Bluebonnet Trails Community Services

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Formula 6: Understanding Alcohol Use Disorder- History, Harm and Hope

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Disclosure to Learners

2026 Texas Council Conference

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To successfully complete this activity, you must:

- Miss no more than 15 minutes of the activity or each session.
- Complete and submit the post-activity evaluation.

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TEXAS Health and Human Services

Texas Department of State Health Services

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- Physicians (CME)
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TEXAS Health and Human Services

Texas Department of State Health Services

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Michael Weaver has received research funding from Novo Nordisk and Eli Lilly.

All financial relationships listed have been mitigated. No other speakers or planning committee members for this educational activity have financial relationships to disclose.

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Christmas 1926 in NYC

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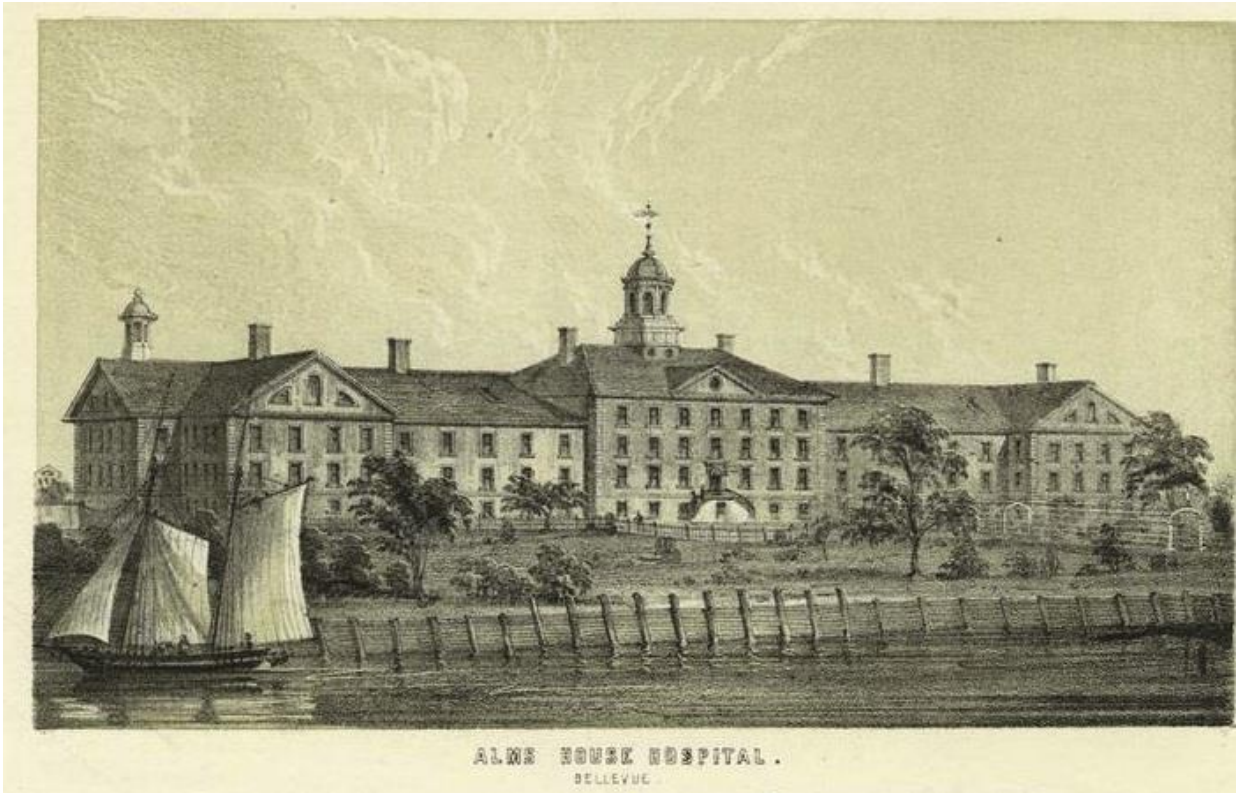
A man stumbles into the emergency room at Bellevue Hospital claiming Santa Claus is after him.

Before hospital staff realized how sick he was the man died. And then another. Then another.

Eventually, hospital staff tallied up more than 60 people made acutely ill by alcohol and eight dead from it. Within the next two days, yet another 23 people had died.

These deaths, as investigators would shortly realize, came courtesy of the U.S. government.

The idea was to scare people into giving up illicit drinking. Instead, by the time Prohibition ended in 1933, the federal poisoning program, by some estimates, had killed at least 10,000 people.



A Moral Imperative (?)

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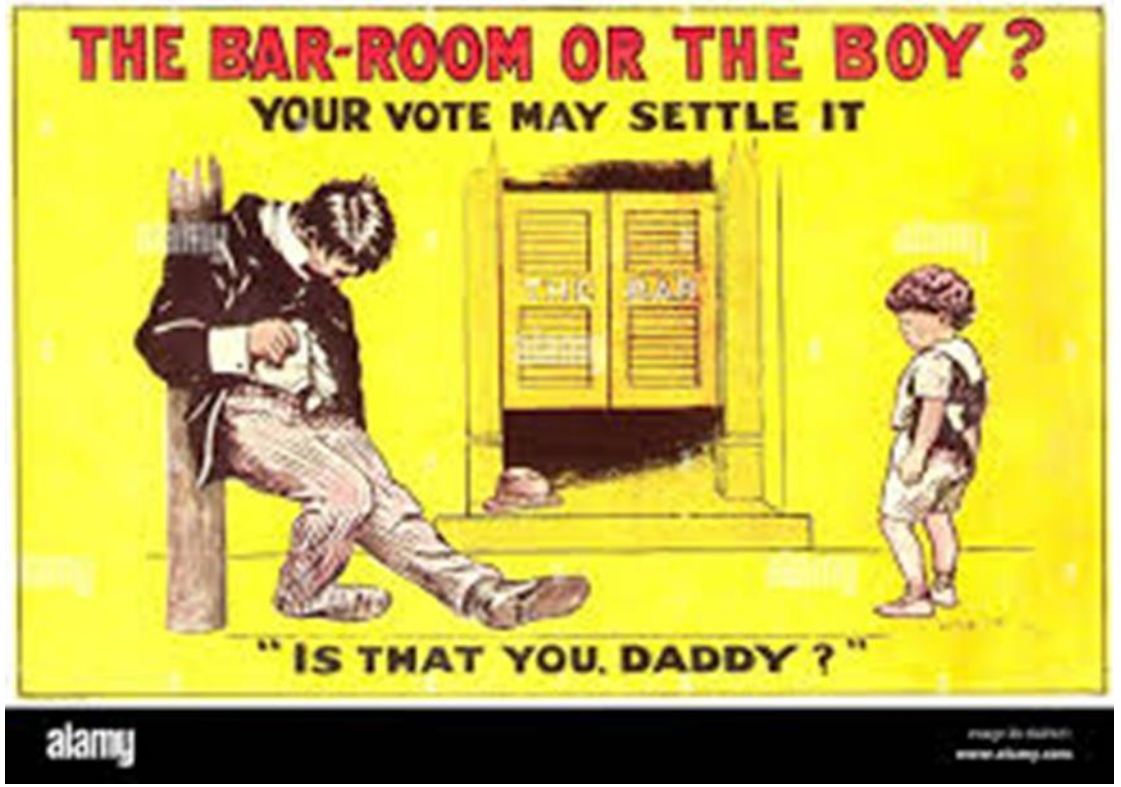
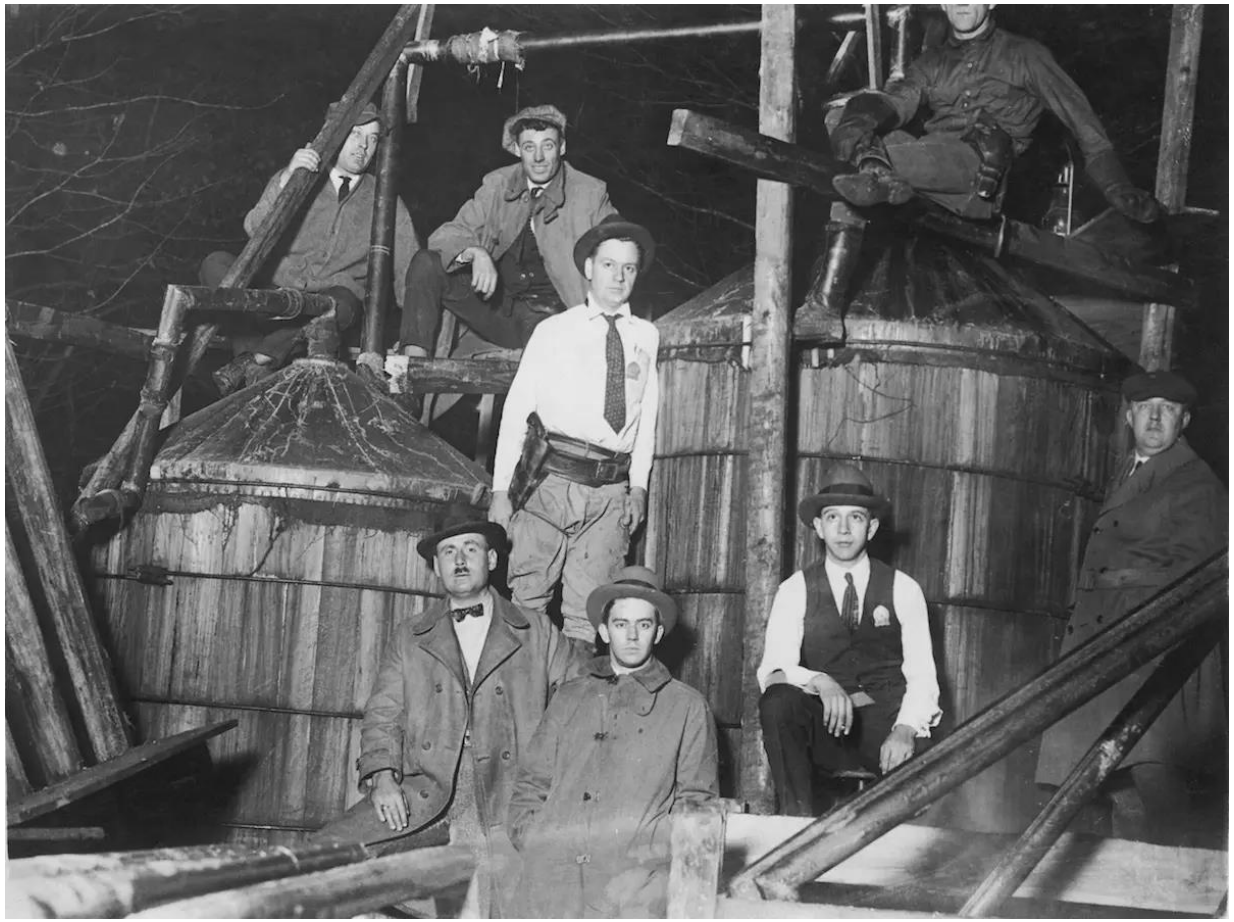
The 18th Amendment bans the manufacture, sale, or transportation of alcoholic beverages in the United States.

The WCTU and ASL helped push the amendment through in 1919, playing on fears of moral decay in a country just emerging from war. The Volstead Act, intended to enforce prohibition, passed shortly later and went into effect on Jan. 1, 1920.





Unintended Consequences

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Prohibition was envisioned as a cure-all for social ills. While alcohol consumption initially declined, enforcement proved nearly impossible.

The illicit alcohol trade flourished, birthing organized crime syndicates led by notorious figures like Al Capone.

Speakeasies replaced saloons, and bootlegging became a lucrative underground industry.

Law enforcement and political officials were often complicit, bribed, or intimidated into turning a blind eye.

The Noble Experiment

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Prohibition's advocates had argued that the elimination of alcoholic beverages would end alcohol use and all its associated evils. The external control on the availability of distilled spirits reduced overall per capita alcohol consumption, but it failed to end alcohol use.

The Public Knew… and drank anyways

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- A December 1926 *New York Times* headline at thread "Government to Double Alcohol Poison Content."
- Wayne Wheeler in a 1926 statement. "The very fact that men will gamble with their lives to get a drink of liquor shows how deeply this habit was fixed . . . To root out a bad habit like that costs many lives and long years of effort."
- By the end of Prohibition in 1933, more than 10,000 Americans had died from imbibing tainted booze.


The New York Times.

GOVERNMENT TO DOUBLE ALCOHOL POISON CONTENT AND ALSO ADD BENZINE

SMITH FOR TRANSIT PEACE; HAS PARLEY WITH WALKER; CITY HEADS SPLIT ON BUSES

Evolution of Understanding

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Ancient to Pre-Modern: Problematic alcohol consumption has been documented throughout history. Early societies, including in China (7000 B.C.), noted the adverse effects of excessive fermentation, and ancient Greek literature often discussed drunkenness.

17th–19th Century: In 1657, Massachusetts took early steps to combat alcohol misuse by restricting the sale of strong spirits. By the 18th and 19th centuries, views shifted, and drunkards began to be seen as victims of a "poisonous drug" rather than just moral weaklings. The term "alcoholism" was officially coined in 1852.

Early 20th Century (Prohibition): In 1920, the 18th Amendment instituted nationwide Prohibition in the US, which was repealed in 1933 after it was found that external controls did not stop abuse.

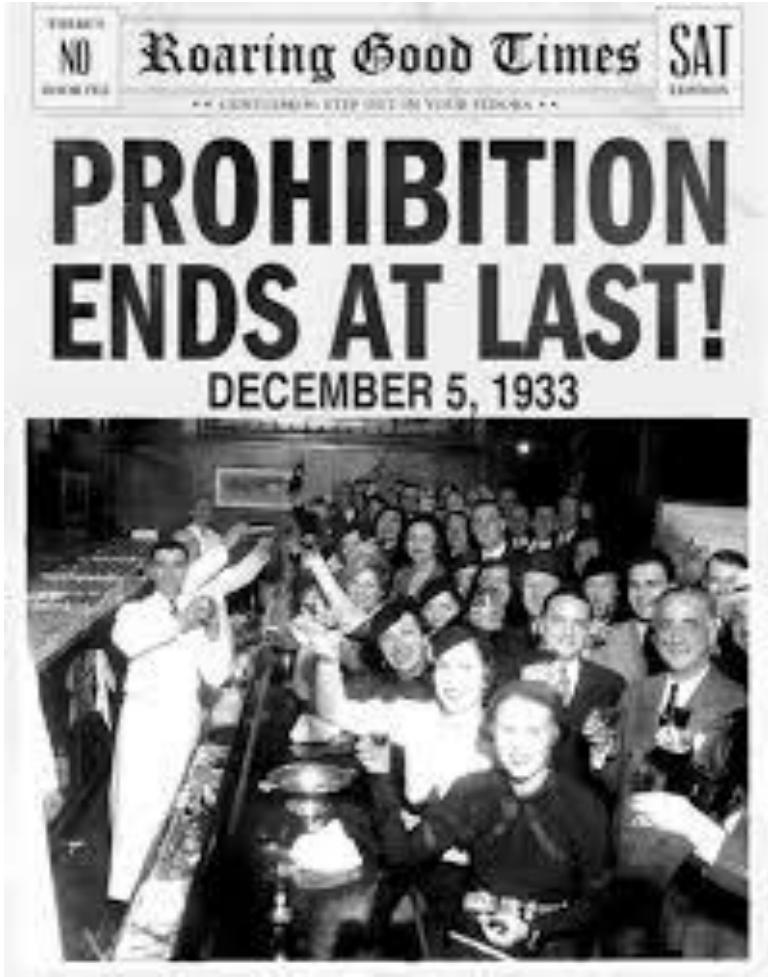
Mid-20th Century (Disease Model): In 1952, the American Medical Association (AMA) officially defined alcoholism as a disease. The 1940s and 1950s saw the development of the "Minnesota Model" of treatment (1948–1950) and the founding of Alcoholics Anonymous (AA).

Late 20th Century–Present: In 1970, the US Congress passed the Hughes Act, establishing the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Modern diagnostics have shifted to the term "Alcohol Use Disorder" to reduce stigma and accurately describe the range of dependence.

From Moral to Medical: The understanding of AUD has moved from a moral failing to a chronic, relapsing brain disease, particularly as research has highlighted genetic factors and brain chemistry changes.

Prohibition Ends

Although the repeal of Prohibition was the result of many factors unrelated to drinking, passage of the Twenty-First Amendment (U.S. Const, amend. XXI) was an acknowledgment that external controls limiting access to alcoholic beverages are not sufficient to prevent alcohol misuse.



The Introduction of Treatment

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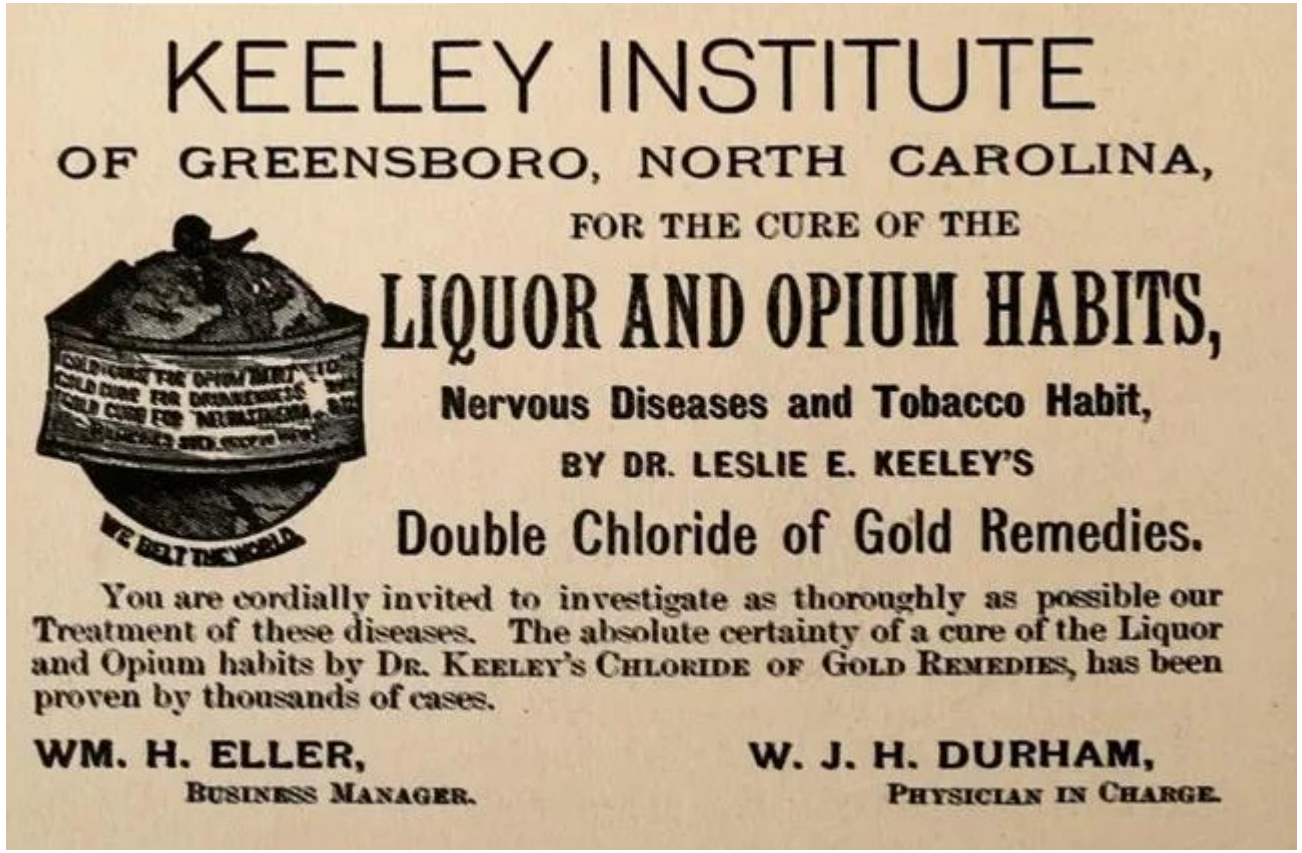
Modern pharmacotherapy for alcohol use disorders was influenced by two events:

1. the repeal of National Prohibition in the United States in 1933 and
2. the establishment of Alcoholics Anonymous (AA) in 1935.

Although these events did not lead directly to the use of medications they contributed to the view that alcoholism is a treatable disease that may be amenable to pharmacotherapy.



Early treatments for AUD

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Beginning in the 1930s, psychotherapy was our primary treatment for alcoholism.

- Available drug therapies lacked scientific support for efficacy.
- Many treatments were based on aversive conditioning.
- This approach aimed to create disgust toward alcohol by:
  - Adding nausea-inducing substances to alcoholic drinks.
  - Pairing these substances with alcohol consumption.

Galant (1936) study:

- Attempted to create alcohol aversion using apomorphine injections while patients drank vodka.
- Only 2 patients remained abstinent beyond 6 months, showing limited effectiveness.

Voegtlin (1940) treatment program:

- Reported a 64% 4-year cure rate in 685 patients using an emetine-based protocol.

Ongoing use of aversion therapy:

Despite limited and mixed evidence, aversion therapy continues to be used.

Early treatments for AUD

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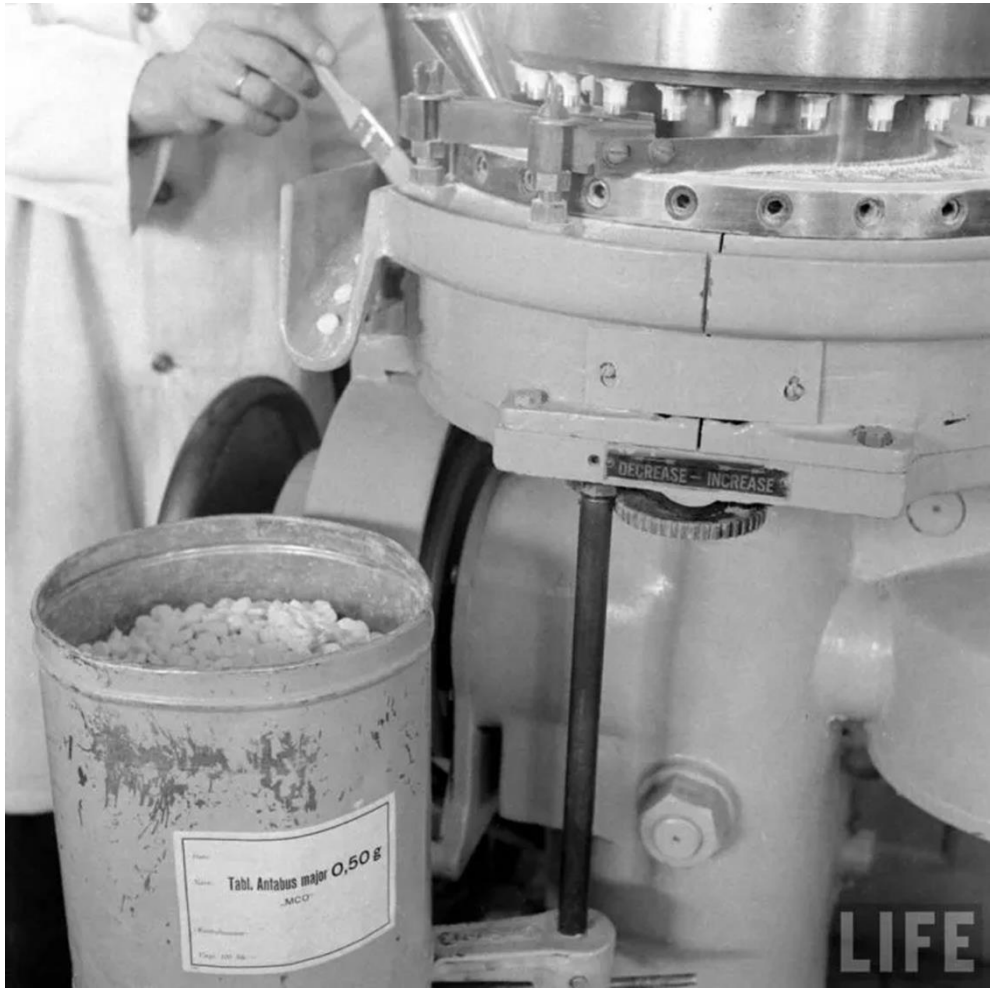
- Psychostimulant approach (1930s–1940s):
  - Researchers explored using psychostimulants to reduce alcohol cravings by boosting mood and energy.
  - Bloomberg (1939):
    - Gave amphetamine to 21 patients with alcoholism.
    - Patients became more alert and energetic.
    - Reported no desire to drink.
  - Reifenstein and Davidoff (1940):
    - Found amphetamine helpful in cases of acute alcohol intoxication.
    - Recommended it for treating depression in institutionalized patients with alcoholism.
- Psychedelic therapy (1960s):
  - Lysergide (LSD) was tested as a way to enhance psychotherapy for alcoholism.
  - Early studies (Canada):
    - Reported significant improvement after a single dose (MacLean et al., 1961; Smith, 1958).
  - Later open-label study (Van Dusen et al., 1967):
    - Included 99 inpatient individuals with alcoholism.
    - Found no higher abstinence rates at 18 months compared to historical controls.
    - Participants often reached a “transcendent” state and gained insight.
    - However, this insight did not translate into reduced alcohol use compared to controls.

Early treatments for AUD

- In 1948, disulfiram was the first medication approved by the U.S. Food and Drug Administration (FDA) to treat alcohol dependence, but its efficacy has not been supported by randomized controlled trials.

- In the 1960s, benzodiazepines replaced older treatments for alcohol withdrawal, but sedative and dependence-producing effects limit their utility in the post-withdrawal period.



Early treatments for AUD

- In the 1980s, the focus shifted to the treatment of co-occurring psychiatric disorders and medications that modify negative mood states, which contribute to relapse to heavy drinking.
- In the 1990s, developments in neurobiology implicated specific neurotransmitter systems underlying alcohol's effects, culminating in the 1994 approval by the FDA of the opioid antagonist naltrexone to treat alcohol dependence.
- In 2006, the FDA approved a long-acting formulation of naltrexone. Acamprosate, an amino acid derivative, first approved in France in 1989, received FDA approval in 2004.

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Alcohol addiction and its treatment
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Quarterly Journal of Studies on Alcohol 1941 2:1 , 98-176

Americans knew their booze was poisoned—and drank it anyway
Ravenna, Isabel. National Geographic. April 10, 2025.

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Overview of the Neurobiology of Alcohol Use Disorder (AUD)

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- Alcohol affects multiple neurotransmitter systems.
- The expectation and consumption of alcohol stimulates dopamine in the reward regions of the brain (mesolimbic system). These regions project to parts of the brain that regulate motivation and cognitive control (orbitofrontal and prefrontal cortices).
- Alcohol also interacts with endogenous opioids, GABA, endocannabinoids, and other neurotransmitter systems (neuroendrocine, serotonergic, noradrenergic).
- Repeated cycles of alcohol use and cessation changes the above brain circuits involved.
- **These alcohol-related circuit disruptions are amenable to pharmacological treatment**

Overview of Presumed Actions of Pharmacotherapies for Alcohol Use Disorder

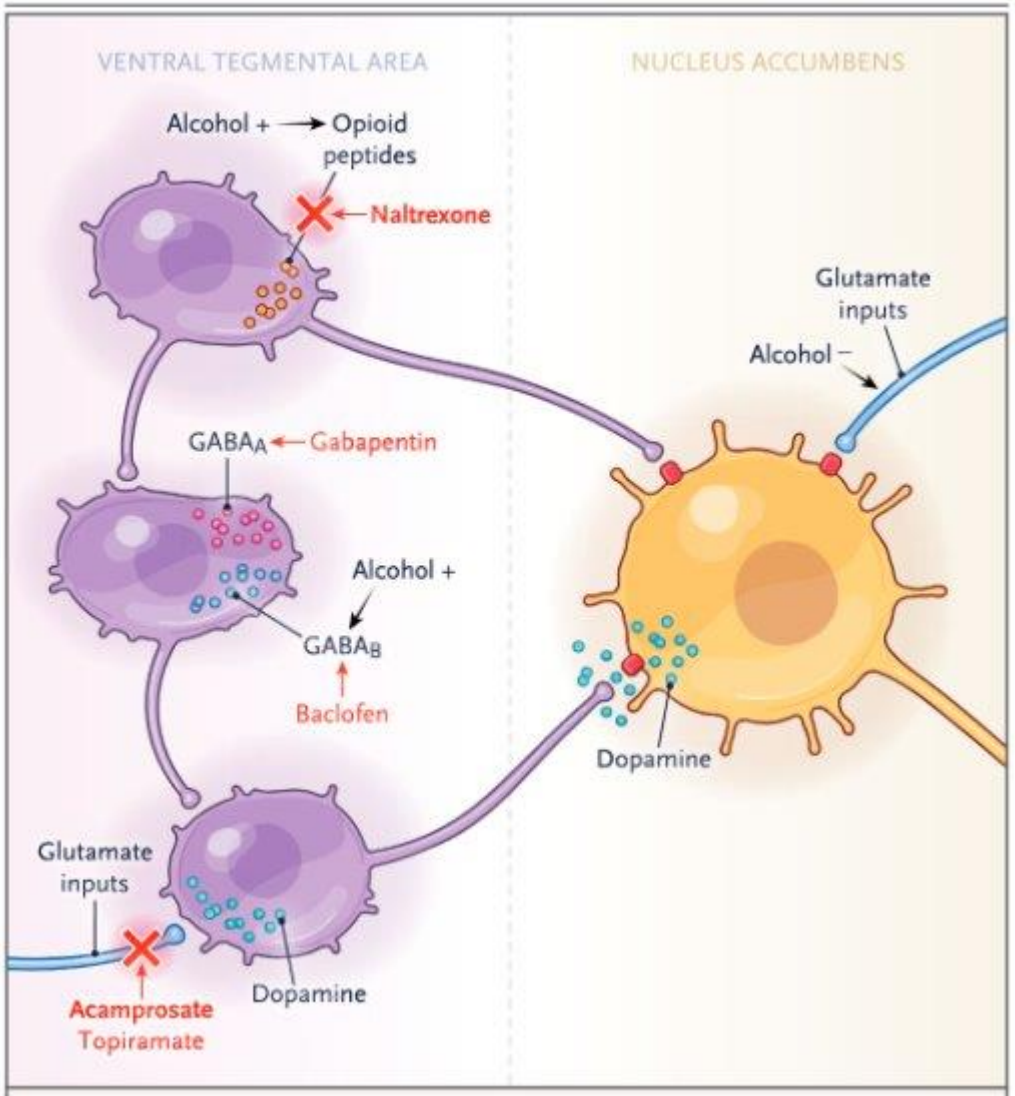

Figure 1. Overview of Presumed Actions of Pharmacotherapies for Alcohol Use Disorder.

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.

Haber, Paul S. "Identification and treatment of alcohol use disorder." *New England Journal of Medicine* 392.3 (2025): 258-266.

FDA Approved Treatments for AUD

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- **Disulfiram:** Irreversibly binds and inhibits the enzyme aldehyde dehydrogenase.
  - Leads to build up of the intermediate metabolite plasma acetaldehyde. Causes flushing, palpitations, nausea/vomiting, sweating, dizziness, etc.
  - The disulfiram-ethanol reaction can occur up to two weeks after discontinuation.
  - Approved dose is 250 mg a day, some patients require more.
  - Cannot be used in patients with liver disease

- **Naltrexone:** μ-preferring opioid antagonist.
  - Reduces the opioid mediated reward
  - 50 mg per day orally or 380 mg per month intramuscular injection
  - Can be used in early liver disease (LFTs <5x UNL) but not advanced liver illness

- **Acamprosate:** NMDA receptor antagonist.
  - Mechanism unclear, possibly indirectly decreases dopamine reward.
  - 666 mg TID, with new studies showing 999 BID is equivalent
  - Can be used in liver disease

Non-FDA Approved Treatments for AUD With Strong Evidence

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- **Topiramate**: GABA A agonist & Glutamate antagonist; FDA approved for migraines, epilepsy, and weight loss*
  - Doses from 100-300 mg; requires slow increase in twice daily dose from 50 mg over 6-8 weeks
  - Tends to be less tolerable due to drowsiness, memory impairment ("Dopamax"), parasthesias
  - Renally cleared but in advanced liver disease can cause hepatic encephalopathy
- **Gabapentin**: Indirectly increases GABA activity, FDA approved for partial-onset seizures, postherpetic neuralgia, and RLS.
  - Doses from 600 to 3,600 mg
  - Renally cleared, relatively safe in liver disease
  - Doses over 1,800 mg associated with dizziness, somnolence, ataxia, and peripheral edema
  - Becoming controlled substance in some states an estimated 1% of US population misuses gabapentin.
- **Nalmefene**: Antagonist at μ & δ-opioid receptors, partial antagonist at κ-opioid receptors
  - Not approved by FDA but approved by EMS
- **Combination Treatments:**
  - Study of Acamprosate + Naltrexone showed no benefit above Naltrexone
- **Naltrexone + Gabapentin better than either alone**

Investigational/Novel Non-FDA Approved Treatments for AUD

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- **Baclofen:** GABA-B agonist for muscle spacsticity
- **Sodium Oxybate:** GABA metabolite for narcolepsy
- **Semaglutide:** Glucagon-like peptide-1 used for diabetes & obesity
- **Varenicline:** Acetylcholine partial agonist for smoking cessation.
- **Ondansetron:** 5-HT3 antagonist for nausea/vomiting
- **Psychedelics:** LSD and psilocybin

Professional Practice Guidelines

VA/DoD Practice Guidelines

- First Line for AUD
  - Topiramate
  - Disulfiram
  - Acamprosate
  - Naltrexone

APA Practice Guidelines

- Moderate to Severe AUD
  - Naltrexone
  - Acamprosate
  - Disulfiram
- Alternative Treatments
  - Topiramate
  - Gabapentin

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Questions?