



Outpatient Treatment of Alcohol Use Disorder

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Even a Little Alcohol Can Harm Your Health

Recent research makes it clear that any amount of drinking can be detrimental. Here's why you may want to cut down on your consumption beyond Dry January.

Alcohol-Related Deaths Are Rising Among Women

The gap between male and female fatalities is narrowing, including for people 65 and older. Here's how to know if you need to cut back on your drinking.

Middle-Aged Adults Are Binge Drinking and Using Marijuana at Record Levels

Moderate Drinking Has No Health Benefits, Analysis of Decades of Research Finds

The review found that the methodology of many previous studies was flawed and that risk of myriad health problems increased significantly after less than two drinks a day for women and after three for men.

Canada's New Guidelines for Alcohol Say 'No Amount' Is Healthy

The guidance builds on growing evidence, after decades of sometimes conflicting research, that even small amounts of alcohol can have serious health consequences.

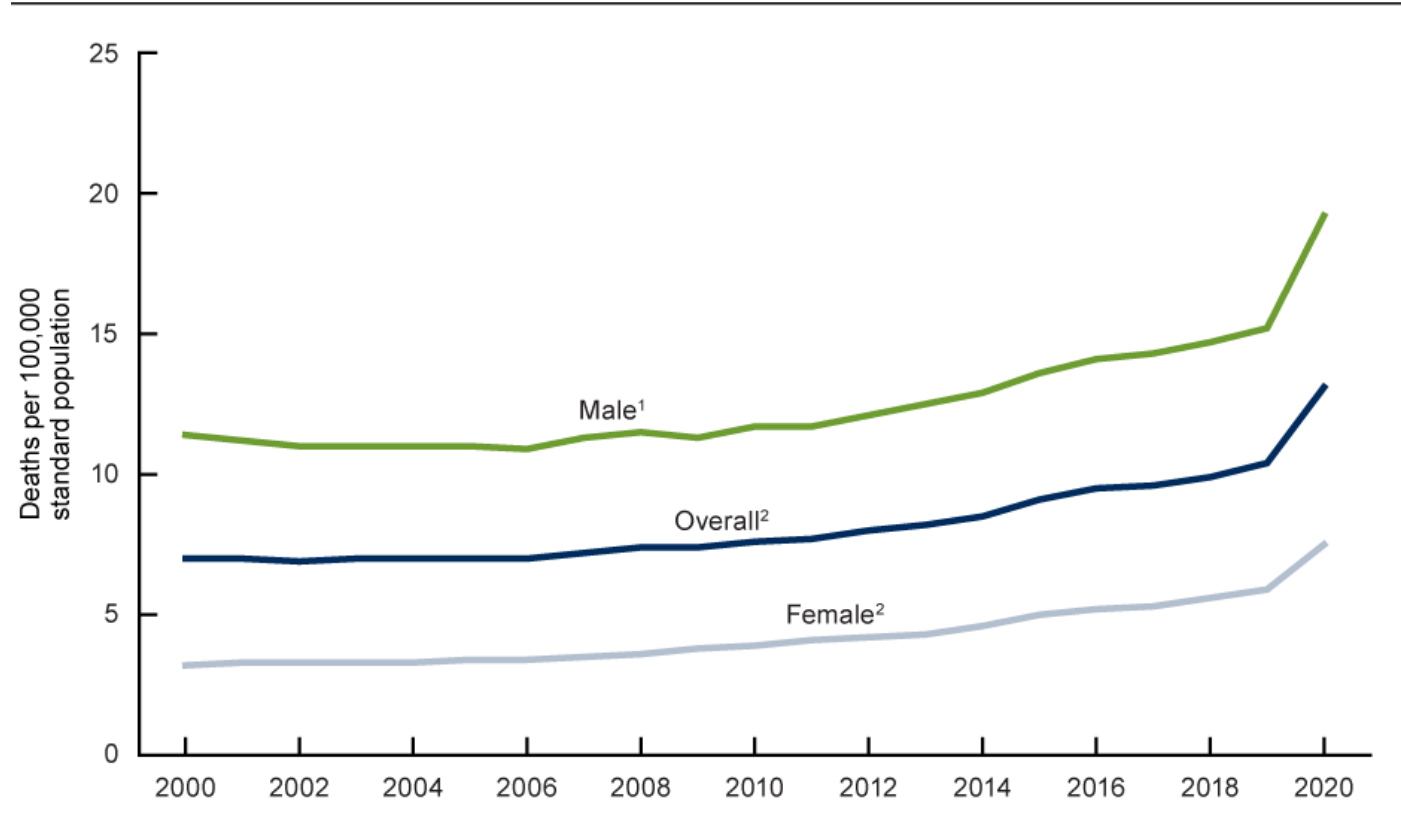
Agenda

- Background: epidemiology and low risk use
- Screening
- Management of alcohol use disorder
- New and notable
- Take Home Points

Background

- Alcohol use is responsible for 140,000 deaths annually
- Alcohol-related deaths have been rising for past 2 decades and rose further during pandemic
- Binge drinking among adults 35-50 reached highest ever level in 2022

Figure 1. Age-adjusted rates of alcohol-induced deaths, by sex: United States, 2000–2020



1. Spencer et al. NCHS Data brief 448

2. NIH press release 8/17/2023 Monitoring the future 2022

Terminology

- Excessive drinking/at risk drinking:
 - Heavy alcohol use (NIAAA definition):
 - > 7 drinks/week (women)
 - > 14 drinks/week (men)
 - Binge alcohol use
 - > 3 drinks in one sitting (women)
 - > 4 drinks in one sitting (men)



1. US Department of agriculture dietary guidelines for Americans 2020-2025
2. Infographic: CDC population health, chronic disease prevention and health promotion 4/19/2022

Alcohol and health benefits

- Historically, some studies suggested that moderate alcohol intake might have health benefits
- There are now concerns about bias in study design
 - 2016: Negligible reductions in all cause mortality
 - 2017: Cardio-protective effects are questionable
 - 2022: Cohort of UK adults
 - Light alcohol use was associated with other positive health behaviors
 - Adjusting for health behavior, all amounts of alcohol were associated with CVD risk

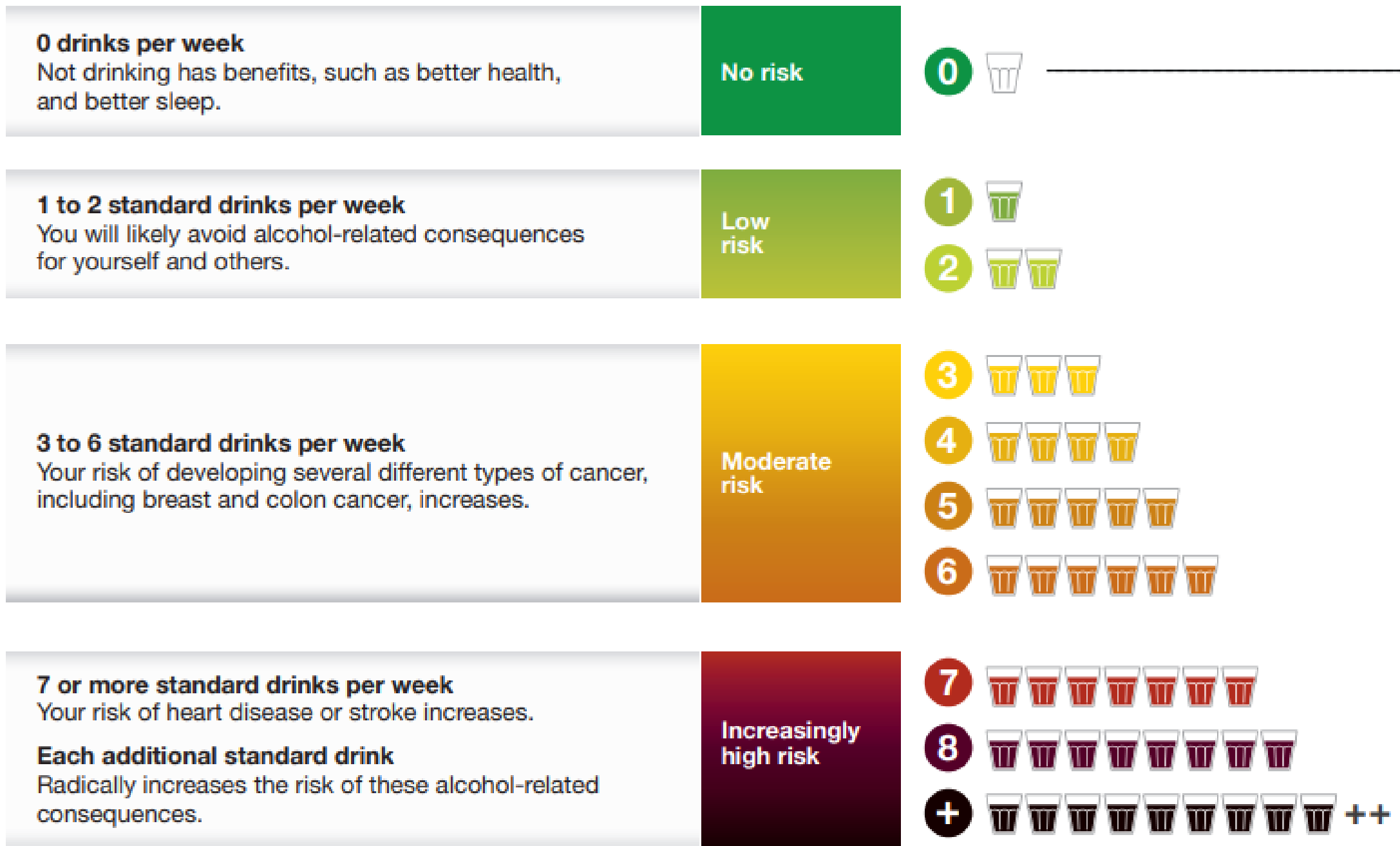
1. Stockwell J Stud Alcohol Drugs 2016

2. Zhao et al. J Stud Alcohol Drugs. 2017

3. Biddinger et al JAMA Netw Open 2022

Alcohol and health benefits

- No difference in mortality between people with no lifetime alcohol use, **We shouldn't recommend alcohol use for health benefits**
- Nonsignificant difference in mortality between people drinking 2-3 drinks/day **We shouldn't recommend alcohol use for health benefits**
- Increased mortality for people drinking >2 drinks/day
 - Mortality risk for women are larger than for men



Conditions associated with or exacerbated by alcohol use

- Breast cancer
- Colon cancer
- Rectal cancer
- Mouth/throat cancer
- Hepatocellular carcinoma
- Esophageal cancer
- Hypertension
- Heart failure
- Atrial fibrillation
- Cardiomyopathy
- Hemorrhagic stroke
- Violence and injury
- Infectious disease (TB, HIV, pneumonia, hepatitis, COVID)
- OSA
- Seizure disorder
- Cognitive impairment
- Depression and suicide
- Pregnancy complications
- Liver disease
- GERD
- Sexual dysfunction

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Screening

- USPSTF: all adults in primary care be screened for unhealthy alcohol use
- Single item screen: How many times in the past year have you had 4 (or 5) drinks in a day?

Screening: AUDIT-C

Please circle the answer that is correct for you.

1. How often do you have a drink containing alcohol?					SCORE
Never (0)	Monthly or less (1)	Two to four times a month (2)	Two to three times per week (3)	Four or more times a week (4)	_____
2. How many drinks containing alcohol do you have on a typical day when you are drinking?					
1 or 2 (0)	3 or 4 (1)	5 or 6 (2)	7 to 9 (3)	10 or more (4)	_____
3. How often do you have six or more drinks on one occasion?					
Never (0)	Less than Monthly (1)	Monthly (2)	Two to three times per week (3)	Four or more times a week (4)	_____
TOTAL SCORE					
Add the number for each question to get your total score.					_____

Maximum score is 12. A score of ≥ 4 identifies 86% of men who report drinking above recommended levels or meets criteria for alcohol use disorders. A score of > 2 identifies 84% of women who report hazardous drinking or alcohol use disorders.

How are we doing?

- Cross-sectional EMR review from 2014-2016
- Reviewed 19,213 primary care visits
- Patients screened in 2.6% of visits
- Alcohol counseling in 0.8% of visits
- Least likely to be screened when seen for a new problem or a pre-surgical visit

Brief intervention

“You are drinking more than is medically safe.”

“I’m especially worried that alcohol may be contributing to (your specific medical disease).”

“I strongly recommend that you cut down (or quit), and I want to help.”

“Are you willing to consider making changes in your drinking?”

... after brief intervention, consider assessment for AUD and treatment options

Many people who are struggling with alcohol use need support to stop drinking. Can I share with you some resources that others have found helpful?

It sounds like it has been hard for you to stop drinking. Alcohol use disorder is treatable. Are you interested in talking about treatment options?

Even more terminology

DSM-IV

Alcohol dependence

Alcohol abuse



DSM-5

Alcohol use disorder (AUD)

- Mild, moderate or severe

Impaired control

- More than intended
- Persistent desire or unsuccessful attempts to cut down
- Time spent obtaining
- Cravings

Impaired social function

- Use causing problems
- Continued use despite
- Important social, recre

Risky use

- Use in situations in wh
- Use despite known physical or psychological problem caused or exacerbated by alcohol

Pharmacologic

- Withdrawal
- Tolerance

Mild AUD: 2-3 criteria

Moderate AUD: 4-5 criteria

Severe AUD: 6 or more

use

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What is recovery?

- SAMSHA: “Recovery is a process of change through which people improve their health and wellness, live self-directed lives, and strive to reach their full potential.”
- DSM-V: remission is not meeting any AUD criteria (except cravings)
- Research outcomes: abstinence, average alcohol use, number of drinking days, number of heavy drinking days
 - New research outcomes: AUD in remission + cessation of heavy drinking

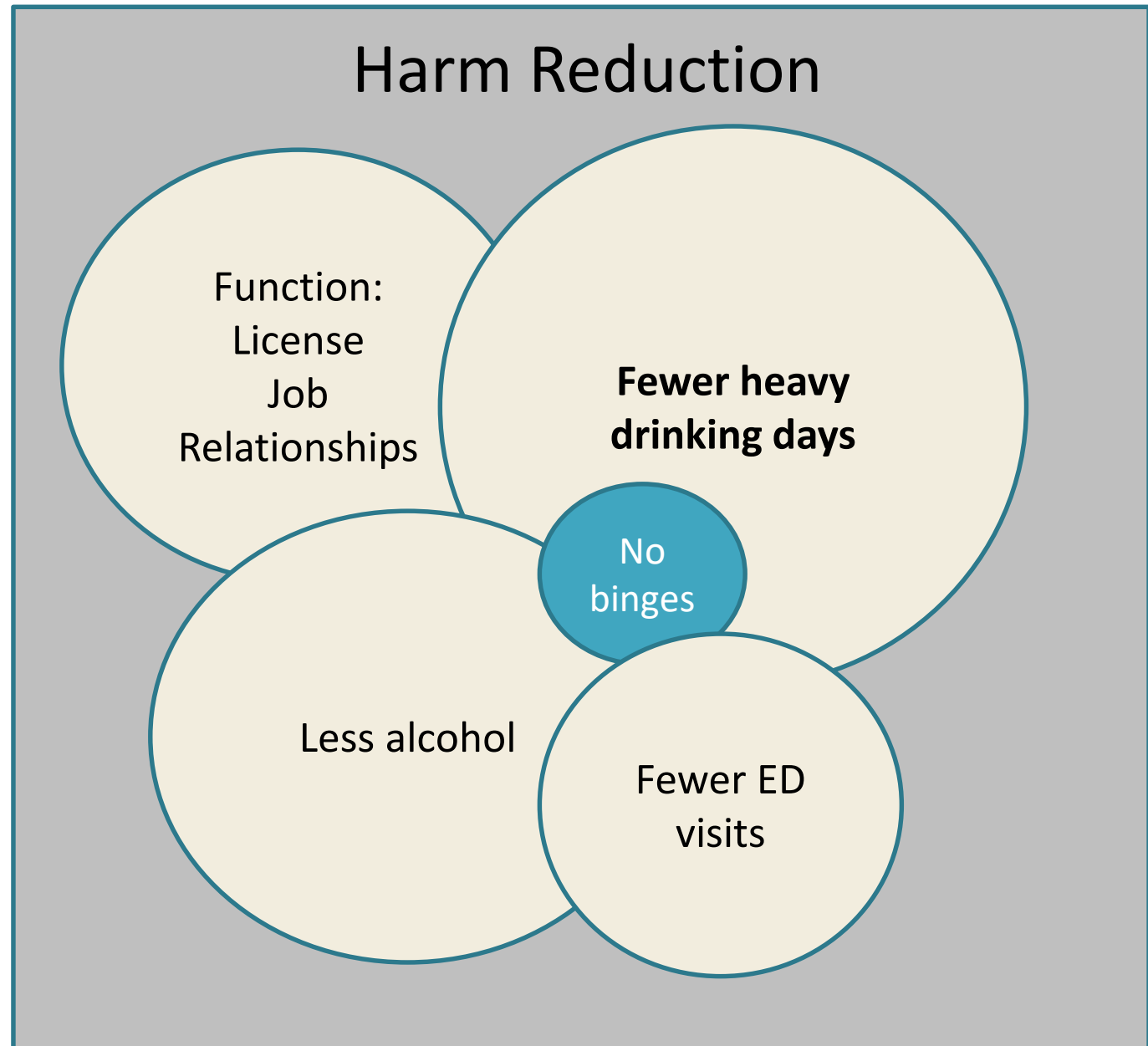
Goals of treatment



Abstinence

Among people with AUD who don't seek treatment, expectation for abstinence was a common reason to avoid treatment

Treatment goals



Harm Reduction Goals for AUD

- Reduced alcohol consumption is associated with lower risk of death¹
- Decreased drinking rates can be sustained over time (12 months) and are associated with improved function²
- Function at completion of treatment was a better predictor of psychological and social outcomes at 10 years than abstinence³
- Reduction in alcohol consumption is associated with improved **blood pressure, LFTs, and quality of life** among people who do not abstain in the year following treatment⁴

1. Laramee et al. E bio Medicine 2015

2. Witkiewitz et al. Alcoholism: Clinical and Exp Research 2019

3. Witkiewitz et al. J Addict Med 2020

4. Witkiewitz et al. Alcohol Clin Exp Res 2018

Approaches to AUD treatment



Mutual support groups



Counseling



Pharmacotherapy

Psychotherapy and medication

- Common to recommend multimodal treatment¹⁻²
- Medication alone is acceptable for patients uninterested in other treatment based on RCT data³

Therapy only	Placebo only	Therapy + placebo	Naltrexone + placebo	Naltrexone + placebo + Therapy	Acamprosate + placebo	Acamprosate + placebo + Therapy	Naltrexone + Acamprosate	Naltrexone + Acamprosate + Therapy
WORST Still improved	Middle	BEST ★	BEST ★	BEST ★	Middle	Middle	No added benefit to naltrexone alone	No added benefit to naltrexone alone
							More side effects	More side effects

1. Reus et al Am J Psychiatry 2018
2. VA Practice Guidelines for Substance Use Disorder Treatment 2021
3. Anton et al. JAMA 2006

Psychotherapy and medication

- Meta-analysis that combined all SUD studies:
 - CBT + Medication superior to medication alone
- Systematic review specific to alcohol:
 - 3/9 studies showed improvements when therapy was added to medication
 - 10/19 studies showed improvement when medications were added to therapy
- Conclusion: medication has a key role to play!

Medications for AUD

Sidebar 3: Pharmacotherapy

Alcohol Use Disorder

Recommended: naltrexone, topiramate

Suggested: acamprosate, disulfiram

Suggested as second line: gabapentin

American psychiatric association:

Recommended/First line: naltrexone or acamprosate

Second line: disulfiram

Consider: topiramate, gabapentin

1. Reus et al Am J Psychiatry 2018
2. VA Practice Guidelines for Substance Use Disorder Treatment 2021

Medications for AUD: J Addict Med

- 2022 systematic review and meta-analysis
- Baclofen, **disulfiram**, **acamprosate**, and **naltrexone** improved abstinence and reduced heavy drinking
- Topiramate was difficult to tolerate

Naltrexone

Mechanism

- Opioid receptor antagonist
- Decrease rewards of drinking

Use

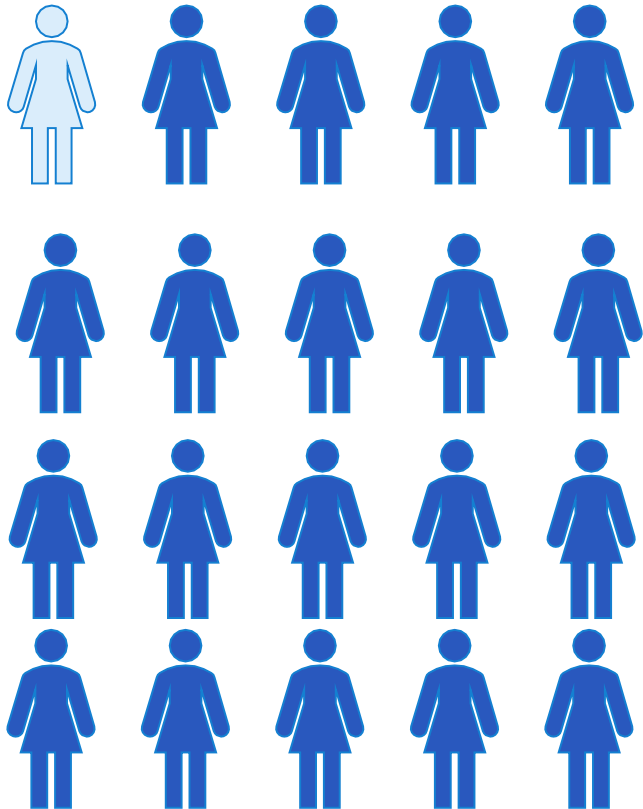
- Decrease cravings
- Decrease alcohol use
- Increase abstinence

Dosing

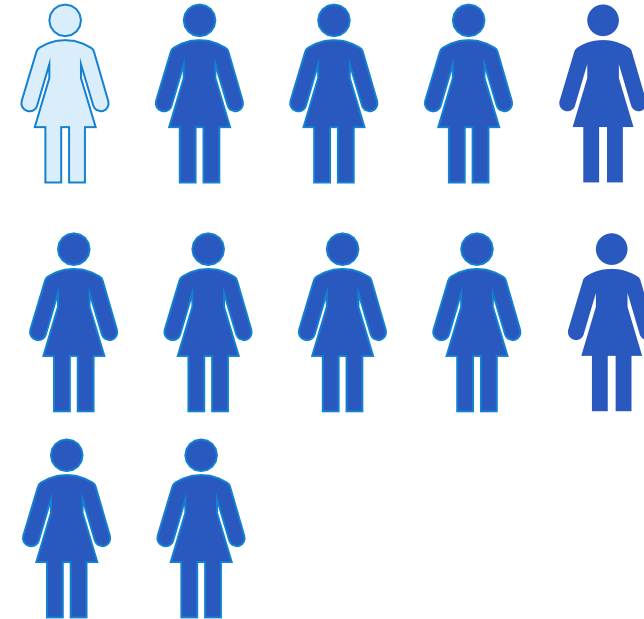
- Oral: 50-100 mg/day
- IM: 380 mg q28 days

Oral naltrexone: benefits

To prevent one return to any drinking...



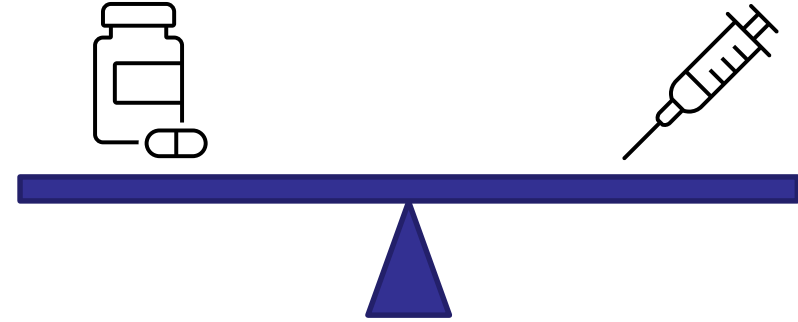
To prevent one return to heavy drinking...



IM Naltrexone benefits

- Longer time to first day of heavy drinking
- Lower median number of heavy drinking days
- Outcomes may be improved in some studies when patients are abstinent for 7 days before injection
- Barriers: cost, insurance, education

Oral or IM?



- No RCTs for people with AUD
- Retrospective chart review of 32 veterans showed longer time to relapse in people with IM (150 days) vs. PO (50 days) naltrexone¹
- Consider IM for patients who struggle with non-adherence

Naltrexone: side effects



**Interacts with
opiates:**

**Must be off
chronic opioids
at least 10 days**

**First line in people
without severe liver
disease or opioid
use**

CrtCl <30



**Possible
dysthymia?**

**No difference in
depression in
2007 VA cohort**

Naltrexone and hepatotoxicity

- Historic concerns about hepatotoxicity
- No adverse liver events in high risk patient populations:
 - Ongoing alcohol use
 - Opioid use disorder
 - Hepatitis C
 - People experiencing homelessness

Acamprosate

Mechanism

- NMDA receptor modulation
- Prevent symptoms of prolonged withdrawal

Use

- Increase abstinence
- May be most effective if started after 2 weeks abstinence

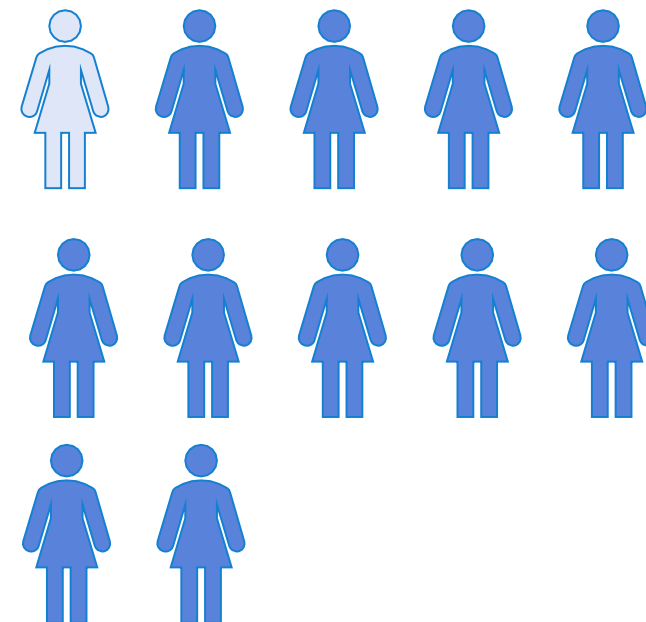
Dosing

- 666 mg TID

Acamprosate

- Safe in cirrhosis
- Efficacy similar to naltrexone for abstinence goals

To prevent 1 person from returning to drinking¹... ***



Acamprosate: drawbacks



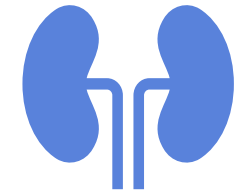
Three times a
day dosing!

No effect
for drinking
binge

Option for people with
severe liver disease

Most effective for
abstinence goals

of
/SI
(AUD also
increases SI)



Renally
cleared

CrtCl 30-50:
333 TID

CrtCl <30:
avoid use

1. APA Practice Guideline for Pharmacologic Treatment of AUD. 2018
2. VA Practice Guidelines for Substance Use Disorder Treatment 2021
3. Kranzler et al. JAMA 2018

Disulfiram

Mechanism

- Inhibits acetaldehyde dehydrogenase
- Aversive response

Use

- Complete abstinence
- May be helpful in open label settings with high adherence

Dosing

- 250 mg daily

Disulfiram: drawbacks



Drug-drug
interactions

And

Drug-food
interactions



Alcohol
disulfiram
reaction
lethargy
hemocyanin
instability

Not first line

Can consider in highly
selected patient
population



Can trigger
psychosis
(rare)

Off-label: topiramate

- 2014 Cochrane review¹ shows evidence is heterogeneous
- 2014 meta-analysis² showed reduced heavy drinking, but evidence is heterogeneous
- 2018 meta-analysis³ showed reduced drinking, reduced heavy drinking, reduced heavy drinking
- 2023: Reduced heavy drinking, reduced heavy drinking, reduced heavy drinking about alcohol use⁴

Considered a first line option in VA guidelines

Considered for people who “prefer” it over naltrexone/acamprosate in APA guidelines

heavy drinking, but evidence

drinking, reduced

any other medication for

reduced positive expectations

1. Pani et al. Cochrane Database, 2014
2. Blodgett et al. Al Clin Exp Res, 2014
3. Pallacuer et al. Addiction, 2018

4. Votaw et al. Addiction 2023

Topiramate

Mechanism

- Enhancing GABA receptors
- Decreasing rewards in opioid receptors

Use

- Increase abstinence
- Decrease alcohol consumption
- Decrease cravings

Dosing

- 25 mg daily x 1 week
- Increase 25-50 mg/day every week
- Goal dose: 100 mg BID

Topiramate: drawbacks



Side effects:

weight loss,
sedation,
cognitive
impairment,
paresthesia

1. Off-label option for reducing consumption and cravings or increasing abstinence
2. Side effects may limit use



Contraindications:

Renal stones
Hepatic
encephalopathy

Gabapentin for AUD

- Cochrane review in 2014 → insufficient evidence, limited by heterogeneity¹
- Systematic review and meta-analysis 2019 → combined 7 RCTs²
 - Range of doses from 300-3600 mg/day; typically 1000-2000
 - No decrease in return to heavy drinking or number of drinks per day
 - No increase in abstinence
 - May decrease percent heavy drinking days
- JAMA Internal Medicine 2020 → double blind RCT of 96 people with symptoms of alcohol withdrawal to goal dose 300/300/600³
 - Reduced heavy drinking days (NNT 5.4), increased abstinence (NNT 6.2)
 - ~1/3 of participants didn't complete the trial; assumed to be drinking

1. Pani et al. Cochrane database 2014

2. Kranzler et al. Addiction 2019

3. Anton et al. JAMA Intern Med 2020

Gabapentin

Mechanism

- Unknown: influences gaba and glutamate tone
- ?reduce sx of alcohol withdrawal and improve sleep?

Use

- Decrease number of drinking days
- People with prior alcohol withdrawal
- CKD dose adjustments available

Dosing

- Start 300 mg qHS, increase by 300 mg on a daily basis to goal of 12-1800 mg

Baclofen

- 17 RCTs with 1818 participants
- Increased percentage of days abstinent compared with placebo and reduced return to use¹, less heavy drinking²
- No difference in number of drinks per drinking day, craving, anxiety, depression¹
- Unable to compare to naltrexone or acamprosate
- Increased fatigue, dizziness, somnolence

1. Agabio et al. Cochrane database 2023

2. Bahji et al. J Addict Med 2022

Return to use

Expected and common part of chronic disease!

Assess adherence

Intensify support and consider referral

Consider switching medications

No data to support combination therapy

How long should we continue?

- Some guidelines recommend at least 6-12 months
- In practice, no reason to stop if patient is experiencing benefit and not experiencing side effects
- Suggested criteria for discontinuation: stable recovery, engagement with treatment or strong social support, reduced cravings

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Psilocybin + therapy for AUD?

- Psilocybin may enhance neuroplasticity → better response to psychotherapy
- RCT: psilocybin vs. diphenhydramine
- Medication given in two 8 hour sessions
- 12 therapy sessions with 2 therapist team
- 25-65 years old, mostly white

Psilocybin + therapy for AUD?

- Therapy alone lowered alcohol use!
- Abstinence also lower in the psilocybin group
- Blinding is challenging
- Not ready for general practice

	Mean (SD)	
	Diphenhydramine (n = 45)	Psilocybin (n = 48)
% of Heavy drinking days		
Screening	48.57 (28.73)	56.48 (31.77)
Week 4 ^c	21.31 (20.14)	24.11 (26.29)
Follow-up ^d	23.57 (26.67)	9.71 (26.21)

GLP-1 Agonists and AUD

- GLP-1 agonists decrease appetite, increase satiety, and may change rewards from food and drink
- RCT: Placebo vs. exenatide for AUD
- 26 weeks of treatment + 6 months follow-up
- 127 pts randomized

GLP-1 Agonists and AUD

- No difference between placebo and exenatide in terms of heavy drinking days
- No pancreatitis in any group
- Exploratory subgroup analysis:
 - BMI < 25: *increased* alcohol use with exenatide
 - BMI >30: *decreased* alcohol use with exenatide

AUD and the gut microbiome

- Pilot study: 46 people with moderate alcohol related hepatitis and AUD randomized to lactobacillus vs. placebo x6 months
 - MELD improved at 1 month in LGG group
 - 16/24 LGG people reduced drinking at 6 months compared with 4/24 in placebo per report
- 2021 phase 1 RCT suggested fecal transplant was associated with fewer AUD-related events at 6 months

1. In general, less alcohol use is healthier than more alcohol use
2. Patients should be screened annually for alcohol use using validated tools
3. People with alcohol use disorder should be offered referral to specialty services *and* medications for alcohol use disorder

4. Naltrexone and acamprosate are first-line medications for alcohol use disorder
5. Treatment of alcohol use disorder remains an active and exciting area of research – but we shouldn't neglect the treatments we already have!

Does It Help With the Regret, Too? Hangovers Meet IV Drips.

High-powered revelers are trying to hack their hangovers with concierge infusions.

Substance Abuse Is Climbing Among Seniors

Many aging baby boomers have long histories with drugs, cannabis and alcohol. "The field wasn't ready for that," said one expert.

The Jell-O Shot Renaissance

Across the country, bars are serving jiggly, alcoholic concoctions that are nothing like the college party version.

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