University of California
San Francisco

Updates on Management of Unhealthy Alcohol Use

Triveni DeFries, MD MPH
Department of Internal Medicine | San Francisco General Hospital
University of California, San Francisco
Substance Use Warmline, National Clinician Consultation Center

NATIONAL CLINICIAN CONSULTATION CENTER

Translating science into care

The National Clinician Consultation Center (NCCC) offers on-demand, cost-free clinical support and guidance – for clinicians, by clinicians.

To reach our team: 844-ASK-NCCC (844-275-6222)
Submit your clinical inquiry online: nccc.ucsf.edu

HIV/AIDS Warmline	HIV treatment, ARV management, complications, and co-morbidities	**Perinatal HIV Hotline**	Pregnancy, infant feeding and HIV
Hepatitis C Warmline	HCV testing, staging, monitoring, treatment	**Substance Use Warmline**	Substance use evaluation and management
PrEPline	HIV pre-exposure prophylaxis options and monitoring	**PEPline**	Bloodborne pathogen (HIV, HBV, HCV) exposure management

A program of the Goldschmidt Collective

The National Clinician Consultation Center is part of the AIDS Education and Training Center(AETC) Program and is located at the University of California, San Francisco (UCSF) / San Francisco General Hospital. It is supported by the Health Resources and Services Administration(HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $2,250,000 with 0% financed with non-governmental sources.

AETC AIDS Education & Training Center Program
National Clinician Consultation Center

UCSF

Disclosures:

- No conflicts to report
- Will discuss off label use of medications

Learning Objectives

1. Describe the rising burden of alcohol-related harm and the corresponding treatment gap
2. Use the spectrum of unhealthy alcohol use to identify appropriate interventions
3. Select medications for alcohol use disorder to match patient goals and co-morbidities
4. Identify updated treatment and counseling resources based in harm reduction

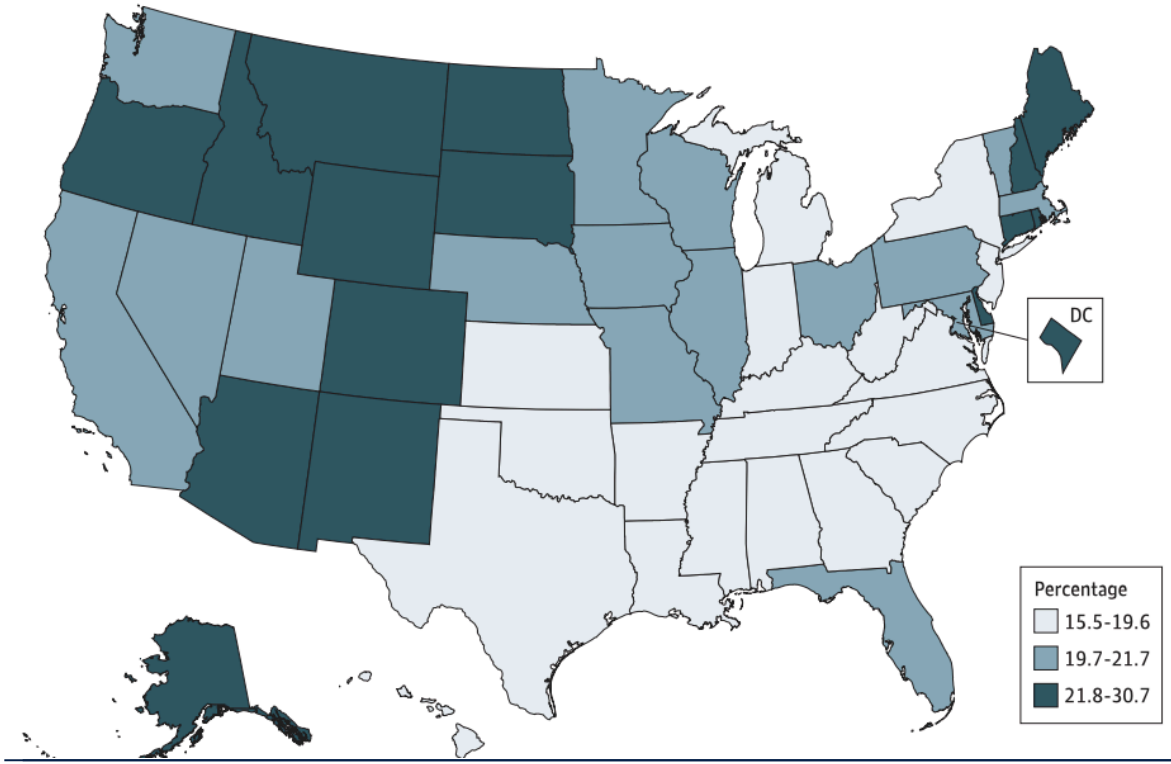
Recommended language for reducing alcohol-related stigma

	Instead of…
Alcohol use disorder	Alcohol abuse, dependence, alcoholism
Alcohol misuse	Alcohol abuse
Person with alcohol use disorder	Alcoholic, addict
Person in recovery from AUD	Recovering alcoholic
Person who misuses/engages in alcohol	Alcohol abuser, drunk
Alcohol-associated liver disease	Alcoholic liver disease
Alcohol-associated hepatitis/cirrhosis/pancreatitis	Alcoholic hepatitis/cirrhosis/pancreatitis
Medically-managed withdrawal	Detox
Recurrence of use/Return to use	Relapse

NIAAA Spectrum Vol 14 Issue 1, 2022

Part I. Unhealthy alcohol use in public health

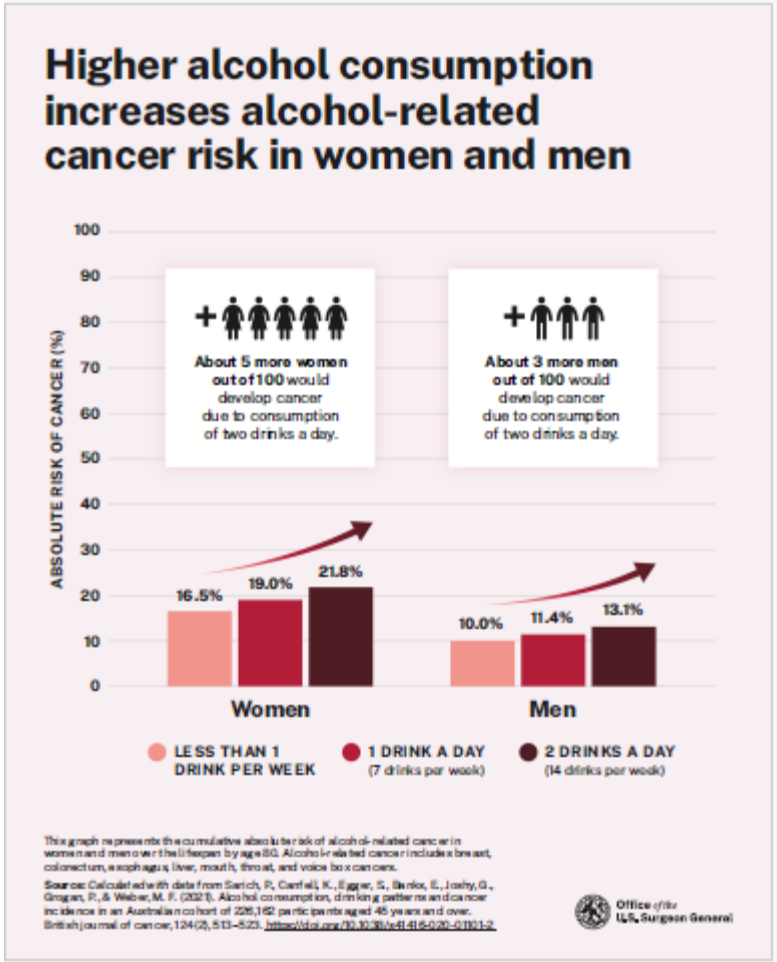
Figure. Estimated Percentage of Total Deaths Attributable to Excessive Alcohol Use Among US Adults Aged 20 to 49 Years, 2015 to 2019



- 4th leading cause of preventable mortality
- Cross sectional study 694,600 deaths from 2015-2019
- **13% (1 in 8) of annual US deaths** attributable to excessive alcohol use
- In CA, 1 in 4 deaths among 20-34yo and 1 in 5 among 35-49yo

Esser et al. Jama Open 2022.

UCSF



In the U.S., pursuant to 27 U.S.C. 215, every alcoholic beverage sold in the United States must currently have the following health warning label:

> "GOVERNMENT WARNING: (1) According to the Surgeon General, women should not drink alcoholic beverages during pregnancy because of the risk of birth defects. (2) Consumption of alcoholic beverages impairs your ability to drive a car or operate machinery, and may cause health problems."[66]

This label statement has remained unchanged since its inception in 1988.[67]

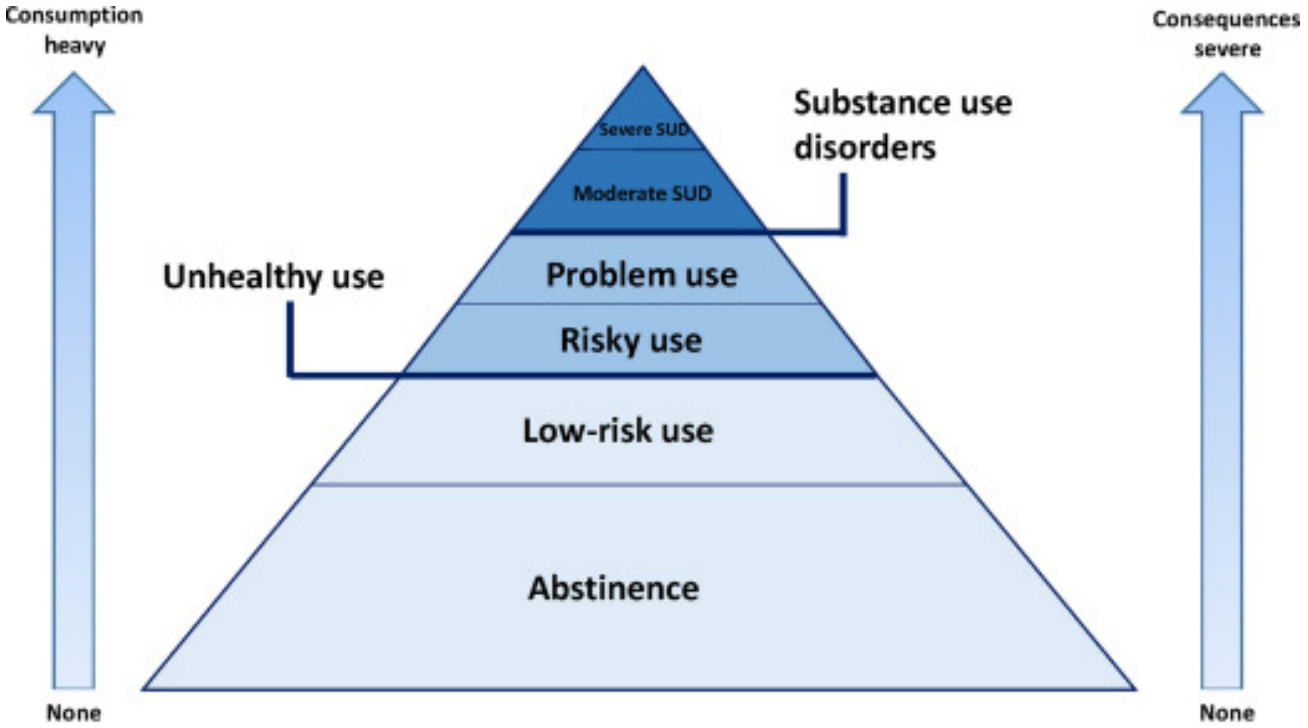
The power to change the label statement lies with Congress.[66] Given the conclusive evidence on the cancer risk from alcohol consumption and the Office of the Surgeon General's responsibility to inform the American public of the best available scientific evidence, the Surgeon General recommends an update to the Surgeon General's warning label for alcohol-containing beverages to include a cancer risk warning.

Surgeon General's Report: https://www.hhs.gov/surgeongeneral/reports-and-publications/alcohol-cancer/index.html
Morford KL, Tetrault JM, O'Connor PG. Alcohol and Cancer Risk. JAMA. 2025;334(10):908–909. doi:10.1001/jama.2025.11229

UCSF

Part II. Assessing unhealthy alcohol use

Unhealthy alcohol use is a spectrum

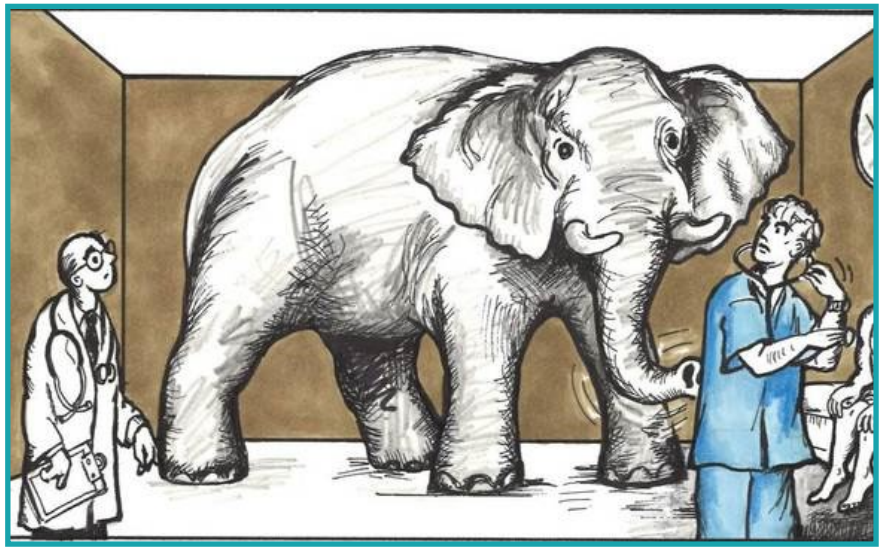


McNeely, J., et al. *Screening for Unhealthy Alcohol and Drug Use in General Medicine Settings*, Medical Clinics of North America, Volume 106, Issue 1, 2022, Pages 13-28.

UCSF

Unhealthy alcohol use goes undetected

- USPSTF recommends screenings in primary care settings in adults, and providing persons engaged in risk or hazardous drinking with brief behavioral counseling interventions (B recommendation)



Bazzi & Saitz, 2018; US Preventive Task Force, 2018; Edelman & Tetrault, 2019; Chatteron et al, 2022

UCSF

Part III. Treatment of AUD

Medications for AUD

FDA Approved:

1. **Naltrexone**
2. **Acamprosate**
3. Disulfiram

Non-FDA Approved:

1. **Topiramate**
2. **Gabapentin**
3. Baclofen
4. Ondansetron
5. Varenicline
6. Nalmefene

McPheeters M, O'Connor EA, Riley S, et al. Pharmacotherapy for alcohol use disorder: a systematic review and meta-analysis. *JAMA*. 2023;330(17):1653–1665.

UCSF

Case #1:

40 Y patient with severe AUD seen in the hospital

They have cut back from 6-8 beers daily to 4/day

Severe cravings whenever they try to quit, not confident they can stop. Goal to cut back.

PMH:
HTN
Depression
Knee pain

Meds: HCTZ, pantoprazole, sertraline, thiamine, folate, MVI

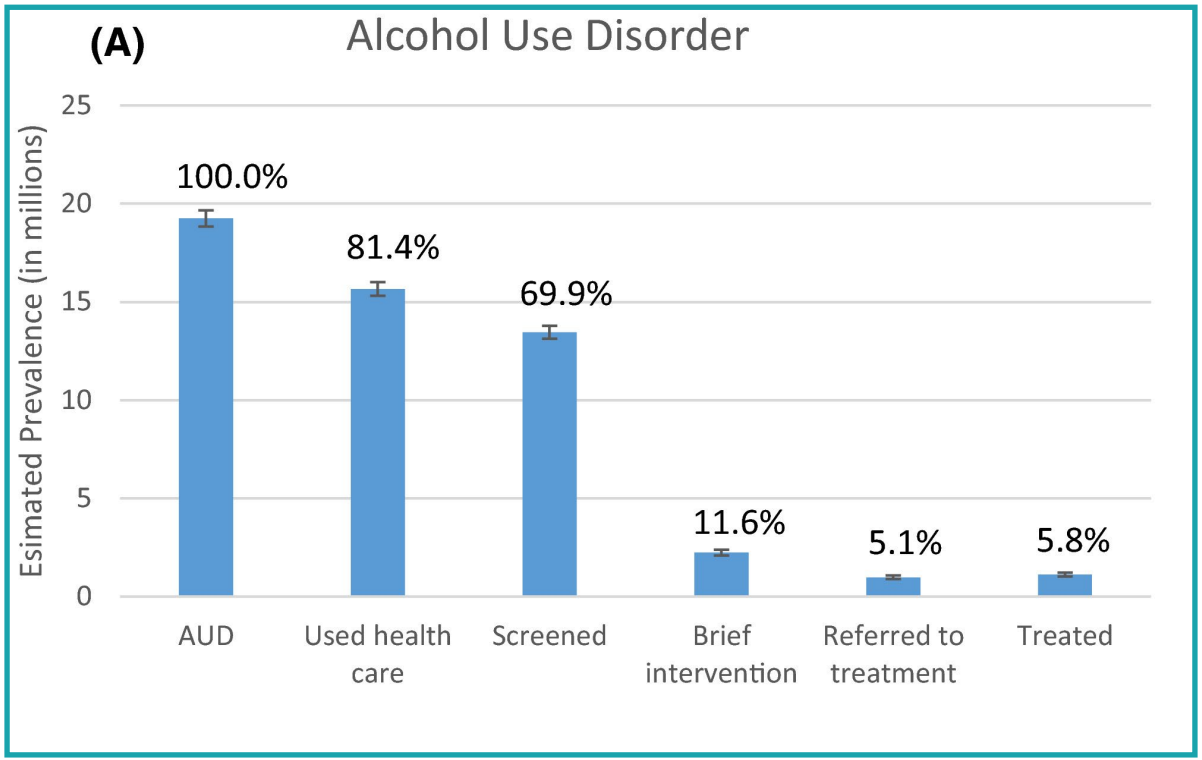
FH: brother and father with AUD

AST 65, ALT 21
T. Bili .1
Albumin 3, INR 1.1
Cr 0.82

Which medication do you recommend?

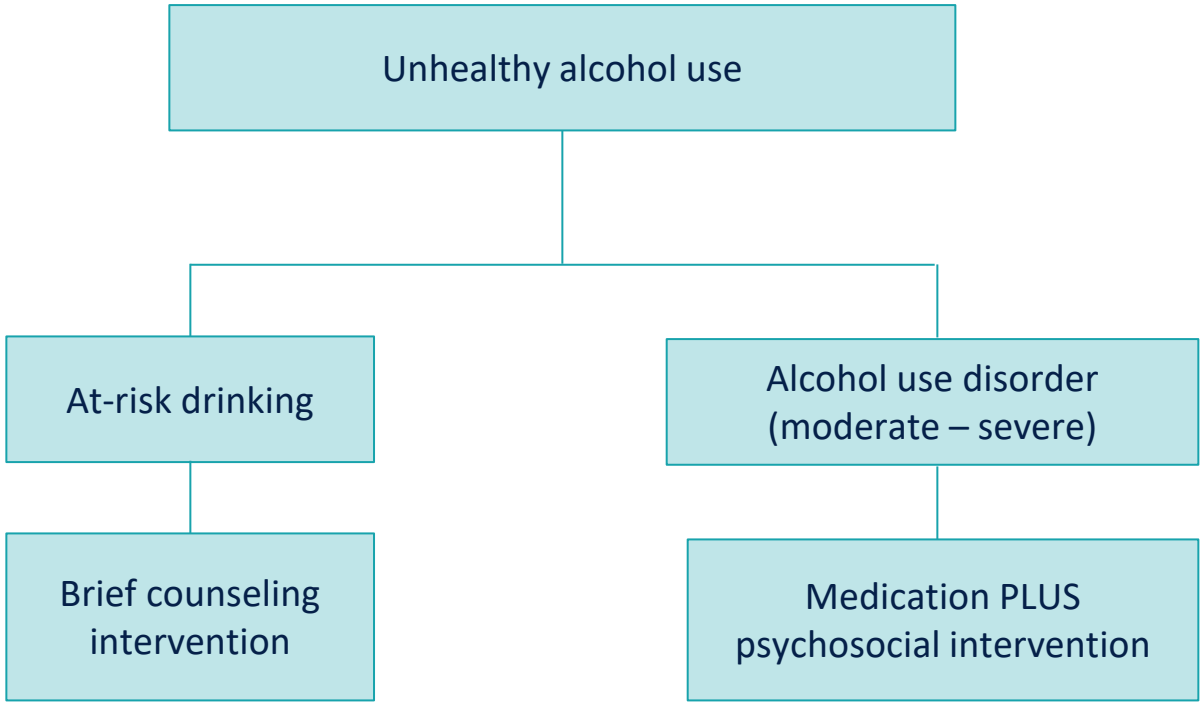
A. Acamprosate
B. Disulfiram
C. Baclofen
D. Naltrexone
E. Topiramate
F. Naloxone
G. Gabapentin

AUD Cascade of Care



Mintz CM, et al.,2021

UCSF



McQueen J, Howe TE, Allan L, Mains D, Hardy V. Brief interventions for heavy alcohol users admitted to general hospital wards. Cochrane Database of Systematic Reviews 2011, Issue 8. Art. No.: CD005191.

AUD treatment gap

- 7.6% of patients with unhealthy alcohol use receive treatment
- 1.6% people received pharmacotherapy
- Racial disparities in treatment

Han, 2020; Han et al., 2021; Oldfield et al., 2020; Acevedo et al, 2024

Table. Comparisons of NNT for Medications for AUD vs Medications Commonly Prescribed in Primary Care

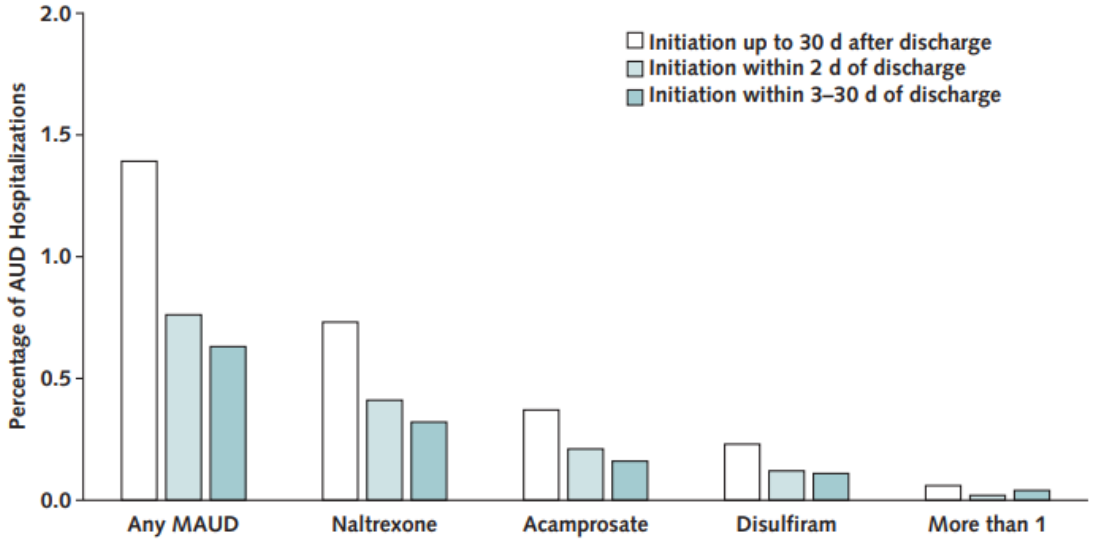
Indication and medication or treatment	Outcome	NNT (95% CI)
AUD		
Naltrexone (oral)	Lower rate of return to heavy drinking (range, 12-24 wk)	11 (5-41)
	Abstinence (range, 12-36 wk)	18 (4-32)
Acamprosate	Abstinence (range, 12-52 wk)	11 (1-32)
Depression in primary care		
TCAs	Response or remission (range, 4-12 wk)	8 (7-16)
SSRIs	Response or remission (range, 4-24 wk)	6 (6-42)
Asthma		
Antileukotriene added to same dose inhaled corticosteroids	Prevent use of oral corticosteroids needed to manage acute asthma exacerbation (range, 6-16 wk)	22 (16-75)
Diabetes		
Metformin	Prevent type 2 diabetes by study end (range, 1-4 y)	14 (10-22)

Abbreviations: AUD, alcohol use disorder; NNT, number needed to treat; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

Busch AB, Greenfield SF, Huskamp HA. Expanding Alcohol Use Disorder Medications in Primary Care. *JAMA Intern Med.* Published online March 03, 2025. doi:10.1001/jamainternmed.2024.8325

Hospitalization is an opportunity to start medications for AUD

Figure. Initiation of medication treatment for AUD after alcohol-related hospitalizations.



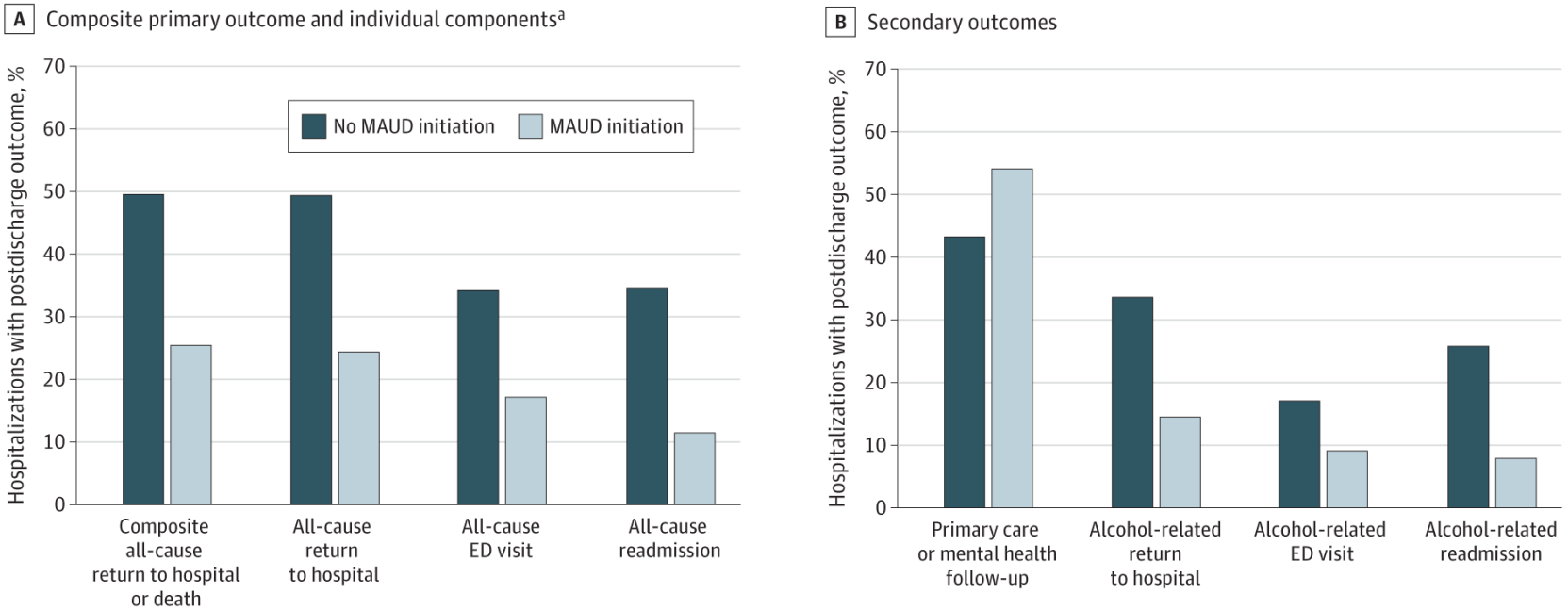
AUD = alcohol use disorder; MAUD = medications for AUD.

Bernstein EY, Baggett TP, Trivedi S, et al. Pharmacologic treatment initiation among Medicare beneficiaries hospitalized with alcohol use disorder. Ann Intern Med. 2023;176:1137-1139.

UCSF

Outcomes After Initiation of Medications for Alcohol Use Disorder at Hospital Discharge

JAMA Netw Open. 2024;7(3):e243387. doi:10.1001/jamanetworkopen.2024.3387



Unadjusted Posthospitalization Care Patterns After Alcohol-Related Hospitalizations at 30d Return to hospital includes emergency department (ED) visits and hospital readmissions and observation stays. MAUD indicates medications for alcohol use disorder.

[a]Mortality not shown due to the Centers for Medicare & Medicaid Services cell suppression policy threshold for display of data (values <11 individuals).

UCSF

Medication Selection for AUD:

Target Goals

- Reduce drinking: Naltrexone, Gabapentin, Topiramate
- Abstinence: Acamprosate, Disulfiram, Naltrexone, Topiramate

Target Comorbidities

- Decompensated Liver Disease: Acamprosate, Gabapentin, Topiramate
- Adherence Challenges: XR Naltrexone
- Concurrent Opioid Use: NOT naltrexone
- Concurrent Stimulant Use: XR-Naltrexone, Topiramate
- Renal Disease: Dose reduce acamprosate, gabapentin
- Anxiety: Gabapentin
- Insomnia: Gabapentin, Topiramate
- H/o withdrawal: Gabapentin

FDA-Approved: (1) Naltrexone

Dosage	• Oral 50-100 mg/day • Intramuscular 380 mg/month
Mechanism	Opioid receptor antagonist that reduces rewarding effects of alcohol
Effectiveness	• Number Needed to Treat (NNT) = 20 to prevent return to any drinking • NNT = 12 to prevent return to heavy drinking
Pros	• OK to use if actively drinking • Daily oral AND long-acting injectable options • Cheap and available • May combine with gabapentin

Cons	• Liver concerns
	  • Avoid if Child-Pugh C or greater, or alanine aminotransferase (AST)/aspartate aminotransferase (ALT) >5x upper limit of normal
	  • Monitor liver function tests
	• Gastrointestinal effects, headache, dizziness
	• Abstinence from opioids prior to initiation
	• Opioids not as effective for analgesia

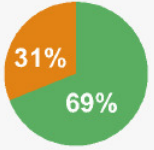
Jonas, JAMA, 2014; Anton et al., 2011; Murphy et al, Addiction, 2021

Naltrexone is safe in patients with cirrhosis

A retrospective study of a nationwide cohort of Veterans

Patients with cirrhosis with new initiation of Naltrexone

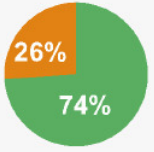
N = 2,940



Liver enzymes checked within 3 months

Patients with liver enzyme elevation*

N = 62



Drug Induced Liver Injury using RUCAM criteria

N = 0

Each figure represents approximately 30 patients with cirrhosis

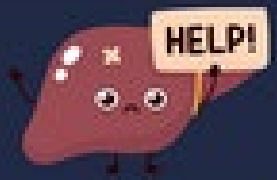
* Liver enzyme elevation was defined as ALT >5x ULN or ALP >3x ULN

ULN, Upper limit of normal; ALT, alanine transaminase; ALP, alkaline phosphatase; RUCAM, Roussel Uclaf Causality Assessment Method

Things We Do For No Reason™

Avoiding Naltrexone for Alcohol Use Disorder in Liver Disease

Why You Think You Should Delay Naltrexone Use



1980's study associated high dose naltrexone use with hepatocellular injury →

FDA Black Box Warning

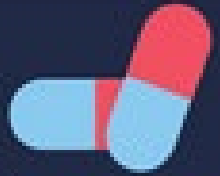
Why Delay of Naltrexone May Be Harmful or Unnecessary

Retrospective studies on naltrexone use:

- ↓ AST, ALT
- ↓ Mortality
- ↓ Rehospitalization
- ↓ ED visits

FDA Black Box Warning Removed

What You Should Do Instead



Prescribe naltrexone for patients with AUD

A: Do not avoid!
B: Do not avoid!
C/Acute alcoholic hepatitis: Consider naltrexone or acamprosate

Journal of Hospital Medicine
Alcohol Use Disorder

D Lee and J Buyske, July 2025
#Visual Abstract by @Leah_Jones9

Food for Thought

Home | JAMA Psychiatry | Vol. 83, No. 1

Viewpoint

Over-the-Counter Naltrexone to Address Unhealthy Alcohol Use

Olga Terechin, MD[1]; Sofia E. Matta, MD[1]; Joji Suzuki, MD[1]

» Author Affiliations | Article Information

UCSF

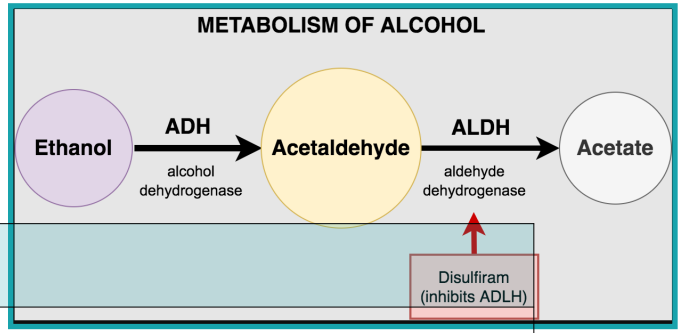
FDA-Approved: (2) Acamprosate

Dosage	666 mg orally three times a day
Mechanism	Modulates glutamate neurotransmission
Effectiveness	Maintains abstinence, NNT = 12 to prevent return to any drinking in 8-24 weeks Effective in European studies, Abstinence prior to initiation
Pros	• Safe for the liver • Can use in setting of opioid use

Cons	• TID adherence
	• Requires renal dosing
	  • 50% reduction for moderate renal impairment
	  • Contraindicated if CrCl<30
	• Diarrhea in 10-15%
	• Takes 5-8 days for full effect
	• Limited to patients with goal of abstinence

Jonas, 2014; Rosner et al, Cochrane Database Syst Rev, 2010; Donoghue et al, 2015; Maisel et al, 2012; Cheng et al, BMJ 2020

FDA-Approved: (3) Disulfiram



Dosage	• 250-500 mg by mouth daily
Mechanism	• Inhibits aldehyde dehydrogenase • Causes aversive alcohol-disulfiram reaction
Effectiveness	• Meta-analysis of blind trials showed no difference than placebo though medium efficacy if open-label trials are included • More effective in supervised administration
Pros	• Use in highly structured environment (e.g. opioid treatment program) or for patients with history of success with disulfiram
Cons	• Very unpleasant • Adherence critical (and caution "hidden" alcohol in mouthwash, etc) • Must have goal of abstinence • Concerning in setting of pregnancy, CAD, psychosis, liver disease

Skinner et al, 2014; Jonas et al, JAMA, 2014

UCSF

Non-FDA approved: (1) Topiramate

*1st line option along with naltrexone (VA/DoD)

- Goal either abstinence or nonharmful drinking. NNT = 5.29* (Adjusting with adverse events, NNT 6.12 - 7.52)
- Titrate up to 300mg/day over 8 weeks but 100-200mg/day may be effective.
  - To stop, taper by 25-50mg per day over 1 week
- Beneficial for people with seizures, insomnia, obesity. May be particularly useful with co-occurring PTSD, Cocaine Use Disorder, TBI.
- Significant adverse effects dose-dependent: cognitive impairment, paresthesia, sedation, appetite suppression, taste alteration, teratogenic
- Renally adjust

TABLE 2. Titration Schedule for 200 mg Daily Target Dose

Week	Morning Dose, mg	Night-time Dose, mg	Total Daily Dose, mg
1	—	25	25
2	25	25	50
3	25	50	75
4	50	50	100
5	50	100	150
6	100	100	200

Adapted from Kranzler et al., 2014.

Kranzler, 2014; Feinn et al, 2016; Guglielmo et al, 2015; Blodgett et al, 2014; Jonas, 2014; Batki et al, 2014, Morley et al, 2024
*VA/DoD Guidelines 2021

Non-FDA approved: (2) Gabapentin

- Studied at 900-1800 mg/day with mixed evidence; Effect for decreased drinking days
- May be useful for people with h/o withdrawal
- Can also use for non-severe alcohol withdrawal
- Dose adjust for CKD
- May combine with other AUD medications
- May be helpful with neuropathic pain, insomnia
- Misuse potential?

Johnson et al., JAMA, 2006; Mason et al, 2014; Falk et al., 2019; Anton et al., 2020; Kranzler et al, 2019

UCSF

Non-FDA approved: (3) Baclofen

- Safe for use in liver failure, but mixed evidence
- Concern for significant harms: In 165K patients in France treated with meds for AUD, baclofen was associated with hospitalization (HR 1.1) and mortality (HR 1.3) in dose response relationship

Jonas, 2014; Chaignot et al, 2018

Medication Selection for AUD:

Target Goals

- Reduce drinking: Naltrexone, Gabapentin, Topiramate
- Abstinence: Acamprosate, Disulfiram, Naltrexone, Topiramate

Target Comorbidities

- Decompensated Liver Disease: Acamprosate, Gabapentin, Topiramate
- Adherence Challenges: XR Naltrexone
- Concurrent Opioid Use: NOT naltrexone
- Concurrent Stimulant Use: XR-Naltrexone, Topiramate
- Renal Disease: Dose reduce acamprosate, gabapentin
- Anxiety: Gabapentin
- Insomnia: Gabapentin, Topiramate
- H/o withdrawal: Gabapentin

Case #1: Medications for AUD

40 Y patient with severe AUD seen at clinic

They have cut back from 6-8 beers daily to 4/day

Severe cravings whenever they try to quit, not confident they can stop. Goal to cut back.

PMH:
HTN
Depression
Knee pain

Meds: HCTZ, pantoprazole, sertraline, thiamine, folate, MVI

FH: brother and father with AUD

AST 65, ALT 21
T. Bili .1
Albumin 3, INR 1.1
Cr 0.82

Which medication do you recommend?

A. Acamprosate
B. Disulfiram
C. Baclofen
D. Naltrexone
E. Topiramate
F. Naloxone
G. Gabapentin

UCSF

Case #1:

40 Y patient with severe AUD starting naltrexone. Is oral or injectable naltrexone more effective?

- Trials have not shown a significant difference in clinical efficacy between the two formulations in terms of reduction in heavy drinking days, overall alcohol consumption, or acute healthcare utilization at 3 months
- **Both formulations are associated with substantial reductions in heavy drinking, but neither demonstrates clear superiority in direct efficacy outcomes.**
- **Injectable naltrexone may improve adherence**

.Extended-Release Naltrexone Versus Oral Naltrexone for Substance Use Disorders: A Systematic Review and Meta-Analysis.

JAMA Internal Medicine

RCT: Oral vs Extended-Release Injectable Naltrexone for Hospitalized Patients With Alcohol Use Disorder

POPULATION

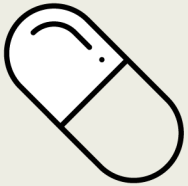
199 Men, 49 Women

Hospitalized adults with alcohol use disorder and recent heavy drinking

Mean age, 49.4 y

INTERVENTION

248 Participants randomized; both groups initiated treatment as inpatients and continued postdischarge

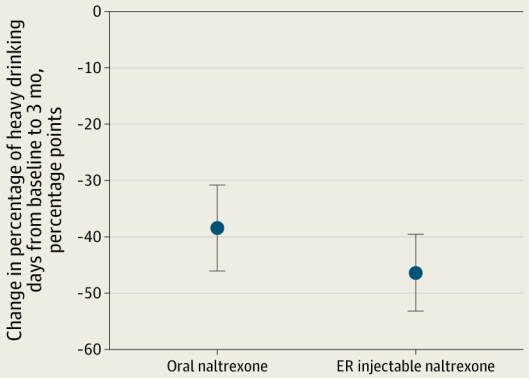


125 Oral naltrexone
Oral naltrexone, 25 mg, daily for 3 d, then 50 mg daily with titration to potential maximum 100 mg daily dose

123 ER injectable naltrexone
Extended-release (ER) injectable naltrexone, 380 mg, on day of hospital discharge, with second and third doses 1 and 2 mo later

FINDINGS

At 3-mo follow-up, percentage of heavy drinking days in the past 30 d was reduced in both groups compared with baseline, but there was no significant difference between the groups



Between-group difference in change in primary outcome at 3 mo:
−8.17 percentage points (95% CI, −18.97 to 2.62)

SETTINGS / LOCATIONS

1 Massachusetts hospital

PRIMARY OUTCOME

Change from baseline to 3-mo follow-up in percentage of heavy drinking days in the past 30 d, derived from self-reported number of drinks consumed each day in the past 30 d using the Timeline Followback calendar method

Magane KM, Dukes KA, Fielman S, et al. Oral vs extended-release injectable naltrexone for hospitalized patients with alcohol use disorder: a randomized clinical trial. *JAMA Intern Med.* Published online April 21, 2025. doi:10.1001/jamainternmed.2025.0522

Case #2: 65yo patient with depression, severe AUD, HTN with abnormal liver tests.

- "*I want to stop but short-term, it's more realistic to cut back first*"

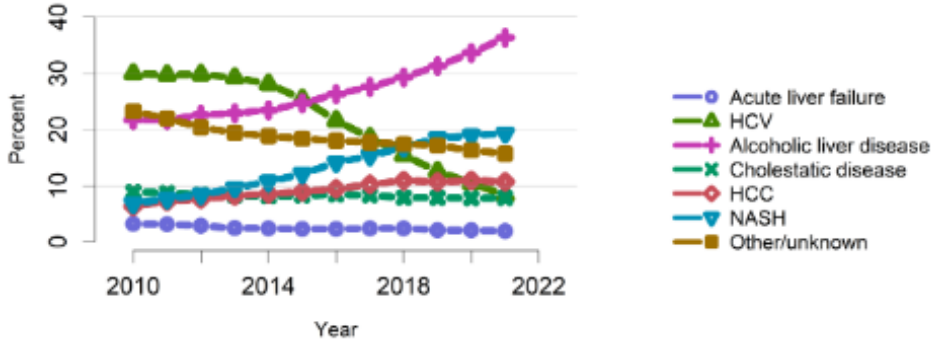
- Recent work up
  - AST 199, ALT 100, T bili 2.4, albumin 3.4, INR 1.6, Cr 1.0, Elevated AFP
  - US shows cirrhosis, no ascites
  - Ruled out other causes of liver disease
- Child Class B
- Medications: Benazepril, Sertraline

Which medication do you recommend?

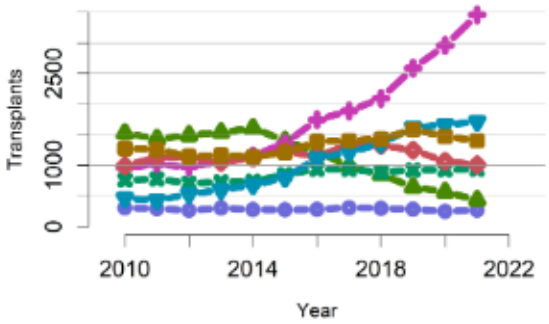
A. Acamprosate
B. Disulfiram
C. Baclofen
D. Naltrexone
E. Topiramate
F. Naloxone
G. Gabapentin

Alcohol-associated Liver Disease (ALD)

- Covid-10 pandemic has led to increase in ALD
- ALD is now leading indication for liver transplantation, replacing HCV
- 50% increase in waiting list registration for liver transplantation



Distribution of adults waiting for LT by diagnosis



Total LT by diagnosis

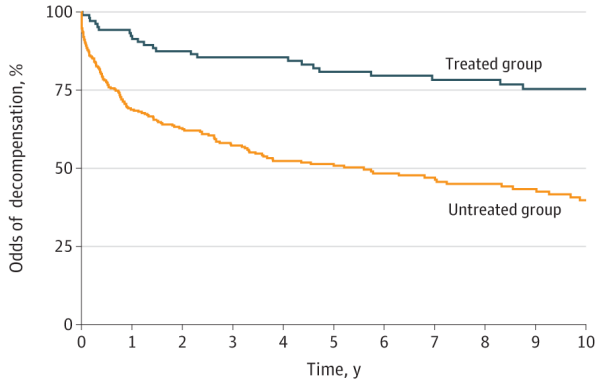
Kwong et al. OPTN/SRTR 2021 Annual Data Report: Liver; Cholankeril et al Hepatology 2021.

UCSF

Alcohol-associated Liver Disease (ALD)

- Low rates of AUD treatment:
  - For cirrhotic-stage ALD, 12% of patients received behavioral therapy after diagnosis of AUD, whereas 1% received behavioral and pharmacotherapy and 0.4% received pharmacotherapy alone (Rogal et al, Hepatology, 2020)
- Despite benefit:
  - MAUD use is associated with a 68% reduced hazard for all-cause mortality (HR 0.32, 95% CI 0.18-0.59, p <0.001) (Rabiee et al. Hepatology Communications, 2023)

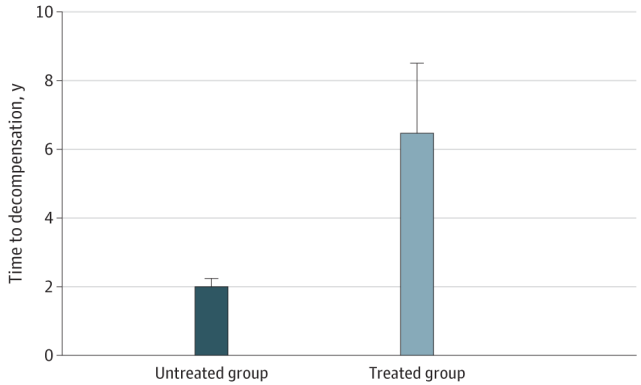
A Kaplan-Meier analysis of association between treatment and decompensation



No. at risk

Treated group	105	97	89	84	77	69	62	60	56	52	48
Untreated group	301	193	164	137	111	95	76	70	61	51	41

B Mean time to decompensation in untreated group vs treated group



Original Investigation | Gastroenterology and Hepatology

May 20, 2022

Incidence and Progression of Alcohol-Associated Liver Disease After Medical Therapy for Alcohol Use Disorder

Augustin G. L. Vannier, BA[1,2,3]; Jessica E. S. Shay, MD, PhD[1,2,3]; Vladislav Fomin, MD[1,2,3]; et al

Table 3. Odds Ratios for Developing Hepatic Decompensation After Medical Addiction Therapy

Medical addiction therapy	Adjusted odds ratio (95% CI)	*P* value
Any pharmacotherapy	0.35 (0.23-0.53)	<.001
Naltrexone	0.27 (0.10-0.64)	.005
Gabapentin	0.36 (0.23-0.56)	<.001
Topiramate	0.43 (0.17-0.99)	.05
Baclofen	1.06 (0.39-2.69)	.91
Acamprosate	1.99 (0.99-4.059)	.06
Disulfiram	2.59 (0.54-13.26)	.24

JAMA Netw Open. 2022;5(5):e2213014. doi:10.1001/jamanetworkopen.2022.13014

UCSF

Case #2: Medications for AUD

Co-occurring liver disease

- 65yo male with depression, HTN, alcohol-associated cirrhosis, Childs Pugh B. His goal is to decrease drinking.
- Consider Addiction Medicine-Hepatology collaborations

Which medication do you recommend?

A. Acamprosate
B. Disulfiram
C. Baclofen
D. Naltrexone
E. Topiramate
F. Naloxone
G. Gabapentin

Case #3 26-year-old female hospitalized with alcohol-associated hepatitis

- Last drink was day before admission
- High MELD
- Not responding to medical therapy

How long would she need to wait before being able to receive a liver transplant?

a.) 12 months
b.) 6 months
c.) She is a candidate now

“6-month rule” for liver transplantation

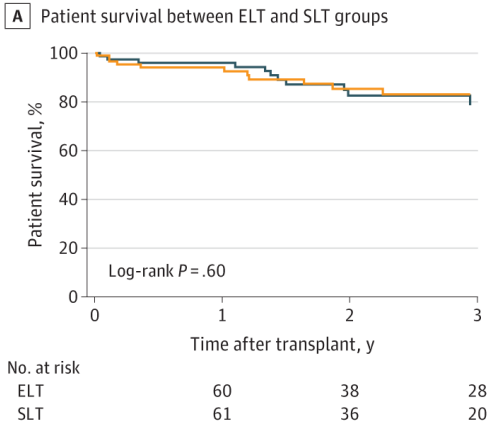
- Until recently, >85% of LT programs in US and near majority of 3rd party payors required 6 months of pre-LT abstinence
- **“6 month rule”**
  - Devised from 1997 consensus conference with 2 goals:
    - Allow recovery time from acute effects of alcohol-associated hepatotoxicity, potentially avoiding unnecessary LT
    - Evaluate pt commitment to alcohol abstinence while implementing preventative strategies against future relapse
  - Soon became a surrogate for predicting future drinking in LT candidates with ALD
  - Excludes potential candidates for LT with severe AH who are medical nonresponders or not eligible for medical therapy

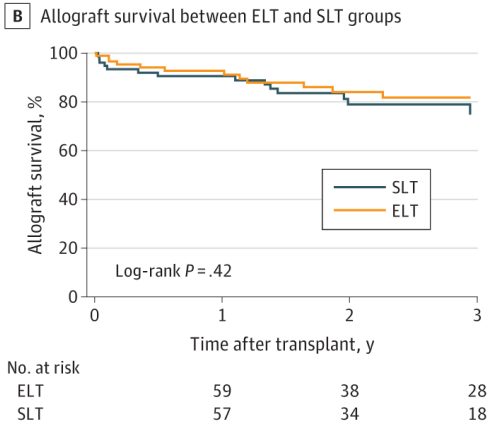
Slide adapted from C Sherman

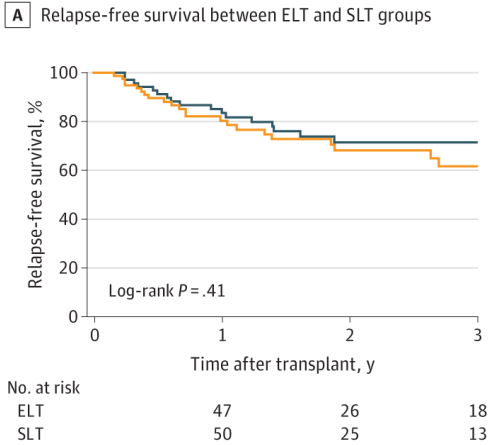
Crabb et al. AASLD Practice Guidelines. 2019.
Leong and Im. Clin Liver Dis. 2012.
Louvet et al. Hepatology. 2007.

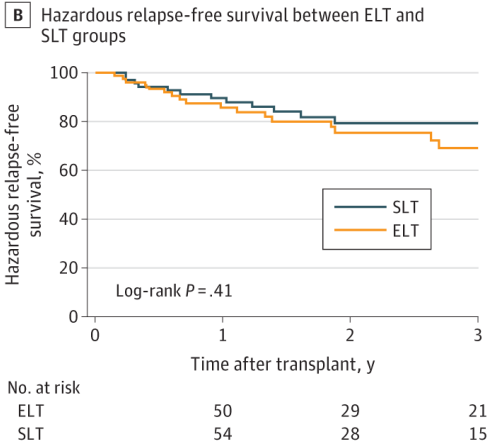
UCSF

- Post- **liver transplant** outcomes in patients with alcohol-associated liver disease and <6 months of abstinence?
- **No significant difference** in 1-year patient survival, allograft survival, or return to alcohol use.









Herrick-Reynolds et al, JAMA Surg, 2021.

Not all patients with ALD need 6 months of abstinence to be considered for transplant

- AASLD 2019 Guideline for ALD
  - "**Liver transplantation may be considered in carefully selected patients** with favorable psychosocial profiles in severe AH not responding to medical therapy"
  - "Candidate selection for liver transplantation in alcohol-associated cirrhosis **should not be based solely on a fixed interval of abstinence**"
- ACG 2018 Guideline for ALD
  - "**LT may be considered for highly selected patients** with severe AH"

Case #4:

62 yo patient with DM (a1c 10, on insulin), BMI 40, kidney stones, MASH who screens positive on AUDIT-C during annual clinic screening. You discuss how they use alcohol to calm anxiety and they meet criteria for AUD. You consider which of the following medication options to decrease drinking?

a) Naltrexone
b) Acamprosate
c) Disulfiram
d) Topiramate
e) Gabapentin
f) Semaglutide

- Semaglutide, a GLP-1RA, is currently being studied as a potential therapy for AUD
- May offer dual benefit with co-occurring conditions such as type 2 diabetes or obesity
- Randomized trials underway

Subhani et al. Association between glucagon-like peptide-1 receptor agonists use and change in alcohol consumption: a systematic review. EClinicalMedicine. 2024 Nov 14;78:102920.

JAMA Psychiatry

RCT: Once-Weekly Semaglutide in Adults with Alcohol Use Disorder

POPULATION

14 Men, 34 Women

Non-treatment-seeking adults meeting criteria for alcohol use disorder

Mean (SD) age, 39.9 (10.6) y

SETTINGS / LOCATIONS

1 US academic medical center

INTERVENTION

48 Participants randomized and analyzed

24 Semaglutide
Once-weekly semaglutide

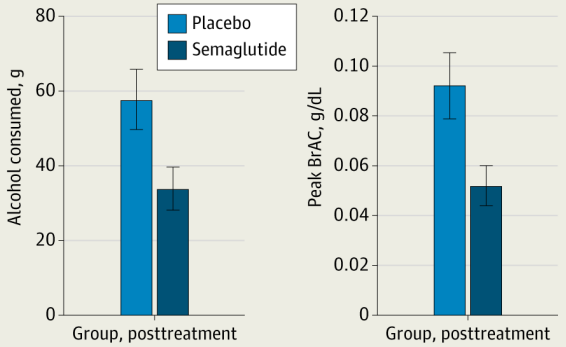
24 Placebo
Placebo injections

PRIMARY OUTCOME

Estimated alcohol consumed over 120 min during laboratory self-administration (estimated alcohol consumed in grams and peak breath alcohol concentration [BrAC] in g/dL)

FINDINGS

Among participants consuming alcohol in a laboratory session following 8 wk of treatment, those in the semaglutide group drank significantly less alcohol than those in the placebo group



Mean (SD) alcohol consumed: Semaglutide: 33.62 (20.72) g; placebo: 57.19 (28.15) g
Mean (SD) peak BrAC: Semaglutide: 0.052 (0.029) g/dL; placebo: 0.092 (0.046) g/dL
Effect sizes: Alcohol consumed: β, −0.48; 95% CI, −0.85 to −0.11; *P* = .01; peak BrAC: β, −0.46; 95% CI, −0.87 to −0.06; *P* = .03

Hendershot CS, Bremmer MP, Paladino MB, et al. Once-weekly semaglutide in adults with alcohol use disorder: a randomized clinical trial. *JAMA Psychiatry*. Published online February 12, 2025. doi:10.1001/jamapsychiatry.2024.4789

Case #4:

62 yo patient with DM (a1c 10, on insulin), BMI 40, kidney stones, MASH who screens positive on AUDIT-C during annual clinic screening. You discuss how they use alcohol to calm anxiety and they meet criteria for AUD. You consider which of the following medication options to decrease drinking?

a) **Naltrexone**
b) Acamprosate
c) Disulfiram
d) Topiramate
e) **Gabapentin**
f) **Semaglutide**

Case #5: Alcohol Withdrawal

40yo patient with history of AUD in hospital.

PAWSS >4

+ Risk factors for severe withdrawal

CIWA = 18

a.) CIWA monitoring
b.) Vitamin and mineral repletion
c.) Gabapentin 600-900mg TID
d.) Symptom-triggered benzodiazepine protocol
e.) All of above

Who will develop severe withdrawal?

- History of delirium tremens (DT) most predictive in hospitalized patients
- Prediction of Alcohol Withdrawal Severity (PAWSS) is a screening tool to predict severe withdrawal in a medically ill patient
- PAWSS Scores ≥4 suggest high risk. Prophylaxis and/or treatment may be indicated

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Maldonado et al, 2015

Part A: Threshold Criteria: ("Y" or "N", no point)

Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days? OR did the patient have a "+" BAL on admission? _____

IF the answer to either is YES, proceed with test:

Part B: Based on patient interview: (1 point each)

1. Have you been recently intoxicated/drunk, within the last 30 days? _____
2. Have you ever undergone alcohol use disorder rehabilitation treatment or treatment for alcoholism? (i.e., in-patient or out-patient treatment programs or AA attendance) _____
3. Have you ever experienced any previous episodes of alcohol withdrawal, regardless of severity? _____
4. Have you ever experienced blackouts? _____
5. Have you ever experienced alcohol withdrawal seizures? _____
6. Have you ever experienced delirium tremens or DT's? _____
7. Have you combined alcohol with other "downers" like benzodiazepines or barbiturates, during the last 90 days? _____
8. Have you combined alcohol with any other substance of abuse, during the last 90 days? _____

Part C: Based on clinical evidence: (1 point each)

9. Was the patient's blood alcohol level (BAL) on presentation ≥ 200? _____
10. Is there evidence of increased autonomic activity? (e.g., HR > 120 bpm, tremor, sweating, agitation, nausea) _____

Total Score: _____

Notes: Maximum score = 10. This instrument is intended as a SCREENING TOOL. The greater the number of positive findings, the higher the risk for the development of AWS.
A score of ≥ 4 suggests HIGH RISK for moderate to severe (complicated) AWS; prophylaxis and/or treatment may be indicated.

Wood et al, 2018; Maldonado et al, 2014

UCSF

Treatments of alcohol withdrawal

- **Benzodiazepines**
  - Prevent seizures so generally considered 1st line
  - Symptom triggered protocols
  - Consider reserving for high risk of severe withdrawal given concerns for delirium, CNS depression and misuse
  - Longer-acting (chlordiazepoxide) preferred; Shorter-acting without active metabolites (lorazepam) preferred for impaired liver function or risk of oversedation
- **Phenobarbital**
  - Prevents seizures
  - Monotherapy or as adjunct to benzodiazepines
- **Gabapentin**
  - As effective as benzodiazepines in treating symptoms other than seizures and DT
  - Best as adjunct or for mild-moderate alcohol withdrawal symptoms in low risk patients
  - Can continue for maintenance treatment of AUD
- **Others:** Carbamazepine, Adjunctive AEDs or Dexmedetomadine

- Of 22,899 hospitalizations among 16,323 adults diagnosed with alcohol withdrawal syndrome at Kaiser Northern California
- Benzo-sparing order set implementation was associated with relative decreases in benzodiazepine exposure, ICU use, and LOS

Table 1. Elements of BZD-Sparing Order Set for Alcohol Withdrawal Syndrome

Pathway	Treatment	Dosing
Observation (criteria: PAWSS < 4 and CIWA-Ar < 8): thiamine, folic acid, multivitamin, and maintenance fluid	Thiamine[a]	Day 1-3: 200 mg by mouth 2 times daily
		Day 4+: 100 mg by mouth daily
	Folic acid[b]	Day 1+: 1 mg by mouth daily
	Multivitamin[a]	Day 1+: 1 tablet by mouth daily
	Maintenance fluid	Day 1+: 20 mEq/L potassium chloride in 5% dextrose and 0.45% sodium chloride at 100 mL/h by IV route continuously
Prevention and active withdrawal (criteria: PAWSS ≥ 4 and CIWA-Ar ≥ 8): gabapentin or valproic acid, then clonidine, then lorazepam, with treatment from observation pathway	Gabapentin	Loading dose: 1200 mg by mouth
		Day 1-3: 800 mg by mouth 3 times daily
		Day 4-5: 600 mg by mouth 3 times daily
		Day 6-7: 300 mg by mouth 3 times daily
	Gabapentin (low dose)	Loading dose: 1200 mg by mouth
		Day 1-5: 300 mg by mouth 3 times daily
		Day 6-10: 300 mg by mouth 2 times daily
		Day 11-20: 600 mg by mouth at bedtime
	Valproic acid[c]	Day 1-5: 250 mg by mouth 2 times daily
		Day 1-10: 500 mg by mouth at bedtime
	Clonidine	Day 1: 0.2 mg by mouth every 8 h for 2 doses and three 0.1 mg/24 h transdermal patches (0.3 mg total)
		Day 3: Remove one 0.1 mg/24 h transdermal patch
		Day 6: Remove one 0.1 mg/24 h transdermal patch
		Day 7: Remove one 0.1 mg/24 h transdermal patch
		Day 8: 0.1 mg/24 h transdermal patch
		Day 10: Remove one 0.1 mg/24 h transdermal patch
	Lorazepam[c]	CIWA-Ar score 16-20: 1 mg by mouth every 4 h as needed
		CIWA-Ar score >21: 2 mg by mouth every 4 h as needed
Severe and complex withdrawal (criteria: admitted to ICU with CIWA-Ar≥15 or not responsive to BZDs): dexmedetomidine with prevention and active withdrawal and observation pathways	Dexmedetomidine	Day 1+: 0.4 µg/kg/h by IV route continuously.
		Titrate by 0.2 µg/kg/h every 10-15 min up to a maximum of 1.4 µg/kg/h to achieve CIWA-Ar score <12 or RASS score −1 to 1.

Smith et al, JAMA Network Open, 2022

Case #5: Alcohol Withdrawal

40yo patient admitted with severe alcohol withdrawal

- With Gabapentin 1800mg/day started in 1st 48 hours,
  - Lower bdz requirement, fewer withdrawal symptoms on Day 3, shorter LOS
  - Well tolerated and continued

a.) CIWA monitoring
b.) Vitamin and mineral repletion
c.) Gabapentin 600-900mg TID → Consider
d.) Symptom-triggered benzodiazepine protocol
e.) All of above

Levine AR, Carrasquillo L, Mueller J, Nounou MI, Naut ER, Ibrahim D. High-Dose Gabapentin for the Treatment of Severe Alcohol Withdrawal Syndrome: A Retrospective Cohort Analysis. Pharmacotherapy. 2019 Sep;39(9):881-888.

Case #6: Alcohol Withdrawal

40yo patient with AUD tells you that they want to stop drinking. You are on a phonecall with them from clinic.

Assessing safety of ambulatory withdrawal management

Can the patient be safely monitored in an ambulatory care setting or at home?	Does the patient need inpatient care?
• Does the patient have safe housing and support? • Can the patient maintain telephone-based contact? • Can the patient follow medication instructions? Take orally? • Does your clinic have the capacity to provide remote monitoring and/or accessibility for patients with alcohol withdrawal syndrome?	• Are they at risk of severe or complicated withdrawal? • Does the patient have a history of seizures or delirium tremens? • Does the patient have acute illness, medical co-morbidities or co-occurring substance use likely to complicate their withdrawal treatment? • Age 65 or over? • Pregnant? • How severe are their symptoms?

ASAM, 2020; B Hurley and A Alvanzo, 2021

UCSF

Who will develop severe withdrawal?

- History of delirium tremens (DT) most predictive in hospitalized patients
- Prediction of Alcohol Withdrawal Severity (PAWSS) is a screening tool to predict severe withdrawal in a medically ill patient
- PAWSS Scores ≥4 suggest high risk. Prophylaxis and/or treatment may be indicated

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Maldonado et al, 2015

Part A: Threshold Criteria: ("Y" or "N", no point)

Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days? OR did the patient have a "+" BAL on admission? _____

IF the answer to either is YES, proceed with test:

Part B: Based on patient interview: (1 point each)

1. Have you been recently intoxicated/drunk, within the last 30 days? _____
2. Have you ever undergone alcohol use disorder rehabilitation treatment or treatment for alcoholism? (i.e., in-patient or out-patient treatment programs or AA attendance) _____
3. Have you ever experienced any previous episodes of alcohol withdrawal, regardless of severity? _____
4. Have you ever experienced blackouts? _____
5. Have you ever experienced alcohol withdrawal seizures? _____
6. Have you ever experienced delirium tremens or DT's? _____
7. Have you combined alcohol with other "downers" like benzodiazepines or barbiturates, during the last 90 days? _____
8. Have you combined alcohol with any other substance of abuse, during the last 90 days? _____

Part C: Based on clinical evidence: (1 point each)

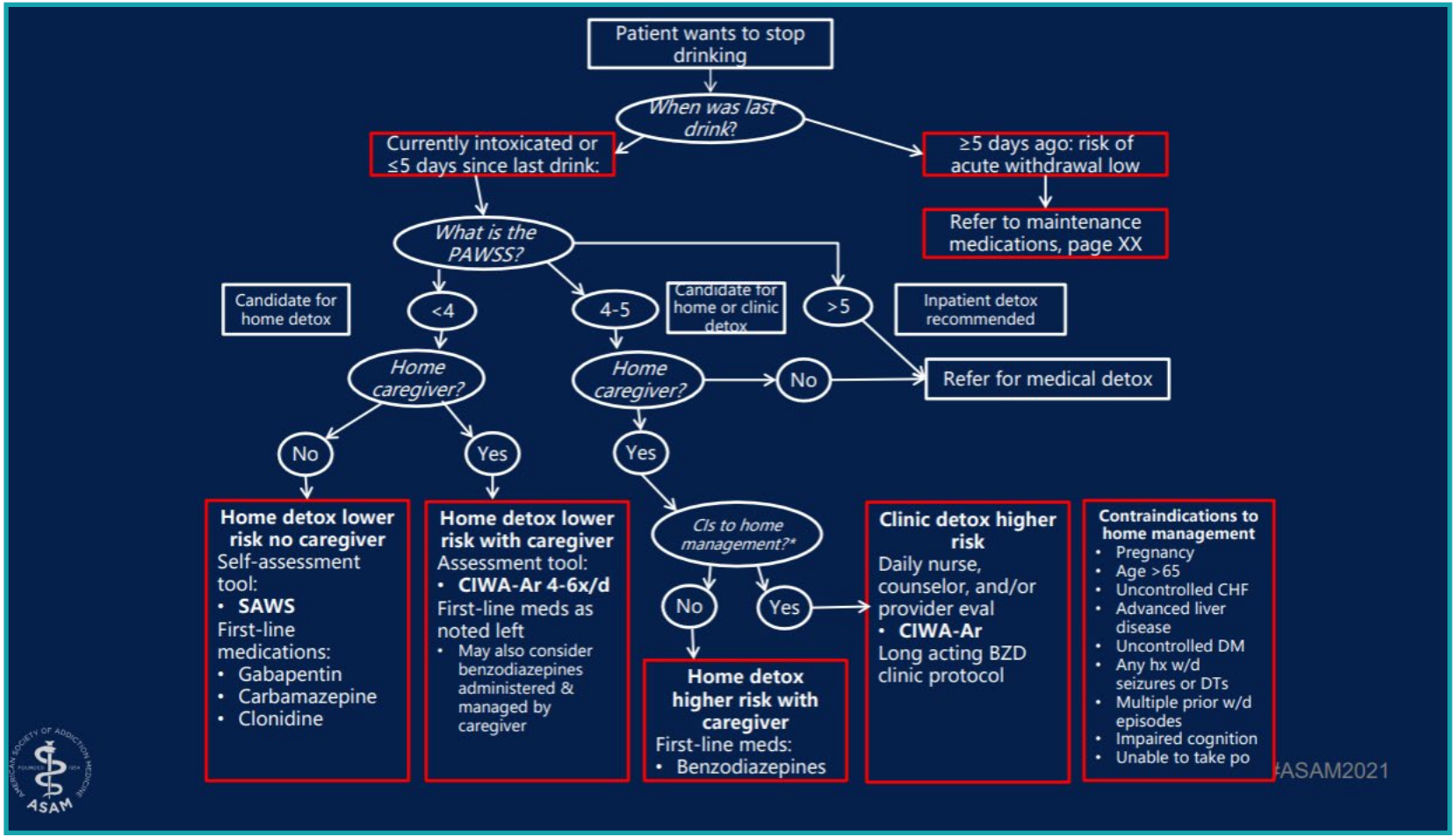
9. Was the patient's blood alcohol level (BAL) on presentation ≥ 200? _____
10. Is there evidence of increased autonomic activity? (e.g., HR > 120 bpm, tremor, sweating, agitation, nausea) _____

Total Score: _____

Notes: Maximum score = 10. This instrument is intended as a SCREENING TOOL. The greater the number of positive findings, the higher the risk for the development of AWS.
A score of ≥ 4 suggests HIGH RISK for moderate to severe (complicated) AWS; prophylaxis and/or treatment may be indicated.

Wood et al, 2018; Maldonado et al, 2014

UCSF



J Blum, M Hoag, J Cram, J Bull, ASAM, 2020

Medications for outpatient withdrawal management

- **Benzodiazepines**
  - Prevent seizures so generally considered 1st line
  - Consider reserving for patients with history or risk of severe withdrawal
  - Significant concerns for delirium, CNS depression and misuse
  - Longer-acting (chlordiazepoxide) preferred
  - Shorter-acting without active metabolites (lorazepam) preferred for impaired liver function or risk of oversedation
- **Gabapentin**
  - As effective as benzodiazepines in treating symptoms other than seizures and DT
  - Best as adjunct or for mild-moderate alcohol withdrawal symptoms in low-risk patients
  - Can continue for maintenance treatment of AUD
  - 1200mg/day in divided doses tapered over 4-6 days
- **Carbamazepine**
  - As adjunct or for lower risk patients who do not tolerate gabapentin
  - More side effects, e.g., dizziness, drowsiness, nausea, drug interactions
  - 800mg/day in divided doses tapered over 5-9 days

Wong J, Saver B, Scanlan JM, et al. The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management. J Addict Med. 2020;14(3S)(suppl 1):1-72.

Monitoring considerations

- Reassess patient frequently, ideally daily, for symptoms and medication reconciliation
- Family member or close contact can help monitor patient and dose medications
- If patient not at risk for severe withdrawal, may not need medications if > 24 hours with no or mild symptoms
- Consider dispensing limited supply q24-72 hours depending on patient risks and adherence

TABLE 1. Alcohol Withdrawal Severity.

Severity Category	Associated CIWA-Ar Range*	Symptom Description
Mild	CIWA-Ar < 10	Mild or moderate anxiety, sweating and insomnia, but no tremor
Moderate	CIWA-Ar 10-18	Moderate anxiety, sweating, insomnia, and mild tremor
Severe	CIWA-Ar ≥19	Severe anxiety and moderate to severe tremor, but not confusion, hallucinations, or seizure
Complicated	CIWA-Ar ≥19	Seizure or signs and symptoms indicative of delirium – such as an inability to fully comprehend instructions, clouding of the sensorium or confusion – or new onset of hallucinations

*Throughout this document, we provide examples for withdrawal severity using the CIWA-Ar, although other scales can be used. Regardless of the instrument used, there is a wide variety in the literature and in practice as to which scores best delineate mild, moderate and severe withdrawal. Classification of withdrawal severity is ultimately up to the judgment of clinicians and the choice of reference range may be based on their particular patient population or capabilities.

Short Alcohol Withdrawal Scale (SAWS)

- Patient-administered tool to assess the severity of alcohol withdrawal.
- Patients indicate how they have felt in the previous 24 hours. Moderate to severe withdrawal ≥ 12 points.
- Clinicians can also use Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar)

Item	*None (0 points)*	*Mild (1 point)*	*Moderate (2 points)*	*Severe (3 points)*
Anxious				
Feeling confused				
Restless				
Miserable				
Problems with memory				
Tremor (shakes)				
Nausea				
Heart pounding				
Sleep disturbance				
Sweating				

Elholm et al, 2010

Ambulatory management of alcohol withdrawal

- Duration of treatment may last between 1-7 days
- Transition to higher level of care if any escalating symptoms, CIWA>20, SAWS>16, distress, altered mental status or seizure
- Recommend regular diet, hydration, safe and relaxing environment, and consider multivitamin containing thiamine and folate
- Don’t forget medications for AUD!

Resource: ASAM Clinical Practice Guideline on Alcohol Withdrawal Management, 2020

Take home points

1. Any healthcare setting is a critical touchpoint for treatment for alcohol use disorder
2. Reduce harm by employing evidence-based interventions across the spectrum of unhealthy alcohol use
3. Select medications for alcohol use disorder to match patient goals and co-morbidities

NATIONAL CLINICIAN CONSULTATION CENTER

Translating science into care

The National Clinician Consultation Center (NCCC) offers on-demand, cost-free clinical support and guidance – for clinicians, by clinicians.

To reach our team: 844-ASK-NCCC (844-275-6222)
Submit your clinical inquiry online: nccc.ucsf.edu

HIV/AIDS Warmline	HIV treatment, ARV management, complications, and co-morbidities	**Perinatal HIV Hotline**	Pregnancy, infant feeding and HIV
Hepatitis C Warmline	HCV testing, staging, monitoring, treatment	**Substance Use Warmline**	Substance use evaluation and management
PrEPline	HIV pre-exposure prophylaxis options and monitoring	**PEPline**	Bloodborne pathogen (HIV, HBV, HCV) exposure management

A program of the Goldschmidt Collective

The National Clinician Consultation Center is part of the AIDS Education and Training Center(AETC) Program and is located at the University of California, San Francisco (UCSF) / San Francisco General Hospital. It is supported by the Health Resources and Services Administration(HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $2,250,000 with 0% financed with non-governmental sources.

AETC AIDS Education & Training Center Program
National Clinician Consultation Center

UCSF

References

White AM, Castle IP, Hingson RW, Powell PA. Using Death Certificates to Explore Changes in Alcohol-Related Mortality in the United States, 1999 to 2017. Alcohol Clin Exp Res. 2020 Jan;44(1):178-187.

Czeisler MÉ, Lane RI, Wiley JF, Czeisler CA, Howard ME, Rajaratnam SMW. Follow-up Survey of US Adult Reports of Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic, September 2020. *JAMA Netw Open.* 2021;4(2):e2037665. doi:10.1001/jamanetworkopen.2020.37665

Werner D. Elucidating the role of alpha-1-containing GABA(A) receptors in ethanol action. 2007.

De Witte P. Imbalance between neuroexcitatory and neuroinhibitory amino acids causes craving for ethanol. 2004.

Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, Gastfriend DR, Hosking JD, Johnson BA, LoCastro JS, Longabaugh R, Mason BJ, Mattson ME, Miller WR, Pettinati HM, Randall CL, Swift R, Weiss RD, Williams LD, Zweben A; COMBINE Study Research Group. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA. 2006 May 3;295(17):2003-17. doi: 10.1001/jama.295.17.2003. PMID: 16670409.

Anton RF, Myrick H, Wright TM, Latham PK, Baros AM, Waid LR, Randall PK. Gabapentin combined with naltrexone for the treatment of alcohol dependence. Am J Psychiatry. 2011 Jul;168(7):709-17.

Anton RF, Latham P, Voronin K, Book S, Hoffman M, Prisciandaro J, Bristol E. Efficacy of Gabapentin for the Treatment of Alcohol Use Disorder in Patients With Alcohol Withdrawal Symptoms: A Randomized Clinical Trial. JAMA Intern Med. 2020 May 1;180(5):728-736. doi: 10.1001/jamainternmed.2020.0249. PMID: 32150232; PMCID: PMC7063541.

R.F. Anton. N Engl J Med, 359 (2008), pp. 715-721

Pollard MS, Tucker JS, Green HD. Changes in Adult Alcohol Use and Consequences During the COVID-19 Pandemic in the US. JAMA Netw Open. 2020.

References

Maldonado JR, Sher Y, Ashouri JF, Hills-Evans K, Swendsen H, Lolak S, Miller AC. The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. Alcohol. 2014 Jun;48(4):375-90. doi: 10.1016/j.alcohol.2014.01.004. Epub 2014 Feb 19. PMID: 24657098.

Sterling SA, Palzes VA, Lu Y, Kline-Simon AH, Parthasarathy S, Ross T, Elson J, Weisner C, Maxim C, Chi FW. Associations Between Medical Conditions and Alcohol Consumption Levels in an Adult Primary Care Population. JAMA Netw Open. 2020 May 1;3(5):e204687. doi: 10.1001/jamanetworkopen.2020.4687. PMID: 32401315; PMCID: PMC7221504.

Esser MB, Sherk A, Liu Y, et al. Deaths and Years of Potential Life Lost From Excessive Alcohol Use — United States, 2011–2015. MMWR Morb Mortal Wkly Rep 2020;69:1428–1433.

Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, Kim MM, Shanahan E, Gass CE, Rowe CJ, Garbutt JC. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. JAMA. 2014 May 14;311(18):1889-900.

Voskoboinik A, Kalman JM, De Silva A, et al. Alcohol abstinence in drinkers with atrial fibrillation. N Engl J Med 2020;382:20-28.

Sharma RA, Subedi K, Gbadebo BM, Wilson B, Jurkovitz C, Horton T. Alcohol Withdrawal Rates in Hospitalized Patients During the COVID-19 Pandemic. JAMA Netw Open. 2021;4(3):e210422.

US Burden of Disease Collaborators. The state of US health, 1990-2010. JAMA. 2013;310(6):591-608.

Collins SE et al. Combining behavioral harm-reduction treatment and extended-release naltrexone for people experiencing homelessness and alcohol use disorder in the USA: a randomised clinical trial, The Lancet Psychiatry, Volume 8, Issue 4, 2021, Appendix A.

Sugarman, D.E., Greenfield, S.F. Alcohol and COVID-19: How Do We Respond to This Growing Public Health Crisis?. J GEN INTERN MED 36, 214–215 (2021). https://doi.org/10.1007/s11606-020-06321-z

References

Batki SL, Pennington DL, Lasher B, Neylan TC, Metzler T, Waldrop A, Delucchi K, Herbst E. Topiramate treatment of alcohol use disorder in veterans with posttraumatic stress disorder: a randomized controlled pilot trial. Alcohol Clin Exp Res. 2014 Aug;38(8):2169-77. doi: 10.1111/acer.12496.

Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings a systematic review and meta-analysis. JAMA. 2014;311:1889-1900.

Spillane S, Shiels MS, Best AF, et al. Trends in Alcohol-Induced Deaths in the United States, 2000-2016. JAMA Netw Open. 2020;3(2):e1921451. Published 2020 Feb 5. doi:10.1001/jamanetworkopen.2019.21451

Bazzi A, Saitz R. Screening for Unhealthy Alcohol Use. JAMA. 2018 Nov 13;320(18):1869-1871. doi: 10.1001/jama.2018.16069. PMID: 30422181; PMCID: PMC6296380

Ng Fat L, Bell S, Britton A. A life-time of hazardous drinking and harm to health among older adults: findings from the Whitehall II prospective cohort study. Addiction. 2020 Oct;115(10):1855-1866. doi: 10.1111/add.15013.

Edelman EJ, Tetrault JM. Unhealthy Alcohol Use in Primary Care-The Elephant in the Examination Room. JAMA Intern Med. 2019 Jan 1;179(1):9-10. doi: 10.1001/jamainternmed.2018.6125. PMID: 30422276.

Smith PC, Schmidt SM, Allensworth-Davies D, Saitz R. Primary care validation of a single-question alcohol screening test. J Gen Intern Med. 2009 Jul;24(7):783-8. doi: 10.1007/s11606-009-0928-6. Epub 2009 Feb 27. Erratum in: J Gen Intern Med. 2010 Apr;25(4):375. PMID: 19247718; PMCID: PMC2695521.

Rehm J, Patra J, Brennan A, et al. The role of alcohol use in the aetiology and progression of liver disease: A narrative review and a quantification. Drug Alcohol Rev. 2021;10.1111/dar.13286.

Jessica L Mellinger, Michael L Volk, Transplantation for Alcohol-related Liver Disease: Is It Fair?, Alcohol and Alcoholism, Volume 53, Issue 2, March 2018, Pages 173–177.

References

Skinner MD, Lahmek P, Pham H, Aubin HJ. Disulfiram efficacy in the treatment of alcohol dependence: a meta-analysis. PLoS One. 2014 Feb 10;9(2):e87366.

Falk DE, O'Malley SS, Witkiewitz K, Anton RF, Litten RZ, Slater M, Kranzler HR, Mann KF, Hasin DS, Johnson B, Meulien D, Ryan M, Fertig J; Alcohol Clinical Trials Initiative (ACTIVE) Workgroup. Evaluation of Drinking Risk Levels as Outcomes in Alcohol Pharmacotherapy Trials: A Secondary Analysis of 3 Randomized Clinical Trials. JAMA Psychiatry. 2019 Apr 1;76(4):374-381. doi: 10.1001/jamapsychiatry.2018.3079. PMID: 30865232; PMCID: PMC6450273.

Rösner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. Cochrane Database Syst Rev. 2010 Sep 8;(9):CD004332. doi: 10.1002/14651858.CD004332.pub2. PMID: 20824837.

Donoghue K, Elzerbi C, Saunders R, Whittington C, Pilling S, Drummond C. The efficacy of acamprosate and naltrexone in the treatment of alcohol dependence, Europe versus the rest of the world: a meta-analysis. Addiction. 2015 Jun;110(6):920-30. doi: 10.1111/add.12875. Epub 2015 Mar 17. PMID: 25664494.

Maisel NC, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? Addiction. 2013 Feb;108(2):275-93. doi: 10.1111/j.1360-0443.2012.04054.x. Epub 2012 Oct 17. PMID: 23075288; PMCID: PMC3970823.

Johansson M, Sinadinovic K, Gajecki M, et al. Internet-based therapy versus face-to-face therapy for alcohol use disorder, a randomized controlled non-inferiority trial. Addiction. 2021;116(5):1088–1100.

Wood E, Albarqouni L, Tkachuk S, et al. Will This Hospitalized Patient Develop Severe Alcohol Withdrawal Syndrome?: The Rational Clinical Examination Systematic Review [published correction appears in JAMA. 2019 Jul 23;322(4):369]. JAMA. 2018;320(8):825-833. doi:10.1001/jama.2018.10574

References

Chaignot C, Zureik M, Rey G, Dray-Spira R, Coste J, Weill A. Risk of hospitalisation and death related to baclofen for alcohol use disorders: Comparison with nalmefene, acamprosate, and naltrexone in a cohort study of 165 334 patients between 2009 and 2015 in France. Pharmacoepidemiol Drug Saf. 2018 Nov;27(11):1239-1248. doi: 10.1002/pds.4635. Epub 2018 Sep 25. PMID: 30251424; PMCID: PMC6282718.

Maldonado JR, Sher Y, Ashouri JF, Hills-Evans K, Swendsen H, Lolak S, Miller AC. The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. Alcohol. 2014 Jun;48(4):375-90. doi: 10.1016/j.alcohol.2014.01.004. Epub 2014 Feb 19. PMID: 24657098.

Blodgett JC, Del Re AC, Maisel NC, Finney JW. A meta-analysis of topiramate's effects for individuals with alcohol use disorders. Alcohol Clin Exp Res. 2014 Jun;38(6):1481-8. doi: 10.1111/acer.12411. Epub 2014 May 5. PMID: 24796492; PMCID: PMC4047180.

Rose AK, Jones A. Baclofen: its effectiveness in reducing harmful drinking, craving, and negative mood. A meta-analysis. Addiction. 2018 Aug;113(8):1396-1406.

White AM, Castle IP, Powell PA, Hingson RW, Koob GF. Alcohol-Related Deaths During the COVID-19 Pandemic. *JAMA.* 2022;327(17):1704–1706. doi:10.1001/jama.2022.4308

Hagman BT, Falk D, Litten R, Koob GF. Defining Recovery From Alcohol Use Disorder: Development of an NIAAA Research Definition. Am J Psychiatry. 2022 Apr 12:appiajp21090963. doi: 10.1176/appi.ajp.21090963. Epub ahead of print. PMID: 35410494.

Perry C, Liberto J, Milliken C, Burden J, Hagedorn H, Atkinson T, McKay JR, Mooney L, Sall J, Sasson C, Saxon A, Spevak C, Gordon AJ; VA/DoD Guideline Development Group*. The Management of Substance Use Disorders: Synopsis of the 2021 U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guideline. Ann Intern Med. 2022 Mar 22. doi: 10.7326/M21-4011. Epub ahead of print. PMID: 35313113.

References

Murphy CE 4th, Wang RC, Montoy JC, et al. Effect of extended-release naltrexone on alcohol consumption: a systematic review and meta-analysis. Addiction. 2021;10.1111/add.15572.

Smith JT, Sage M, Szeto H, et al. Outcomes After Implementation of a Benzodiazepine-Sparing Alcohol Withdrawal Order Set in an Integrated Health Care System. *JAMA Netw Open.* 2022;5(2):e220158. doi:10.1001/jamanetworkopen.2022.0158

Cheng H, McGuinness L A, Elbers R G, MacArthur G J, Taylor A, McAleenan A et al. Treatment interventions to maintain abstinence from alcohol in primary care: systematic review and network meta-analysis *BMJ* 2020; 371 :m3934 doi:10.1136/bmj.m3934

Herrick-Reynolds KM, Punchhi G, Greenberg RS, et al. Evaluation of Early vs Standard Liver Transplant for Alcohol-Associated Liver Disease. *JAMA Surg.* 2021;156(11):1026–1034. doi:10.1001/jamasurg.2021.3748