Treatment of Alcohol Use Disorder in Patients with Liver Disease

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Disclosure Information

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  - Presenter 1 Disclosures: No Disclosures
- Presenter 2: Steven Tate, MD, MSc — Clinical Assistant Professor, Stanford University School of Medicine
  - Presenter 2 Disclosures: No Disclosures
- Presenter 3: Divya Ayyala-Somayajula, MD, MAS — Clinical Assistant Professor of Medicine, Thomas Jefferson University
  - Presenter 3 Disclosures: No Disclosures
- Presenter 4: Thomas Bottyan, MD — Addiction Psychiatrist, VA Northern California Healthcare System
  - Presenter 4 Disclosures: No Disclosures
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  - ® Non-Speaker Author Disclosures: No disclosures

Disclosure Information

- We will be discussing “off-label” uses of the following medications:
  - Baclofen
  - Gabapentin
  - Topiramate
- We will also briefly discuss novel and emerging therapies including GLP-1 receptor agonists, neuromodulation (TMS/tDCS), psychedelics (psilocybin), and ketamine

Learning Objectives

- Evaluate the evidence and safety data for FDA-approved and off-label pharmacotherapies for Alcohol Use Disorder (AUD) in patients with liver disease, including indications and contraindications.
- Develop safe and effective, evidence-based treatment plans for AUD in patients with liver disease.
- Integrate psychosocial, mutual-support, and integrated care models into the management of AUD for patients with liver disease.

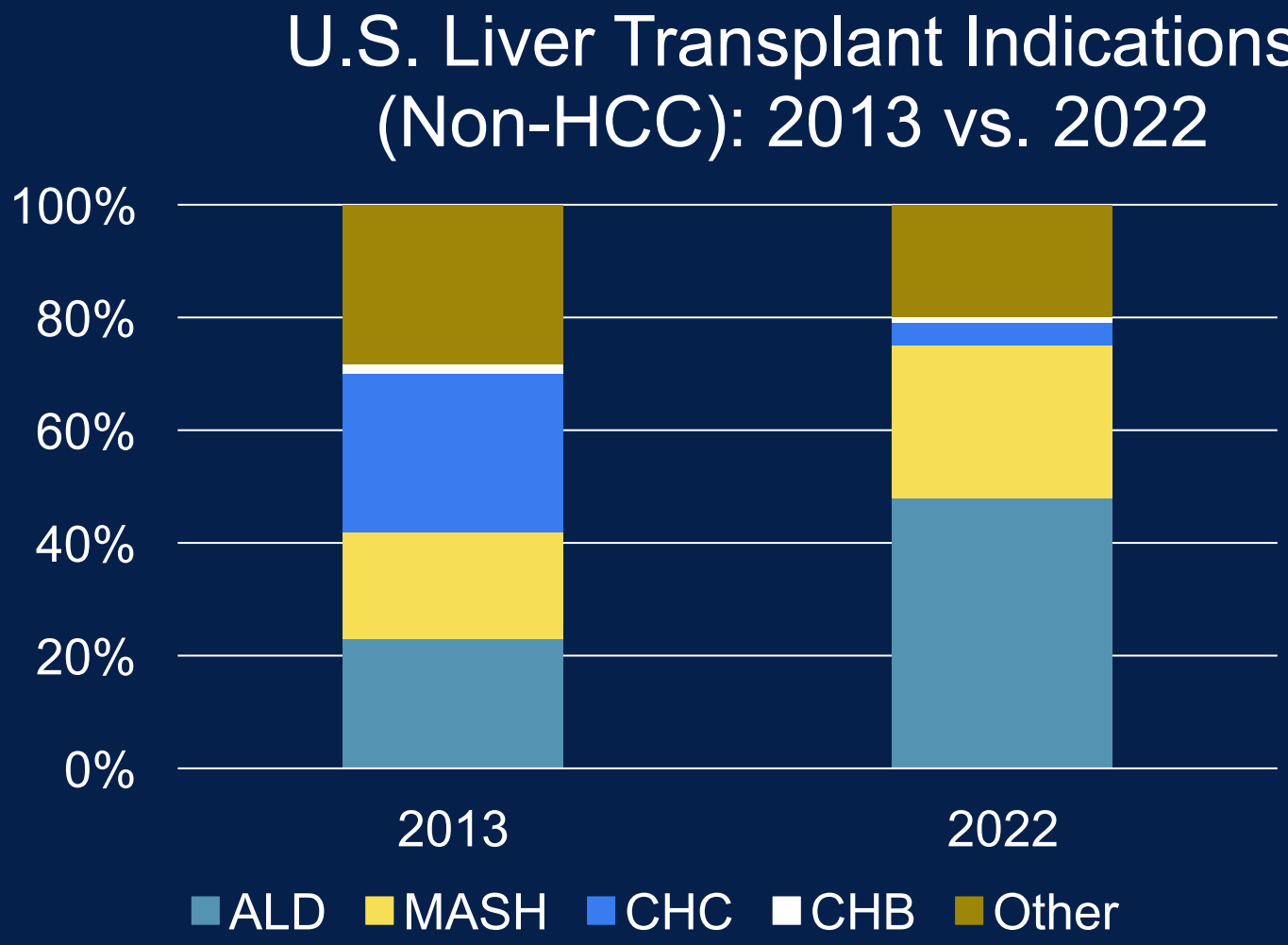
Steatotic Liver Disease (SLD)

CATEGORY	PRIMARY DRIVER	ALCOHOL INTAKE	CLINICAL NOTES
MASLD	Metabolic Dysfunction	<20-30 g/day	Steatosis typically metabolic; alcohol contributes minimally
MetALD	Metabolic + Alcohol Combined	20-60 g/day	Synergistic injury; faster progression risk
ALD	Alcohol Toxicity	>50-60 g/day	Alcohol injury predominates even when metabolic risks coexist.

MASLD = Metabolic Dysfunction-Associated Steatotic Liver Disease
MetALD = Metabolic Dysfunction AND Alcohol-Associated Steatotic Liver Disease
ALD = Alcohol-Associated Liver Disease (ALD)

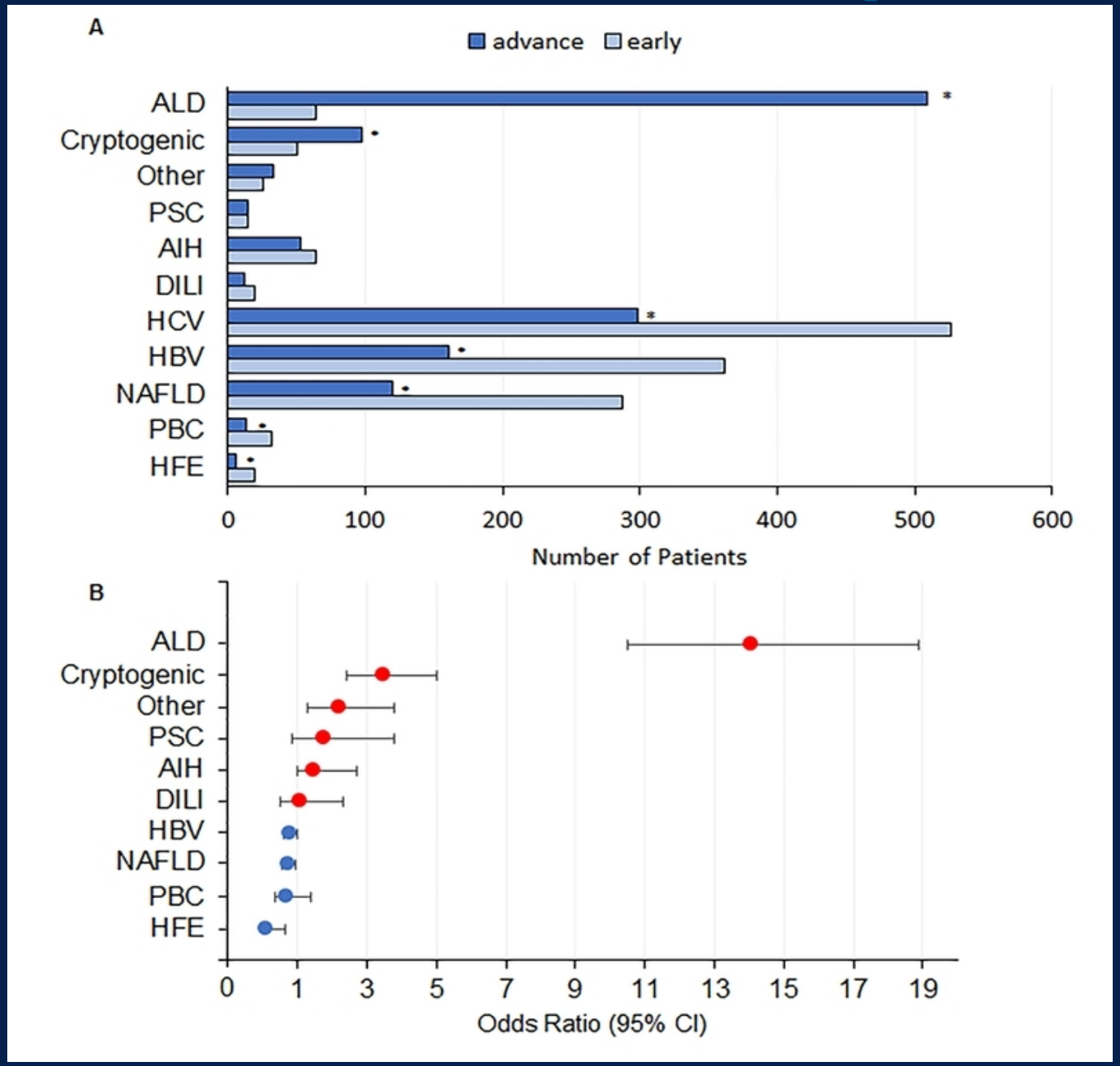
References: Rinella 1

ALD Burden & Epidemiology



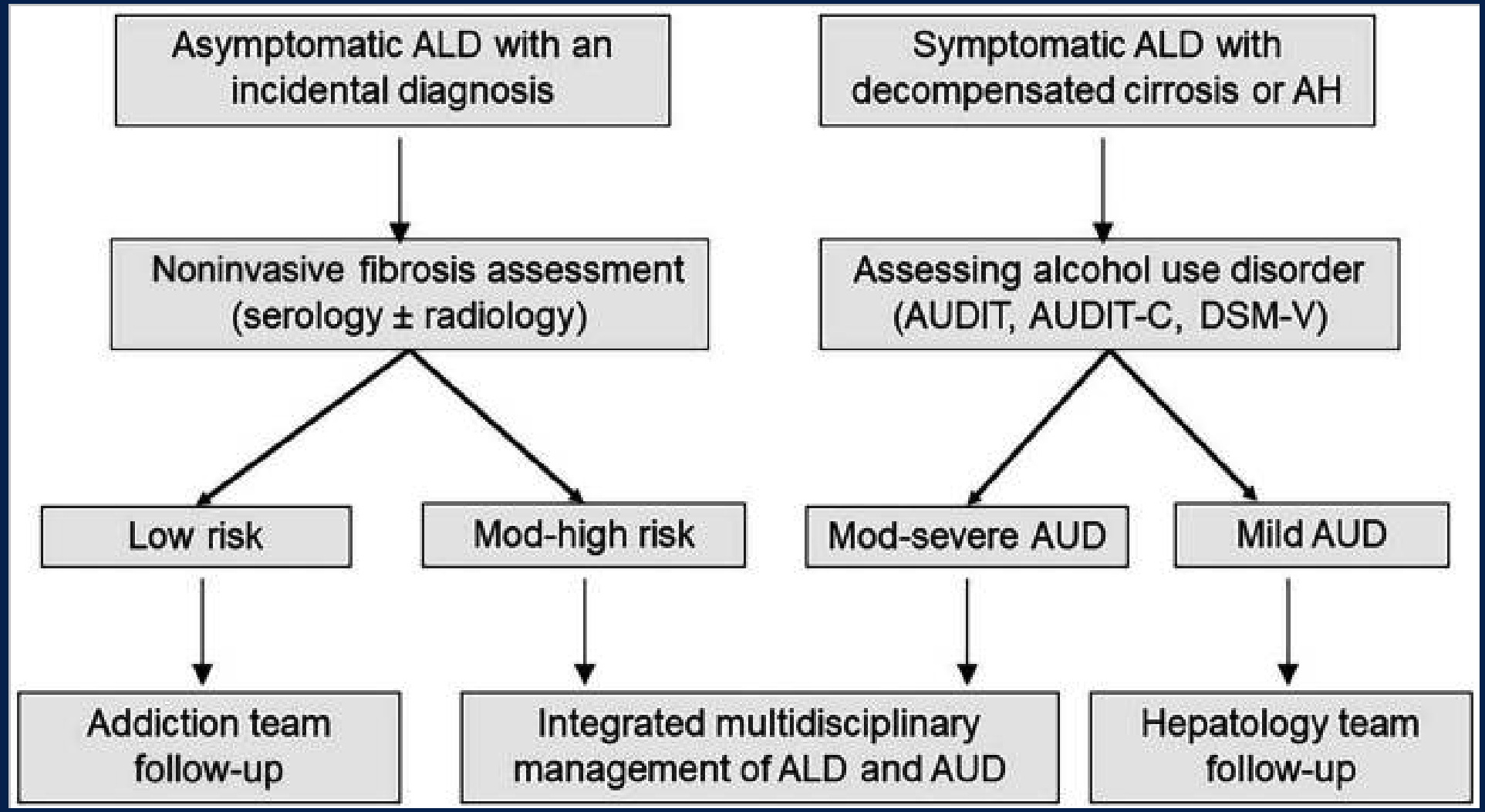
References: Huang 2, Younossi 3

ALD Detection Gap



References: Shah 4

ALD Treatment Gap



References: SAMHSA 5, Mellinger 6, Rogal 7, Sundaresh 8, Joplin 9

Why do ALD patients not participate in treatment even when offered?

AUD/ALD Patients

- Relapse/cessation as an individual strength
- Quitting without treatment is the only way to stop
- AUD severity does not affect relapse risk but rather how abnormal you feel drinking does
- It is a good sign to feel normal when you drink
- Risky drinking is when you get sick from drinking

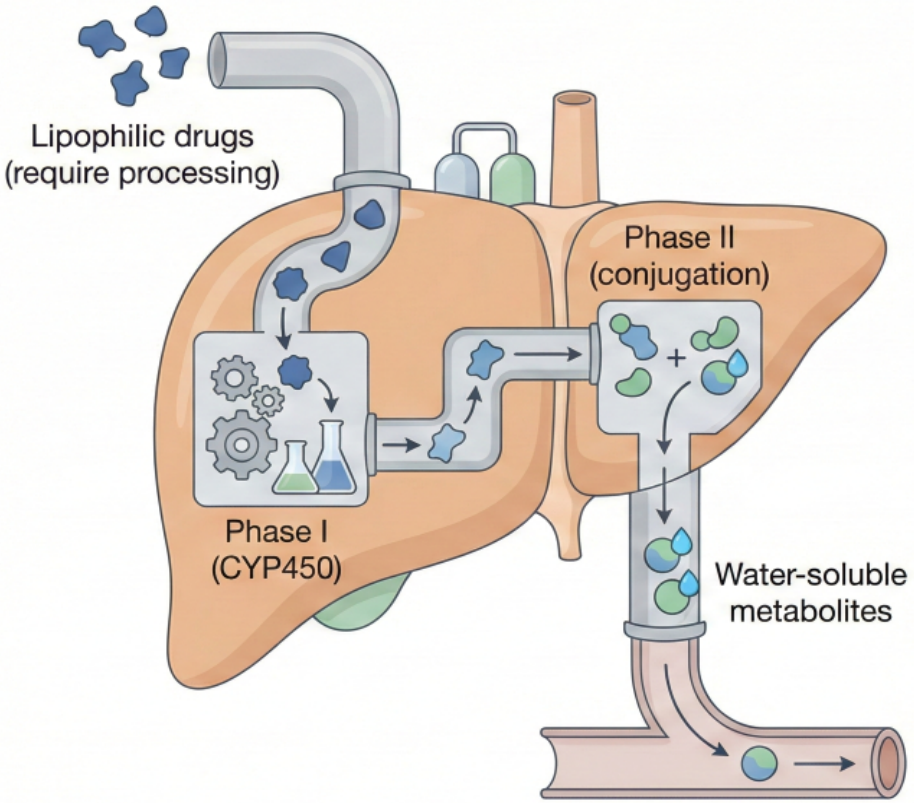
Medical Community

- Alcohol cessation shaped by a broader network of support
- Frame recovery as a combination of self-efficacy + external supports/treatment
- AUD severity effects relapse risk
- Drinking to feel normal is a marker of severe addiction
- Risky drinking/harmful drinking is defined on the amount of alcohol one drinks

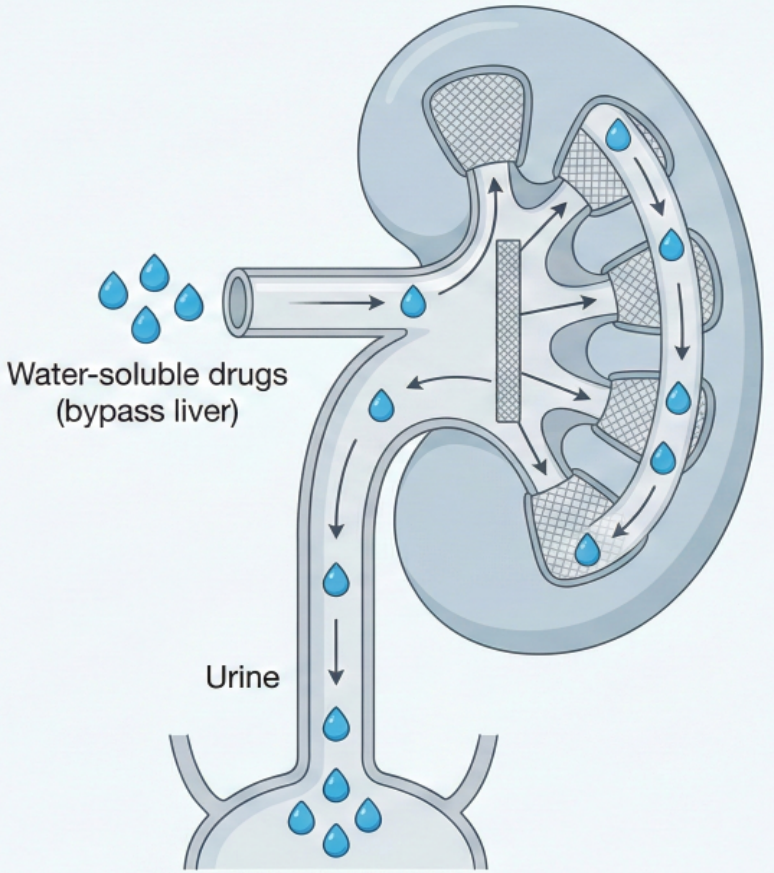
References: Mellinger 6

How AUD Medications Exit the Body

Liver: Chemical Factory (hepatic metabolism)



Kidney: Renal Bypass (renal excretion)



References: Kalra 10, Garza 11, Crabb 12

Renally Cleared	Hepatic Route	Hepatic Route
Acamprosate • First-line evidence • Renal route • Safe in cirrhosis	**Naltrexone (Oral)** • First-line evidence • Reduces heavy drinking • OK in compensated ALD	**Disulfiram** • Hepatic risk • Do NOT Use in ALD
Baclofen • Off-label • Anxiety benefit • Watch sedation • Renal dosing	**Naltrexone (Injectable)** • Extended-release • Evidence weaker than for oral • May help adherence	
Gabapentin • Off-label • Helpful for sleep • Renal dosing		
Topiramate • Off-label • Weight/migraine • Renal dosing • Titrate slow		

References: Haber 13, McPheeters 14

Acamprosate

Mechanism	Modulates glutamatergic (NMDA) signaling and helps rebalance glutamate–GABA tone; exact mechanism not fully defined
Dosing	666mg TID (reduce to 333mg TID if CrCl 30-50 mL/min)
Metabolism	Renally excreted; no hepatic metabolism (safe in ALD)
Safety	Check baseline creatinine Contraindicated if CrCl <30 mL/min Most common AE is diarrhea
Evidence	Strong RCT base NNT ≈ 11 to prevent return to any drinking
Best for	ALD Concomitant/anticipated opioid therapy (does not block opioids) Abstinence goal May be particularly useful in relief drinkers (withdrawal-driven)
Avoid	CKD stage 4–5 Patients unlikely to adhere to TID dosing

References: Haber 13, McPheeters 14, Díaz 15, Micromedex 16

Disulfiram

Mechanism	Inhibits aldehyde dehydrogenase → acetaldehyde buildup → aversive physiologic reaction if alcohol is consumed
Dosing	250–500 mg once daily; start only after ≥12 hours abstinent
Metabolism	Hepatically metabolized (risk of idiosyncratic hepatotoxicity) Can cause acute liver injury, including rare severe or fatal cases
Safety	Check baseline liver function (repeat in 10-14 days) Requires strict abstinence prior to initiation
Evidence	RCT evidence is weak — most trials show no significant benefit vs placebo. Smaller supervised-ingestion studies are not generalizable.
Best for	Consider only in highly selected, supervised, motivated abstinence-oriented patients without liver disease
Avoid	**All ALD / cirrhosis,** acute hepatitis, psychosis, severe heart disease Metronidazole (concurrent or recent); and any alcohol/alcohol-containing products (including OTC syrups, sauces, aftershaves). AST/ALT >3× ULN, TBili >3 mg/dL

References: Haber 13, McPheeters 14, Díaz 15, Micromedex 17

Naltrexone (Oral)

Mechanism	μ-opioid receptor antagonist → reduces alcohol reward, craving, and heavy-drinking reinforcement
Dosing	50 mg PO daily; can load 25 mg ×1–2 days if nausea risk
Metabolism	Hepatic metabolism (active metabolite: 6-β-naltrexol); safe to use in compensated ALD
Safety	Baseline LFTs; repeat if symptoms or dose escalation; GI: nausea (RR 1.73), vomiting (RR 1.53) vs placebo; risk of precipitated withdrawal with opioid use
Evidence	Strong RCT evidence → first-line; Reduces return to any drinking (RR 0.93) and heavy drinking (RR 0.81, NNT ≈ 11); no superiority vs acamprosate in head-to-head trials
Best for	Goal is reduction in alcohol use, strong benefit in reward-driven drinkers
Avoid	Acute hepatitis, liver failure; Do NOT use in current opioid use or those who require opioids

References: Haber 13, McPheeters 14, Díaz 15, Micromedex 18

Naltrexone (Injectable)

Mechanism	μ-opioid receptor antagonist → reduces alcohol reward
Dosing	380 mg IM (gluteal) every 4 weeks (Requires opioid-free period ≥7–10 days)
Metabolism	Hepatic metabolism
Safety	Baseline LFTs; injection-site reactions, GI side effects similar but milder than oral, no opioid use
Evidence	Weaker evidence than oral. No significant benefit for return to heavy drinking, modest reduction in % drinking days. Best evidence is for adherence, not superiority.
Best for	Patients who prefer a monthly injection option; goal reduction in use
Avoid	Acute hepatitis, liver failure; Do NOT use in current opioid use or those who require opioids

References: Haber 13, McPheeters 14, Díaz 15, Micromedex 19

Deep Dive: Naltrexone in ALD

- 52-year-old with alcohol-associated cirrhosis
  - MELD-Na 11, Child-Pugh A
  - Admitted for volume-management; now medically stable
- Goal: reduce drinking (not abstinence)
- Tension: Wants naltrexone, but concern about “hepatotoxicity”

Would you prescribe oral naltrexone 50 mg daily at discharge?

References: McPheeters 14, Díaz 15

Hepatic Safety of Naltrexone in ALD

Study Overview

- 160 adults with AUD (100 LD; 47 cirrhosis; 22 decompensated)
- Compared AST/ALT/Tbili before vs during vs after naltrexone
- Follow-up: Median 10 months

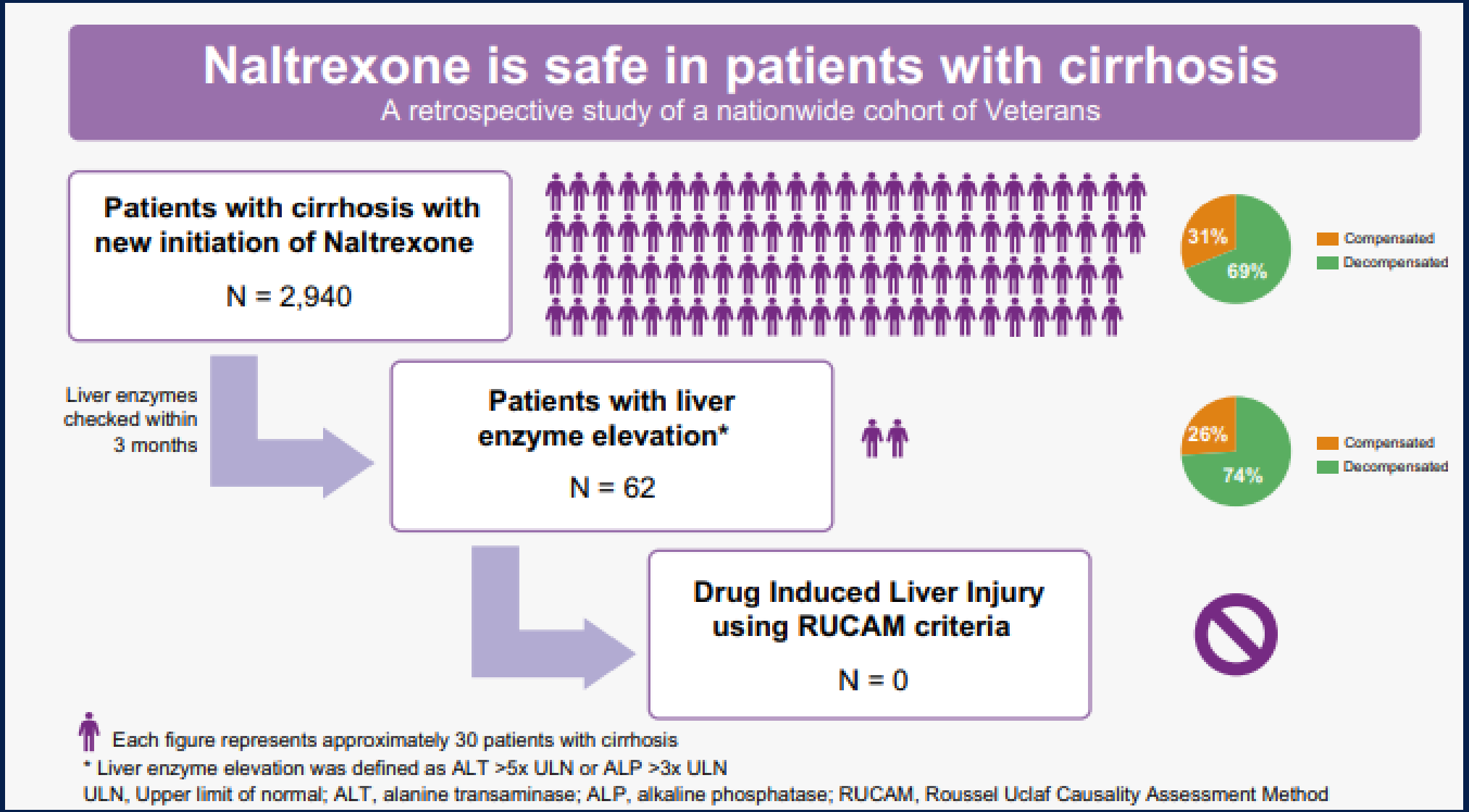
Outcomes & Clinical Takeaways

- AST/ALT improved in LD and cirrhosis groups
- Only 3 liver enzyme elevation cases; none consistent with naltrexone-induced liver injury
- High survival: 95% LD; 90.8% cirrhosis; 81.3% decomp.
- No naltrexone-related deaths

References: Ayyala 20

Thompson et al. 2024

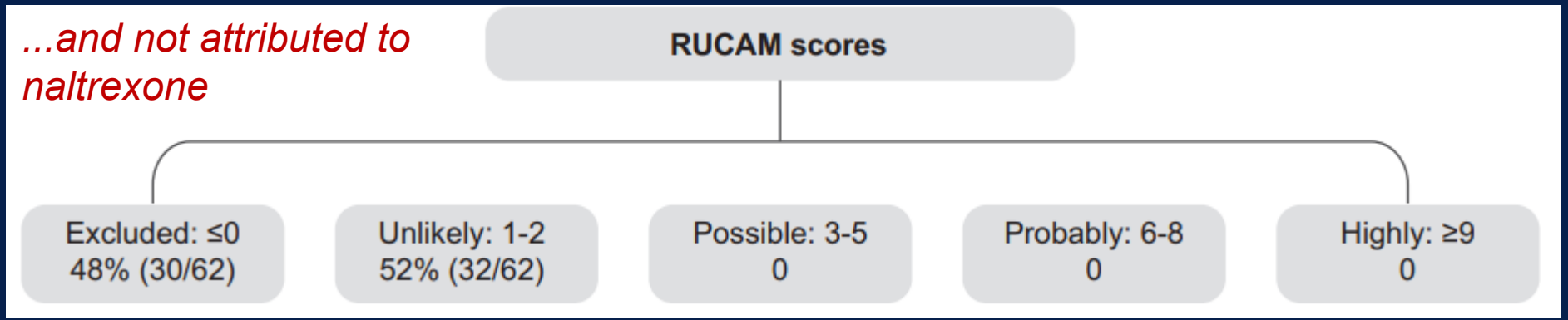
- EMR study with chart review deep dive
- Even a single dose of naltrexone was considered exposure



References: Thompson 21

What were enzyme elevations attributed to? (From chart reviews)

- Most had alternative explanations (77%)
  - Acute alcohol use: 60%
  - Infection: 18%
  - Other medical causes (biliary, pancreatic, shock, AH): ~15%
- High-risk DILI drugs were rare (5%)*No specific cause for liver enzyme elevation could be identified via chart review in 14 (23%) patients*



References: Ayyala 20

But what if...

- This is a very "devil's advocate" interpretation
- *Let's say no specific cause, (23%), was due to naltrexone*
  - *Again, not the actual case!*
- The risk benefit ratio would STILL favor using naltrexone as acute EtOH intoxication was attributed to (60%)

- **Naltrexone *still* mitigates a leading cause of enzyme elevation in Veterans with cirrhosis!**

AAAP, SAMHSA, NIDA Guidelines

- It is not necessary to obtain baseline liver function tests before starting naltrexone – *this can delay effective treatment*
- There is NO empirical evidence to support routine monitoring of LFTs for naltrexone treatment
- Inform patients to contact a healthcare contact a healthcare professional if they develop abdominal pain, nausea, vomiting, fever, dark urine, clay-colored stools, jaundice, or icterus
- Stop naltrexone if LFTs > 10 x ULN **and** any of above are symptoms present and/or requiring emergency or inpatient medical care
  - Restart if no evidence naltrexone was the cause, clinical symptoms resolved, LFTs < 10x ULN

References: Springer 22

Naltrexone Misconceptions

- *You'll get sick if you drink on naltrexone"* → That's disulfiram, not naltrexone
- *"It replaces one addiction"* → Naltrexone is not addictive
- *"It worsens alcohol withdrawal"* → No evidence it worsens withdrawal
- *"It makes people drink more or overdose"* → Actually reduces drinking; increases aversive effects

References: Swift 23

Topiramate

Mechanism	Enhances GABA activity and inhibits AMPA/kainate glutamate receptors; Also inhibits voltage-gated sodium channels → reduces reward, decreases heavy drinking, lowers binge intensity
Dosing	Start: 25 mg nightly. Titrate slowly (weekly) by 25–50 mg. Target: 200–300 mg/day, divided BID.
Metabolism	Primarily renally excreted; limited hepatic metabolism (mostly glucuronidation). Reduce dose 50% in moderate–severe renal impairment
Safety	Paresthesias, taste changes, weight loss; Cognitive slowing (“brain fog”), word-finding difficulty; Sedation, dizziness
Evidence	Moderate strength of evidence (JAMA 2023) ↓ heavy drinking days, % drinking days, drinks per drinking day. Improved abstinence in some RCTs.
Best for	Binge-pattern drinking; patients with weight concerns (appetite/weight effects can be helpful); migraine history; ALD patients needing a renally-cleared option
Avoid	History or risk of hepatic encephalopathy; significant cognitive impairment; severe CKD without dose reduction; concurrent CNS depressants (sedation risk)

References: Haber, 13, McPheeters 14, Díaz 15, Micromedex 24

Topiramate: Not FDA approved but...

First-line recommended:

NALTREXONE*
(oral or extended release injection)

TOPIRAMATE

Sidebar 3: Pharmacotherapy

Alcohol Use Disorder

Recommended: naltrexone, topiramate

Suggested: acamprosate, disulfiram

Suggested as second line: gabapentin

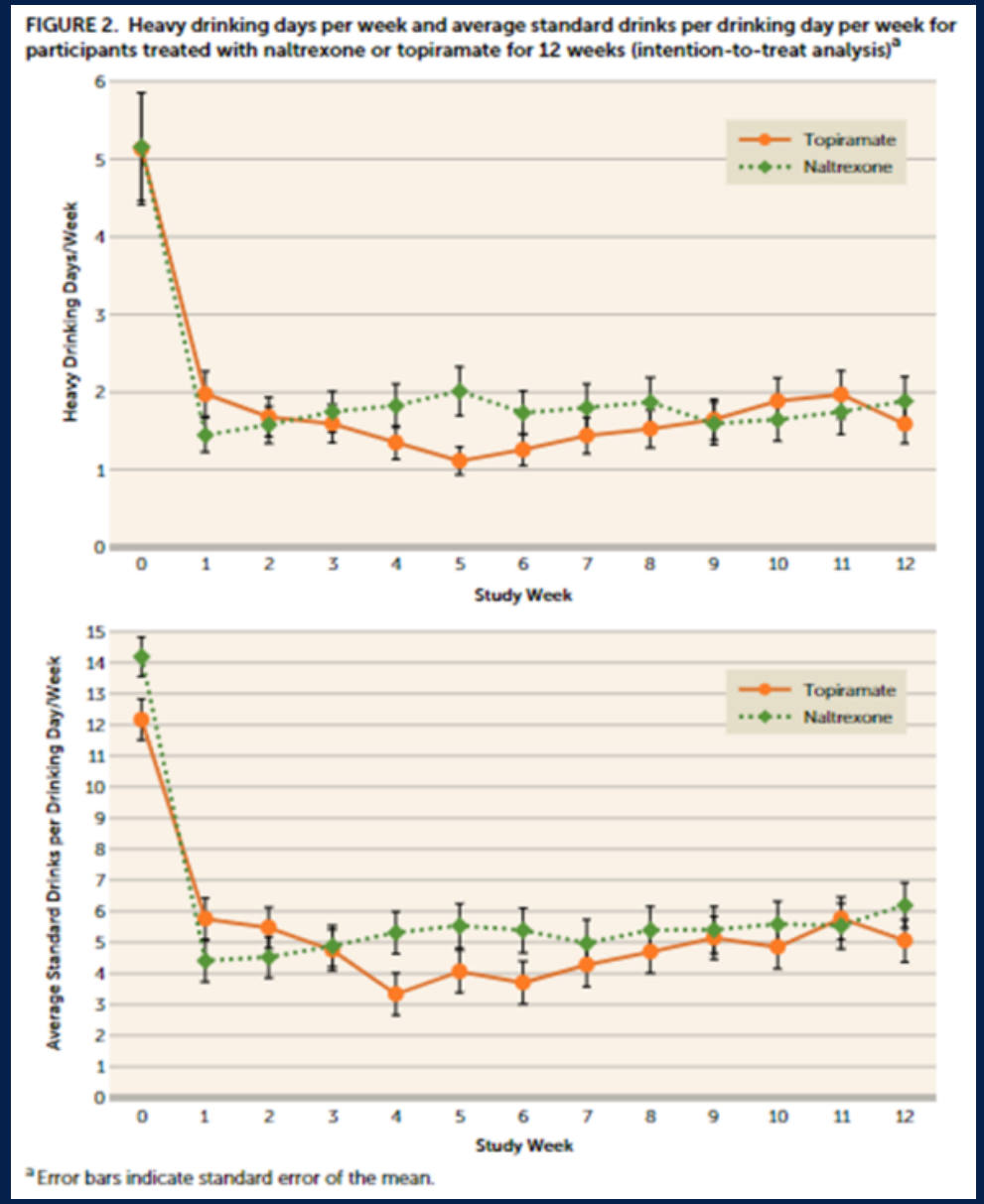
- *"The benefits of topiramate for alcohol consumption outcome outweigh the potential adverse harms … given the overwhelming body of positive evidence for efficacy … the Work Group decided upon a Strong for recommendation." - VA/DoD guidelines*
- Improves abstinence **&** heavy drinking outcomes
  - And does not require pre-treatment abstinence
  - Improves abstinence **&** heavy drinking outcomes
- An AAFP recommended medication as well but not as strong an endorsement in part due to "its adverse-effect profile, which includes paresthesias and cognitive impairment"

References: Perry 25, Poorman 26

Topiramate vs Naltrexone, a 2024 DBRCT

- No difference on heavy drinking days/week or average standard drinks per drinking day/week
- Similar retention, no significant difference in study drop out due to adverse events
- Integrity of the blind: physicians were only able to tell naltrexone vs. Topiramate in 63% of cases, participants only in 45% of cases

- Similar side effect burden, different profile



References: Morley 27

Gabapentin

Mechanism	Binds the α2δ subunit of voltage-gated calcium channels → decreases excitatory neurotransmitter release (e.g., glutamate, norepinephrine). Reduces withdrawal-related insomnia, anxiety, hyperexcitability.
Dosing	900–1800 mg/day, divided doses (commonly 300 mg TID → titrate). Evidence for heavy drinking reduction is strongest at 1800 mg (600 mg TID).
Metabolism	Renally excreted; not hepatically metabolized. Safe in ALD, including cirrhosis (dose-adjust for CKD).
Safety	Sedation, dizziness, ataxia; can worsen encephalopathy; adjust for CKD (risk of accumulation)
Evidence	Reduces heavy drinking days and drinks per drinking day in several RCTs and meta-analyses. Strongest effects seen in those with withdrawal symptoms before treatment initiation.
Best for	Insomnia, anxiety, withdrawal-driven drinking; ALD patients who need a renally cleared option; Patients unable to tolerate/receive acamprosate or naltrexone
Avoid	Severe CKD without dose adjustment; High fall risk, frailty, or baseline cognitive impairment; Caution with concurrent sedatives / benzos

References: Haber 13, McPheeters 14, Díaz 15, Micromedex 28

Baclofen

Mechanism	GABA-B receptor agonist → reduces craving, anxiety-driven drinking; dampens withdrawal-related hyperexcitability
Dosing	10–30 mg PO TID (common clinical range). Some RCTs explore higher doses (60–90 mg/day) — mixed tolerability.
Metabolism	Renally excreted, minimal hepatic metabolism. Safe in cirrhosis, including compensated + decompensated ALD (only AUD med aside from acamprosate formally tested in cirrhosis trials)
Safety	Sedation, dizziness, hypotonia; Caution in hepatic encephalopathy (may worsen mental status); Adjust dose in CKD (accumulation risk)
Evidence	Reduces return to any drinking (RR 0.83) but evidence strength = low; Only drug with RCTs in cirrhosis; Benefits particularly noted in patients with anxiety symptoms
Best for	Patients with cirrhosis (safe across ALD spectrum); Anxiety-driven drinking; Patients who cannot use naltrexone (opioids) or acamprosate (CKD)
Avoid	Hepatic encephalopathy or high risk of mental-status fluctuation; Severe CKD without dose adjustment; Combination with other significant CNS depressants

References: Haber 13, McPheeters 14, Díaz 15, Micromedex 29

Small-Group Vignettes

- Vignette A – Compensated Cirrhosis (Child-Pugh A)
- Vignette B – Decompensated Cirrhosis (Child-Pugh B)
- Vignette C – Decompensated with CKD (GFR between 33-50)
- Vignette D – Decompensated with CKD (GFR < 33)

Vignette A – Compensated Cirrhosis (Child-Pugh A)

- 54-year-old with longstanding alcohol use (4–6 beers daily × 25 years)
- Imaging: nodular liver; small non-bleeding varices
- Labs: AST>ALT, no decompensation symptoms
- Diagnosis: Compensated alcohol-associated cirrhosis (Child-Pugh A)
- Patient does not identify as having AUD

How would you approach treatment?

Compensated Cirrhosis

- Linkage of liver disease to alcohol use
- Emphasizing the single most effective treatment for preventing his liver from further decompensating is alcohol cessation
- Assess openness to alcohol cessation
- Offering behavioral interventions + medication

Renally Cleared

Acamprosate
- First-line evidence
- Safe in cirrhosis
- Caution with GI side effects
- Consider 999 mg BID vs 666 mg TID for enhanced compliance

Baclofen
- Off-label; Anxiety benefit
- Increased risk of hepatic encephalopathy hospitalizations
- 10 mg TID

Gabapentin
- Off-label; Helpful for sleep
- Caution with hepatic encephalopathy
- Cumulative dose of 1800 mg daily

Topiramate
- Off-label
- Small concern for drug induced liver injury so watch labs closely
- Titrate slow to max dose of 75 mg daily

Hepatic Route Selections

Naltrexone (Oral)
- First-line evidence
- Reduces heavy drinking
- Avoid in patients with OUD/narcotic use
- Start at dose of 25 mg daily and titrate up to 50 mg daily

Naltrexone (Injectable)
- Extended-release; May help adherence
- Evidence weaker than for oral
- Avoid in patients with OUD/narcotic use
- 380 mg subq injection every 28 days

Disulfiram
- Associated with acute liver failure
- **Do NOT use in ALD**

Vignette B – Decompensated Cirrhosis (Child-Pugh B)

- 57-year-old with severe AUD (8–10 drinks/day × 30 years)
- Recent hospitalization for hepatic encephalopathy
- Decompensated alcohol-associated cirrhosis
- Ascites + HE, both currently controlled
- On lactulose/rifaximin; resumed weekend drinking
- Labs consistent with Child-Pugh B

Which AUD medication(s) would you start—or avoid?

Decompensated Cirrhosis

- Linkage of liver disease to alcohol use and now potential need of liver transplant to improve his quality and quantity of life
- Emphasizing the single most effective treatment for preventing his liver from further decompensating is alcohol cessation
- Assess openness to alcohol cessation now and how this may play into his post transplant care if he were to receive a transplant
- Offering behavioral interventions + medication therapy

Renally Cleared

Acamprosate

- First-line evidence
- Safe in cirrhosis
- Caution with GI side effects
- Consider 999mg BID vs 666mg TID to ↑ compliance

Baclofen

- Off-label; Anxiety benefit
- increased risk of HE hospitalizations
- Start at 10mg nightly; ↑ to 10mg TID

Gabapentin

- Off-label; Helpful for sleep
- Caution with HE, start with 100mg nightly and slowly increase
- Cumulative dose 1800mg daily

Topiramate

- Off-label
- Small concern for drug induced liver injury
- Watch labs closely
- Titrate slow to max dose of 75mg

Hepatic Route Selections

Naltrexone (Oral)

- First-line evidence
- Reduces heavy drinking
- Avoid in patients with OUD/narcotic use
- Start at 25mg daily x2 weeks;↑ to 50mg daily

Naltrexone (Injectable)

- Extended-release; May help adherence
- Evidence weaker than for oral
- Avoid in patients with OUD/narcotic use
- 380mg subq injection every 28 days

Disulfiram

- Associated with acute liver failure
- **Do NOT use in ALD**

Vignette C – Decompensated with CKD (GFR between 33-50)

- Same patient but now he has CKD. His creatinine is 1.86 with a GFR between 33-50

Renally Cleared

Acamprosate
- First-line evidence
- 333 mg TID with close monitoring of renal function

Baclofen
- Off-label; Anxiety benefit
- increased risk of hepatic encephalopathy
- 5 mg BID adjusted for renal clearance

Gabapentin
- Increased risk of hepatic encephalopathy
- Start at a low dose of 100 mg nightly
- No more than max dose of 1400 mg daily

Topiramate
- Off-label
- Small concern for drug induced liver injury watch labs closely
- 25 mg daily and increase to 50 mg if tolerated

Hepatic Route Selections

Naltrexone (Oral)
- First-line evidence
- Reduces heavy drinking
- Avoid in patients with OUD/narcotic use
- Start 25 mg daily x2 weeks and ↑ to 50 mg daily

Naltrexone (Injectable)
- Extended-release; May help adherence
- Evidence weaker than for oral
- Avoid in patients with OUD/narcotic use
- If not pending transplant, 380mg subq injection every 28 days

Disulfiram
- Associated with acute liver failure
- **Do NOT use in ALD**

Vignette D – Decompensated with CKD (GFR < 33)

- Same patient but now he has CKD. His creatinine is 2.34 with a GFR<33

Renally Cleared

Acamprosate
- Contraindicated with GFR<33

Baclofen
- Avoid use in GFR<33

Gabapentin
- Increased risk of hepatic encephalopathy
- Start at a low dose of 100 mg nightly
- No more than max dose of 300 mg daily

Topiramate
- Off-label
- Small concern for drug induced liver injury watch labs closely
- 25 mg daily and increase to 50 mg if

Hepatic Route Selections

Naltrexone (Oral)
- First-line evidence
- Reduces heavy drinking
- Avoid in patients with OUD/narcotic use
- Start 25 mg daily x2 weeks and increase to 50 mg daily

Naltrexone (Injectable)
- Extended-release; May help adherence
- Evidence weaker than for oral
- Avoid in patients with OUD/narcotic use
- If not pending transplant, 380 mg subq injection every 28 days

Disulfiram
- Associated with acute liver failure
- **Do NOT use in ALD**

MAUDs With Complementary Benefits

- You will vote on 6 short clinical scenarios
- Assume all patients have ALD
- Choose the AUD medication that also helps a co-occurring symptom *(sleep, anxiety, migraines, pruritus, etc.)*

https://ahaslides.com/R24XK

References: Díaz 15, VA/DoD 30, Lindor 31, DailyMed 32, Phimarn 33, Rogal 7

Admitted for AWS + ALD

- 50-year-old with moderate–severe alcohol withdrawal
- Longstanding heavy alcohol use; abrupt cessation yesterday
- Signs of ALD (ascites, thrombocytopenia, ↑bilirubin)
- CIWA 17, tachycardic

Admitted for AWS + ALD

Q: Which of the following is the most appropriate pharmacotherapy for managing her alcohol withdrawal?

A. Scheduled Diazepam
B. Symptom Triggered Lorazepam
C. Loading and then tapering of Gabapentin
D. Loading and then tapering of Phenobarbital

Admitted for AWS + ALD

- Benzodiazepines remain first-line
- Lorazepam or oxazepam preferred in liver disease (short-acting, no active metabolites)
- Longer-acting agents (e.g., diazepam) acceptable without liver disease
- Benzodiazepines can worsen hepatic encephalopathy
- Treat AWS and HE simultaneously
- Alternatives (e.g., gabapentin): limited evidence

References: Jophlin 9, Bahji 34

Admitted for AWS + ALD

Q: Used as adjuncts to benzodiazepines in the treatment of alcohol withdrawal, which of the following medications would not be appropriate for a patient with liver disease?

A. Carbamazepine
B. Clonidine
C. Gabapentin
D. Valproic Acid

Admitted for AWS + ALD

- Gabapentin, Carbamazepine, and Valproic Acid have evidence supporting their use as adjuncts to benzodiazepines in the treatment of alcohol withdrawal.
- Clonidine has limited evidence but is commonly used to manage autonomic hyperactivity and anxiety in alcohol withdrawal.
- Valproic acid should not be used in patients with liver disease.

References: ASAM 35

"I Googled It" Vignette

- “So… I asked ChatGPT about these AUD meds, and it said naltrexone can cause liver failure. I'm already worried about my liver.”

- He crosses his arms and says he’s “not sure about changing anything right now.”

Shared Decision Making

- Affirmations
  - Statements and gestures that recognize client strengths and acknowledge behaviors that lead in the direction of positive change, no matter how large or small.
- Ellicit-Provide-Ellicit
  - Always ask permission to give information
- Risk-benefit analysis
  - "No level of alcohol consumption is safe for our health"

References: Miller 36, WHO 37

Extra - Emerging Therapies

- GLP-1 Receptor Agonists
- Neuromodulation (TMS/tDCS)
- Psychedelics (Psilocybin)
- Ketamine

References: Farokhnia 38, Rehm 39, Bogenschutz 40, Durazzo 41

Psychosocial Interventions

- For Alcohol Use Disorder, behavioral therapies can be as effective as medication.
- AUD & ALD support groups: Alcoholics Anonymous (AA) / Twelve-Step Facilitation (TSF), SMART Recovery, LifeRing Secular Recovery (including “Liver Spot” meetings), Women for Sobriety, American Liver Foundation (ALF), Transplant Center Support Groups

References: VA/DoD 30

Summary of Effectiveness of Psychosocial Interventions

Interventions	First-line Alternatives at Least as Effective as Other Bona Fide Active Interventions or TAU				Added Effectiveness as Adjunctive Interventions in Combination with Pharmacotherapy and/or Other First-line Psychosocial Interventions			
	Alcohol	Opioids	Stimulants/ Mixed	Cannabis	Alcohol	Opioids	Stimulants/ Mixed	Cannabis
Behavioral Couples Therapy	√	N/A	N/A	N/A	?	N/A	N/A	N/A
Cognitive Behavioral Therapy	√	N/A	√	√	√	√/?	N/A	√
Contingency Management/ Motivational Incentives	N/A	N/A	N/A	N/A	?	√	√	√
Community Reinforcement Approach	√	N/A	√	N/A	N/A	N/A	N/A	N/A
Individual Drug Counseling	N/A	N/A	N/A	N/A	N/A	N/A	√	N/A
Motivational Enhancement Therapy	√	N/A	N/A	√	√	N/A	?	?
12-Step Facilitation	√	N/A	?	N/A	√	N/A	N/A	N/A

Symbols: √: Good confidence in effectiveness; ?: Questionable confidence in effectiveness; N/A: Insufficient evidence

AUD & ALD Support Groups

Alcoholics Anonymous (AA)/Twelve-Step Facilitation (TSF) (manualized) compared to other clinical interventions for alcohol use disorder (RCT/quasi-RCT evidence)

Patient or population: adults (> 18 years) with alcohol use disorder, alcohol abuse, or alcohol dependence
Setting: outpatient treatment
Intervention: AA/TSF (manualized)
Comparison: other clinical interventions (e.g. CBT)

Outcomes		Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
		Risk with other clinical interventions	Risk with AA/TSF				
Abstinence	Proportion of participants (%) completely abstinent Follow-up: 12 months	Study population 345 per 1000	418 per 1000 (356 to 490)	RR 1.21 (1.03 to 1.42)	1936 (2 RCTs)	⊕⊕⊕⊕ High	
	PDA Follow-up: 12 months	The mean PDA in the comparison group ranged from 62.3% to 84.0%	MD 3.03 higher (4.36 lower to 10.43 higher)	-	1999 (4 RCTs)	⊕⊝⊝⊝ Very low [a, b, c]	
	LPA Follow-up: 6 months	The mean LPA in the comparison group ranged from 0.47 to 1.71 months	MD 0.60 higher (0.30 lower to 1.50 higher)	-	136 (2 RCTs)	⊕⊕⊝⊝ Low [d, e]	No data available for 12-month follow-up
Drinking Intensity	DDD Follow-up: 12 months	The mean DDD in the comparison group ranged from 4.66 to 5.38	MD 0.17 lower (1.11 lower to 0.77 higher)	-	1516 (1 RCT)	⊕⊕⊕⊝ Moderate [c]	
	PDHD Follow-up: 12 months	The mean PDHD in the comparison group was 13.4%	MD 5.51 lower (14.15 lower to 3.13 higher)	-	91 (1 RCT)	⊕⊕⊝⊝ Low [f]	

References: Kelly 42, Haber 13, LifeRing 43, Krist 4

Final Takeaways – Treating AUD in ALD

- First-line: Acamprosate, oral naltrexone
- Renal: acamprosate, baclofen, gabapentin, topiramate
- Hepatic: naltrexone (oral ± LAI); avoid disulfiram
- Naltrexone: Safe in compensated cirrhosis; consider in decompensated; screen for opioids
- Sleep/withdrawal → gabapentin · Anxiety → baclofen · Binge/weight/migraine → topiramate · Reward ± pruritus → naltrexone
- Transitions matter: Use lorazepam/oxazepam for AWS; start MAUD early; ensure warm handoffs

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