weitzman institute

Translating Research into Practice on Alcohol and Polysubstance Use Disorders
by Educating the Interprofessional Primary Care Team

Welcome to Weitzman Science to Practice: Alcohol Use Disorder!

We will begin the session shortly.

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Translating Research into Practice on Alcohol and Polysubstance Use Disorders
by Educating the Interprofessional Primary Care Team

Welcome to Weitzman Science to Practice: Alcohol Use Disorder!

Session #2:

Translating Peer-Reviewed Research into Clinical Practice:
Medication Treatment for Alcohol Use Disorder

July 8, 2025

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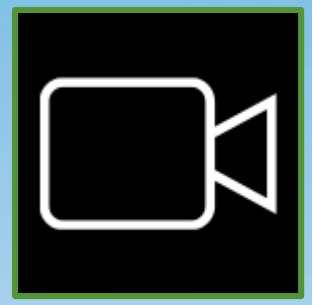

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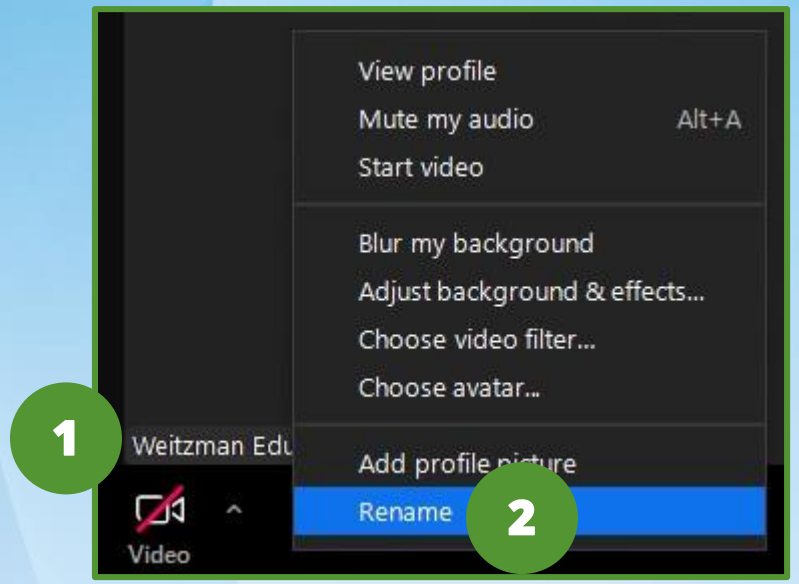

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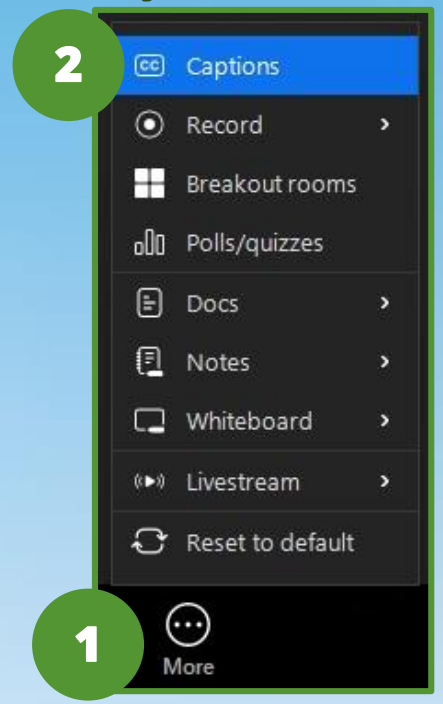

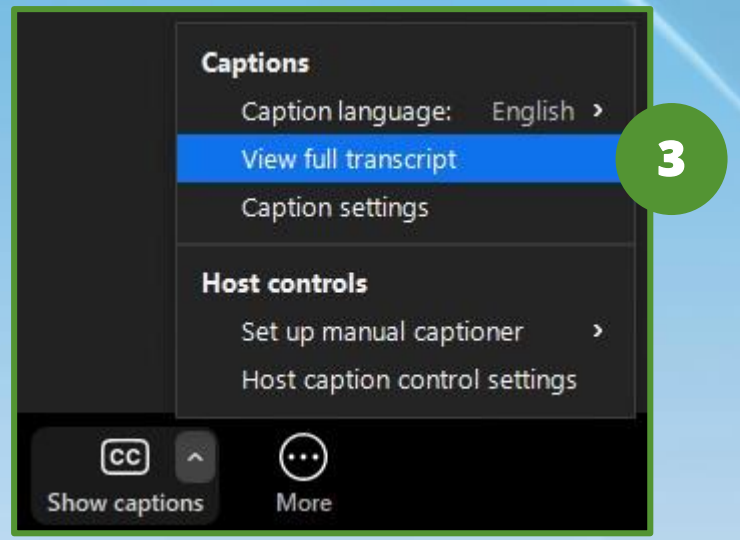

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In support of improving patient care, Moses Weitzman Health System is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

This series is intended for primary care providers (MDs, DOs, NPs, PAs) and behavioral health providers (psychiatrists, psychologists, social workers, therapists).

Please complete the survey and claim your post-session certificate on the WeP after today's session. **Please note: Pharmacists must claim credits within two weeks following today's session or we will not be able to award ACPE credits.**

You will be able to claim a comprehensive certificate on the WeP at the end of the series, July 22, 2025.

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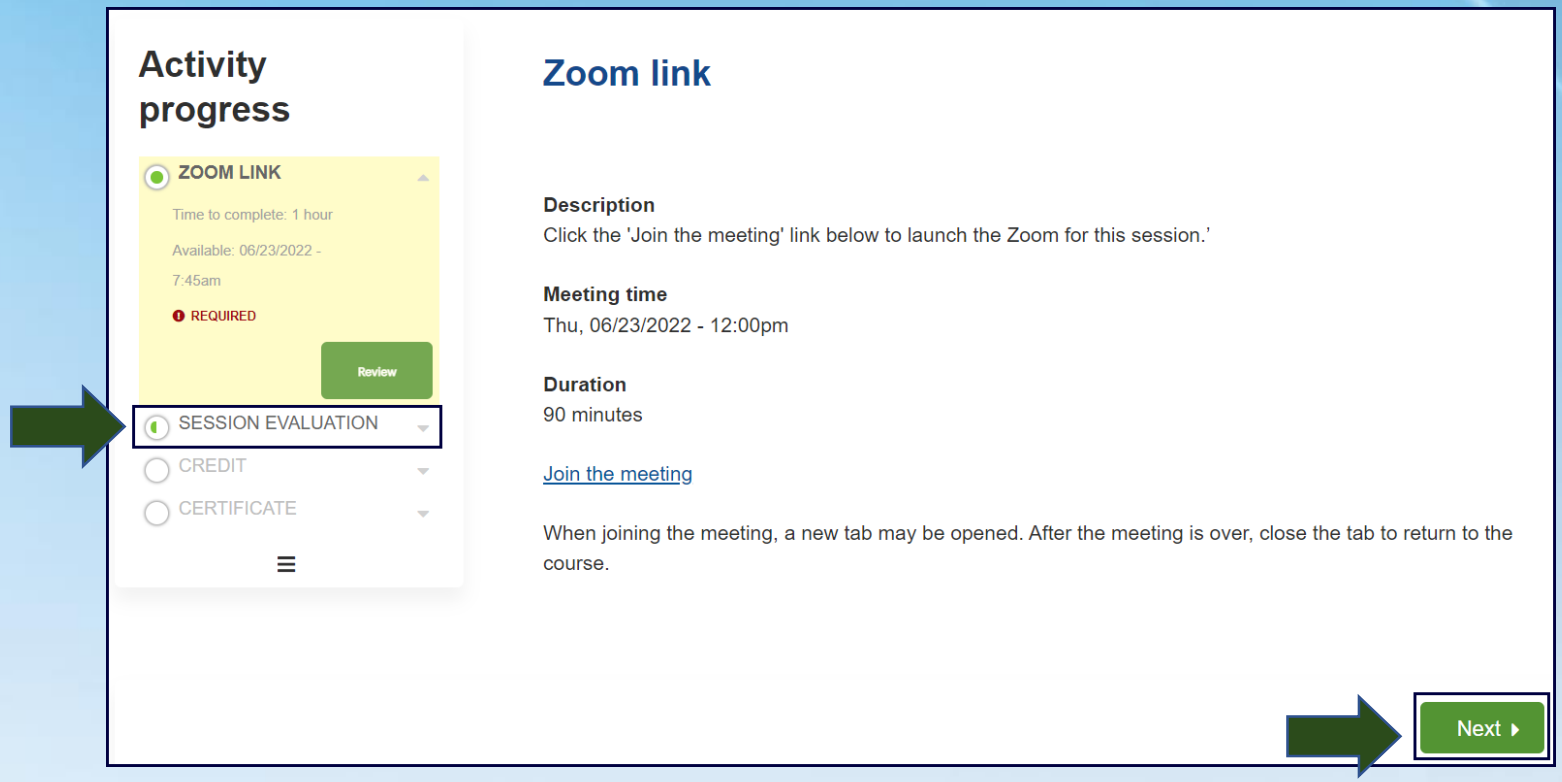

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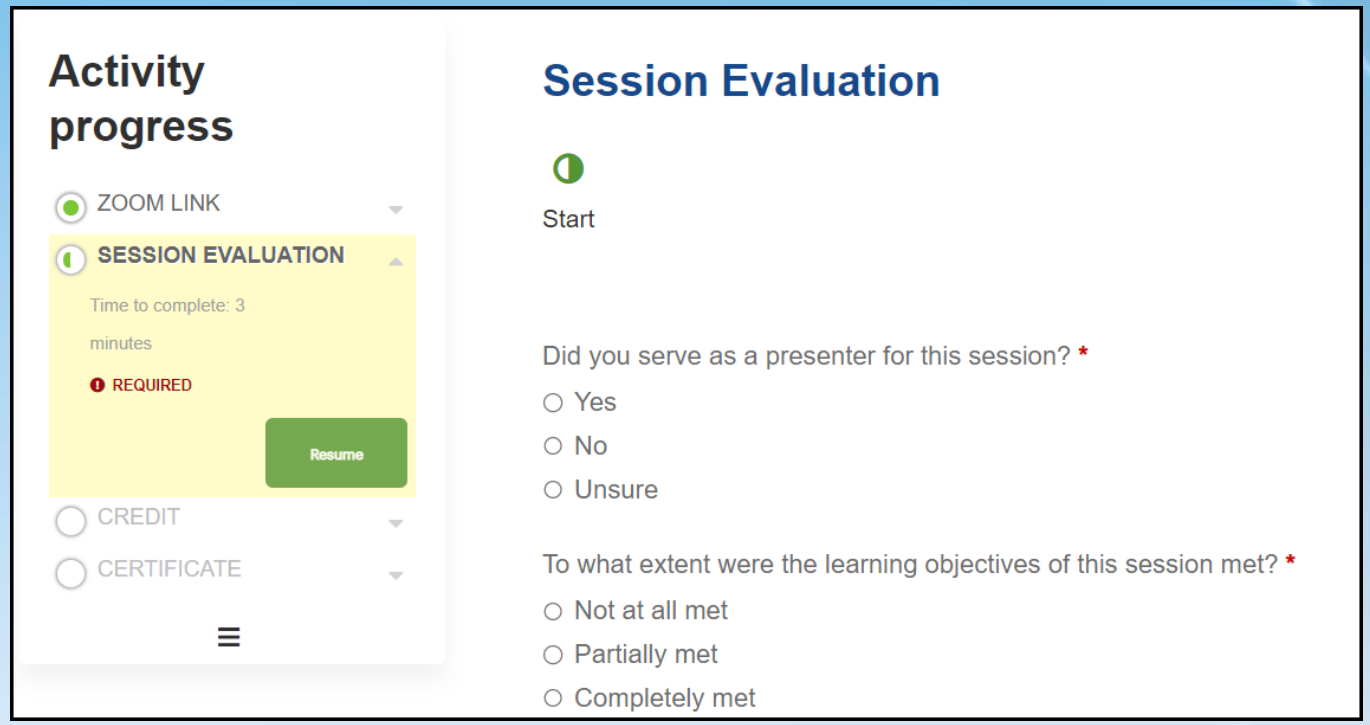

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1. Return to the **Overview tab** of the live activity, *Weitzman Science to Practice: Alcohol Use Disorder: Translating Peer-Reviewed Research into Clinical Practice: Medication Treatment for Alcohol Use Disorder (July 8, 2025)*
2. Scroll down to the **Required Readings, Presentation Slides, and Session Recording** headers

You will then be able to click on **Required Readings, Session Recording, and Presentation Slides** listed below the headers to access the resources.

This Weitzman Science to Practice session has been made available by:

NIH R25 Alcohol and Other Substance Use Research Education Programs for Health Professionals

This project is supported by the National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health under Award Number R25AA031951 to translate research into practice on preventing, screening for, and treating alcohol use disorders in primary care. The content is solely the responsibility of the Weitzman Institute and does not necessarily represent the official views of the National Institutes of Health.

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All Are Welcome

Weitzman Science to Practice Faculty

Aryn Phillips, PhD

Jack Todd Wahrenberger, MPH, MD

Case Presentation: 1

Patient: WG, 62-year-old male
Visit Type: Emergency Department follow-up
Presenting Concern: Follow-up after fall and head injury sustained during a bar fight.

Clinical History:

- WG was seen in the ED last week after a fall during a physical altercation at a bar. Head CT was negative for acute findings. Labs revealed a markedly elevated blood alcohol level and mildly elevated liver function tests (LFTs).
- On exam today, he has healing abrasions on both hands and residual periorbital ecchymosis and swelling on the left side. No stigmata of Liver disease (amazing I know right?).
- You have known WG for over 10 years and have managed his chronic conditions including hypertension, type 2 diabetes, and general preventive care.
- This is not his first alcohol-related injury. When asked about his drinking, he jokes, “Well, I’m Irish, doc—what are you gonna do? I just can’t stop.”

Substance Use History:

- Drinks **12–15 beers on weekend evenings**, with lighter during the week
- Has **never completed a detox or rehab**
- Previously lost housing after being fired from his job due to alcohol-related issues; currently housed and employed (roofer/drywall installer)
- **Acamprosate** was prescribed in the past, but adherence was poor and short-lived
- Previously open to **harm reduction goals** (e.g., drinking fewer days per week, limiting quantity, avoiding driving), but **has not achieved sustained change.**

Case Presentation: 2

Patient: TJ, 35-year-old female
Visit Type: post-hospital discharge
Chief Concern: Follow-up after hospitalization for acute alcohol hepatitis

History of Present Illness:

- TJ is a 35-year-old woman presenting for follow-up after her **third alcohol-related hospitalization** in the past year. Her most recent admission was for **acute alcohol hepatitis**, during which the **gastroenterology team warned of potential irreversible liver damage** if drinking continues.

Previous complications have included:

- One medically supervised alcohol detox (treated with chlordiazepoxide)
- One hospitalization for an upper gastrointestinal bleed related to alcohol use

She reports **daily alcohol consumption**, with:

- **Evening drinking at home**, often alone during the workweek
- **Heavy binge drinking on weekends**, when she doesn't need to work

TJ is currently employed as an **executive secretary**, takes pride in her work, and is **highly motivated to maintain employment**. She explicitly states that she is **not interested in residential rehab** at this time.

She is accompanied by her **partner**, who has **5 years of sustained sobriety** (also my patient but never made the connection before) and is described as very supportive and eager to help her succeed.

Utilization of Medications for Alcohol Use Disorder - MAUD

- Less than 20% of adults with alcohol use disorder (AUD) are actively receiving any form of treatment, including both psychosocial interventions and pharmacotherapy.
- Only about 1.6% of adults with AUD in the United States are prescribed medications for AUD, and large cohort data show that 11.4% receive any medication (including those prescribed at any point in their lifetime).

Parallels Between MAUD and Antihypertensive Therapy

- **The Long Game**: Both conditions represent chronic disorders requiring long-term management rather than acute interventions.
- **Take the Steps**: Both benefit from a stepped-care approach where treatment intensity increases if initial interventions fail.
- **Follow Regularly**: Both require regular monitoring of objective markers (blood pressure vs. drinking patterns) to assess treatment efficacy.
- **We got options**: Both have multiple FDA-approved medication options that target different physiological pathways.
- **Combo**: Both conditions often require combination therapy for optimal outcomes in more severe or treatment-resistant cases.
- **It's not just the meds**: Both benefit from concurrent lifestyle modifications alongside pharmacotherapy.

Parallels -Continued

- High quality blood pressure readings across multiple visits vs. structured Assessments using validated tools (AUDIT and DSM-5)
- Severity Classifications (stage I or II in hypertension vs Mild, Moderate or Severe in AUD)
- Medication Selection with First line Agents moving to combo.
- Routine monitoring and follow up
- Treatment Goals: Similar to how we accept improved but not necessarily "perfect" BP control, AUD treatment success includes reduced drinking and harm reduction, not just complete abstinence.
- Provider education and comfort with prescribing are barriers for both conditions.
- Patient acceptance and stigma affect MAUD more significantly than antihypertensives.

Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis

Melissa McPheeters, Elizabeth A O'Connor, Sean Riley, Sara M Kennedy, Christiane Voisin, Kaitlin Kuznacic, Cory P Coffey, Mark D Edlund, Georgiy Bobashev, Daniel E Jonas

JAMA, 2023

Objective

- To evaluate and compare the efficacy of 9 medications for alcohol use disorder (AUD).
  - Approved by U.S. Food and Drug Administration (FDA) for AUD: acamprosate, disulfiram, naltrexone.
  - Used off-label for AUD: baclofen, gabapentin, varenicline, topiramate, prazosin, ondansetron.

What is a meta-analysis?

- Analysis of findings from a collection of individual studies (Glass, 1976).
- Early meta-analyses were mostly descriptive, but statistical methods of analysis are now used.
- In this study, the authors use the DerSimonian and Laird method, one of the most popular methods in medical research.

Sources: Glass, 1976; DerSimonian & Laird, 1986; DerSimonian & Laird, 2016

What is a meta-analysis?

- DerSimonian and Laird method
  - Uses a random effects model, which assumes that the treatment effect varies across studies.
  - The model estimates the average treatment effect from the studies.
  - Studies are given weights according to the variance observed in that study and the heterogeneity between all studies. Studies with greater within-study variance are given smaller weights.
  - DerSimonian and Laird method uses a particular way to estimate the between-study heterogeneity (method of moments approach).

Sources: Higgins, 2011; DerSimonian & Laird, 2016

Methods – Literature Search & Selection

- Eligible articles:
  - Double-blind randomized clinical trials (RCTs) evaluating one of the 9 medications, comparing medication to placebo or another medication.
  - Population = adults with AUD.
  - >12 weeks of treatment, outpatient setting.
  - Outcomes:
    - Alcohol use: return to drinking, return to heavy drinking, percentage of drinking days, percentage of heavy drinking days (4+/5+), number of drinks per drinking day.
    - Health outcomes: motor vehicle crashes, injuries, quality of life, function, mortality.
    - Adverse events.
      - Allowed studies that compared 2 drugs, non-randomized and open-label trials, subgroup analyses from trials, prospective studies, and case-control studies.

Methods – Literature Search & Selection

- Librarian search of online databases (Pubmed, Cochrane Library, Cochrane Central Trials Registry, PsychINFO, CINAHL, EMBASE) for eligible articles published November 2012 – September 2022. Manual search of references from related reviews or trials.
- Second librarian reviewed searches using Peer Review of Electronic Search Strategies (PRESS) checklist.
- Eligible articles published before November 2012 identified in a published systematic review (Jonas et al, 2014).
- Received article alerts following November 2012 and performed additional Pubmed search in August, 2023, but not new articles identified.

Methods – Literature Search & Selection

- Abstract of each article reviewed by 2 reviewers.
- If deemed possibly eligible by either reviewer, both reviewed full text.
- Studies assessed for:
  - Risk of bias (low, medium, high, or unclear) - randomization, comparability of groups, attrition, measure validity and reliability, approaches to missing data, etc.
  - Strength of evidence (insufficient, low, moderate, high) – risk of bias, consistency, directness, precision.

Methods - Analyses

- DerSimonian and Laird estimator
- Calculate weighted mean differences (WMD) for continuous outcomes and risk ratios (RR) for binary outcomes.
- Calculate numbers needed to treat (NNT) when statistically significant effects were identified for binary outcomes.
  - NNT = the number of patients needed to treat to prevent adverse event among one patient (e.g., return to heavy drinking).
    - NNT = 1/absolute risk reduction

Source: University of Oxford, 2025

Results

- 2,860 articles initially identified, 2,543 deemed ineligible during abstract review.
- 317 articles reviewed, 267 deemed ineligible during full text review.
- Final sample: 50 articles (37 RCTs) from search & 106 articles (81 RCTs) from previous review.
  - 111 articles with alcohol use outcomes, 31 with health outcomes, 99 with adverse events.
  - In 103 articles, all participants met criteria for alcohol dependence.
  - 87 articles included psychosocial interventions along with medication.
  - Ondansetron, varenicline, and prazosin all had low strength of evidence and were not included in further analyses.

Results – Return to Any Drinking & Heavy Drinking

	Acamprosate	Baclofen	Disulfiram	Gabapentin	Naltrexone 50 mg/d, oral	Naltrexone 100 mg/d, oral	Naltrexone Injection	Naltrexone Any dose	Topiramate
Return to any drinking									
No. of studies	20	8	3	3	16	3	2	25	1
No. of participants	6380	995	622	522	2347	946	939	4604	106
Results effect size (95% CI)	RR, 0.88 (0.83-0.93)	RR, 0.83 (0.70-0.98)	RR, 1.03 (0.90-1.17)	RR, 0.92 (0.83-1.02)	RR, 0.93 (0.87-0.99)	RR, 0.97 (0.91-1.03)	RR, 0.96 (0.90-1.03)	RR, 0.95 (0.92-0.99)	Topiramate, 53.8%; placebo, 72.2%
Number needed to treat (95% CI)[c]	11 (1-32)				18 (4-32)				
Strength of evidence	Moderate	Low	Low (no effect)	Low	Moderate	Low (no effect)	Low (no effect)	Moderate	Insufficient
Return to heavy drinking									
No. of studies	7	4	0	3	23	2	2	27	1
No. of participants	2496	483	0	522	3170	858	615	4645	170
Results effect size (95% CI)	RR, 0.99 (0.94-1.05)	RR, 0.92 (0.80-1.06)		RR, 0.90 (0.82-0.98)	RR, 0.81 (0.72-0.90)	RR, 0.93 (0.84-1.01)	RR, 1.00 (0.82-1.21)	RR, 0.86 (0.80-0.93)	Topiramate, 10%; placebo, 14%
Number needed to treat (95% CI)[c]					11 (5-41)				
Strength of evidence	Moderate (no effect)	Low (no effect)	Insufficient	Low	Moderate	Low (no effect)	Low (no effect)	Moderate	Insufficient

Source: adapted from McPheeters et al., 2023

Results – Percentage of Drinking Days & Heavy Drinking Days

					Naltrexone				
	Acamprosate	Baclofen	Disulfiram	Gabapentin	50 mg/d, oral	100 mg/d, oral	Injection	Any dose	Topiramate
Percentage of drinking days									
No. of studies	14	5	2	1	15	3	2	24[d]	8
No. of participants	4916	714	290	112	1992	1023	467	4021	1080
Results effect size (95% CI)[b]	WMD, −8.3 (−12.2 to −4.4)	WMD, −5.55 (−18.79 to 7.69)	No significant difference	No significant difference	WMD, −5.1 (−7.16 to −3.04)	WMD, −2.3 (−5.60 to 0.99)	WMD, −4.99 (−9.49 to 0.49)	WMD, −4.51 (−6.26 to −2.77)	WMD, −7.2 (−14.3 to −0.1)
Strength of evidence	Moderate	Low (no effect)	Insufficient	Insufficient	Moderate	Low	Low	Moderate	Moderate
Percentage of heavy drinking days									
No. of studies	2	9	0	3	7	2	3	13	9
No. of participants	123	1112	0	600	624	423	956	2167	1210
Results effect size (95% CI)[b]	WMD, −3.4 (−6.45 to 5.86)	WMD, −2.16 (−7.34 to 3.02)		No significant difference	WMD, −4.3 (−7.60 to −0.91)	WMD, −3.1 (−5.8 to −0.3)	WMD, −4.68 (−8.63 to −0.73)	WMD, −3.92 (−5.86 to −1.97)	WMD, −6.2 (−10.9 to −1.4)
Strength of evidence	Insufficient	Low (no effect)	Insufficient	Low (no effect)	Moderate	Low	Low	Moderate	Moderate

Source: adapted from McPheeters et al., 2023

Results – Drinks per Drinking Day

	Acamprosate	Baclofen	Disulfiram	Gabapentin	Naltrexone				Topiramate
					50 mg/d, oral	100 mg/d, oral	Injection	Any dose	
Drinks per drinking day									
No. of studies	2	2	0	2	9	1	0	16	7
No. of participants	139	146	0	428	1018	240	0	2011	922
Results effect size (95% CI)[b]	WMD, 0.6 (−1.43 to 2.64)	WMD, 0.85 (−2.23 to 3.93)		No significant difference	WMD, −0.49 (−0.92 to −0.06)	WMD, 1.9 (−1.5 to 5.2)		WMD, −0.85 (−1.44 to −0.26)	WMD, −2.0 (−3.1 to −1.0)
Strength of evidence	Insufficient	Low (no effect)	Insufficient	Low (no effect)	Low	Insufficient	Insufficient	Low	Moderate

Source: adapted from McPheeters et al., 2023

Results

- Health outcomes – insufficient evidence.
- Adverse events –

Figure 7. Summary of Strength-of-Evidence Assessments for Harms Outcomes

Adverse event	Acamprosate	Baclofen	Disulfiram	Gabapentin	Naltrexone	Topiramate	Varenicline
Anxiety	●	●	IE	●	●	IE	●
Cognitive dysfunction	IE	●	IE	▲	IE	▲▲	IE
Diarrhea	▲▲	●	IE	●	●	●	●
Dizziness	●	▲▲	IE	▲▲	▲▲	▲▲	●
Drowsiness	NA	▲▲	IE	NA	NA	NA	NA
Fatigue	NA	●	NA	NA	NA	NA	NA
Headache	●	●	IE	●	●	●	●
Insomnia	●	●	IE	●	●	●	●
Nausea	●●	●	IE	●	▲▲	●	▲▲
Numbness	●	▲	IE	●	IE	▲▲	NA
Rash	●	●	IE	●	●	IE	IE
Sleepiness	NA	▲▲	NA	NA	NA	NA	NA
Study withdrawals due to adverse event	●	●	IE	●	▲▲	▲	●
Suicide attempts or suicidal ideation	IE	●	IE	IE	IE	IE	IE
Taste abnormalities	IE	●	IE	IE	IE	▲▲	IE
Vision changes	IE	●	IE	IE	●	▲	IE
Vomiting	●	●	IE	●	▲▲	IE	●

▲▲ Moderate strength of evidence for adverse event
●● Moderate strength of evidence for no adverse event
▲ Low strength of evidence for adverse event
● Low strength of evidence for no adverse event

Conclusions

- Highest strength of evidence for acamprosate and naltrexone at 50 mg/day.
  - Most studies of acamprosate in U.S. found no efficacy for return to any or heavy drinking, but this may be because recruitment was done through general advertisement vs. in inpatient setting.
- Limited evidence for disulfiram's efficacy.
- Moderate evidence for topiramate, but it was linked to more adverse outcomes.

Limitations

- Limited sample – moderate to severe AUD, middle-aged, White.
- Many studies evaluated medication + other intervention.
- Don’t know much about treatment seeking in these studies.

Polling Question – Are you using MAUD?

- No, I have never prescribed MAUD
- No, I tried in the past but gave up because it just didn't work
- No, but if I got some training, I'd give it a try
- Yes, but only FDA approved medications
- Yes, I am a regular prescriber of MAUD in my patients.

Implications for Practice – the Spectrum of Alcohol Use

- Efficacy and Clinical Outcomes of Pharmacotherapy in **Adults with AUD** – Robust data supporting abstinence, reduction in drinking, and harm reduction.
- Efficacy and Clinical Outcomes of Pharmacotherapy in **Adults with Problem Drinking** - the evidence for pharmacotherapy in adults with problem drinking who do not meet criteria for AUD is limited and of low quality. Most clinical trials and systematic reviews focus on populations with diagnosed AUD, and the generalizability of these findings to individuals with subthreshold or "problem drinking" is uncertain.
- For **adolescents**, the medical literature indicates that psychosocial interventions remain first-line, and pharmacotherapy is rarely used

Brief Pharmacology Review (very brief)

Medication	Dose	Common Side Effects	Monitoring	Clinical Considerations
Naltrexone (oral)	50 mg once daily	Nausea, headache, dizziness; low hepatotoxicity risk	Liver enzymes every 6 months	Contraindicated in cirrhosis, acute hepatitis, or high LFTs; **do not use with opioids**
Naltrexone (injection)	380 mg every 4 weeks	Injection site reactions, nausea, headache, dizziness	Liver enzymes every 6 months	Same contraindications as oral; improves adherence
Acamprosate	666 mg three times daily	Diarrhea (sometimes severe), nausea, anxiety, depression, suicidality	Creatinine and creatinine clearance periodically	Contraindicated if CrCl < 30 mL/min; adjust dose for moderate renal impairment; **TID dosing may reduce adherence**
Gabapentin	Start 300 mg daily; titrate to 900–1800 mg/day	Dizziness, sedation, ataxia	Creatinine and CrCl periodically	**Off-label**; may help with comorbid pain; limited AUD efficacy data
Topiramate	Start 25–50 mg daily; titrate to 100 mg BID	Paresthesia, cognitive dysfunction, somnolence, dizziness, weight loss	Creatinine and CrCl periodically	**Off-label**; adjust for renal impairment; taper required on discontinuation
Disulfiram	250–500 mg daily x 1–2 wks, then 250 mg daily	If alcohol consumed: flushing, nausea, vomiting; also hepatotoxicity	Creatinine, CrCl, and liver enzymes periodically	Requires abstinence to start; limited efficacy data; **aversion-based** therapy
Baclofen	5 mg TID (up to 15 mg TID or more as tolerated)	Sedation, dizziness, muscle weakness	Creatinine, CrCl, and liver enzymes periodically	**Off-label**; limited data for AUD; may be considered for patients unable to use first-line medications

Practical First Line Strategies – "Go to"

- Oral **naltrexone** (50 mg daily) and **acamprosate** (6-6-6 mg three times daily) are the first-line pharmacotherapies with the strongest evidence for efficacy.
- Extended-release injectable naltrexone is also effective and may be preferred in patients with adherence challenges. The choice between oral and injectable formulations should be individualized based on patient preference, adherence likelihood, and cost considerations.
- There is substantive data supporting **disulfiram** but predominantly with supervised administration in open-label RCTs.

Combination Therapy

- Far less studied - current evidence does not support routine use of combination regimens involving FDA-approved or off-label agents for AUD.
- The COMBINE study, a large, multisite randomized controlled trial, found that combination pharmacotherapy with naltrexone plus acamprosate did not provide additional benefit over naltrexone monotherapy or behavioral intervention alone for adults with alcohol use disorder.
- Consider only if people are meeting goals

Special Considerations – Second line

- Disulfiram – Only if Abstinence is the goal of the person and can have supervision from a partner (no cognitive impairment)
- Gabapentin – if neuropathy or history of alcohol withdrawal
- Topiramate – Cocaine use disorder (slow titration)

- Remember: Evidence-based behavioral therapy improves treatment outcomes when added to MAUD

Chat Prompt:

Please type your answer into the chat!

Was there ever a time you thought about suggesting medication for AUD but chose not to?

Going Deeper

- PCSS-MAUD - a national project funded by the Substance Abuse and Mental Health Services Administration to provide free, comprehensive training, guidance, and mentoring on the prevention, diagnosis, and treatment of alcohol use disorder. Learn more at: https://www.pcss-maud.org/

Once-Weekly Semaglutide in Adults with Alcohol Use Disorder: A Randomized Clinical Trial

Christian S Hendershot, Michael P Bremmer, Michael B Paladino, Georgios Kostantinis, Thomas A Gilmore, Neil R Sullivan, Amanda C Tow, Sarah S Dermody, Mark A Prince, Robyn Jordan, Sherry A McKee, Paul J Fletcher, Eric D Claus, Klara R Klein

JAMA Psychiatry, 2025

Background

- Glucagon-like peptide 1 receptor agonists (GLP-1RAs) are incretin mimetic therapies used to treat diabetes and obesity.
  - Semaglutide was approved by FDA to treat diabetes in 2017 and obesity in 2021
  - Administered subcutaneously.
- There have been reports of reduction in alcohol use and craving among those using semaglutide, off-label use to treat AUD already occurring.
  - Pre-clinical evidence that GLP-1RAs reduce voluntary alcohol consumption and alcohol reinforcement.
- Objective: Evaluate the effects of once-weekly semaglutide on alcohol consumption and cravings among non-treatment seeking adults with AUD.

Methods

- Study design: Phase 2 randomized clinical trial.
- Population: non-treatment seeking adults with AUD.

Eligible:

- Age 21-65
- Past-year DSM-V criteria for AUD
- Past-month endorsement of >7 drinks/week among women or >14 drinks/week among men + 2 or more heavy drinking days
- Ability to attend weekly clinic visits and pre-treatment and post-treatment lab sessions.

Ineligible:

- Seeking treatment for AUD or trying to reduce consumption
- Past GLP-1RA use
- Weight loss medication
- BMI <23
- Past-year substance use disorder (other than tobacco or mild cannabis disorder)
- Past-30 day use of illicit drugs
- Ever had diabetes
- Medical or neurological illness inhibiting participation

Intervention

- 9 weeks of clinical visits + final assessment visit
  - Double-blind administration of semaglutide or placebo.
  - Dose administered according to standard practice – 0.25 mg in weeks 1 through 4, 0.5 mg in weeks 5 through 8, possible 1 mg at week 9 based on tolerability.

Outcome measurement

- Pre and post-intervention in-lab alcohol self-administration.
  - Participants given their preferred alcoholic beverage.
  - Given choice to drink or wait 50 minutes for monetary compensation.
  - After 50 minutes, told to drink at their preferred pace to achieve preferred effects over 120 minutes.
  - Investigators assessed volume of alcohol consumed (g-ETOH) and peak breath alcohol concentration (BrAC) (BrAC measured every 30 minutes).

Outcome measurement

- Participants recorded weekly alcohol use using calendar-based methods and daily logs.
- Assessed:
  - Average drinks per calendar day
  - Drinks per drinking day
  - Number of heavy drinking days
  - Number of drinking vs. abstinent days
  - Cravings (Penn Alcohol Craving Scale)
  - Proportion of participants with zero heavy drinking days
  - Cigarettes consumed per day
- Collected data on body weight, blood pressure, side effects, adverse events, depression symptoms.

Analyses

- Lab outcomes: residualized change models, regressing post-intervention outcome on assigned medication group and controlling for pre-intervention outcome and sex.
- Weekly reported outcomes: linear mixed models for each of the outcomes.
  - Included random effects for participants, fixed effects for time period and medication group, an interaction of treatment x time, and controlled for baseline outcome and sex.
- Computed Cohen d values.
  - Small: d = 0.2, Medium: d = 0.5, Large: d = 0.8
- Used intention to treat principles.

Results

- Recruited and randomized 48 participants.
- Most were female, had high BMI, moderate AUD severity.
- 42 participants completed all clinical visits. 25 participants chose to drink during lab visits.

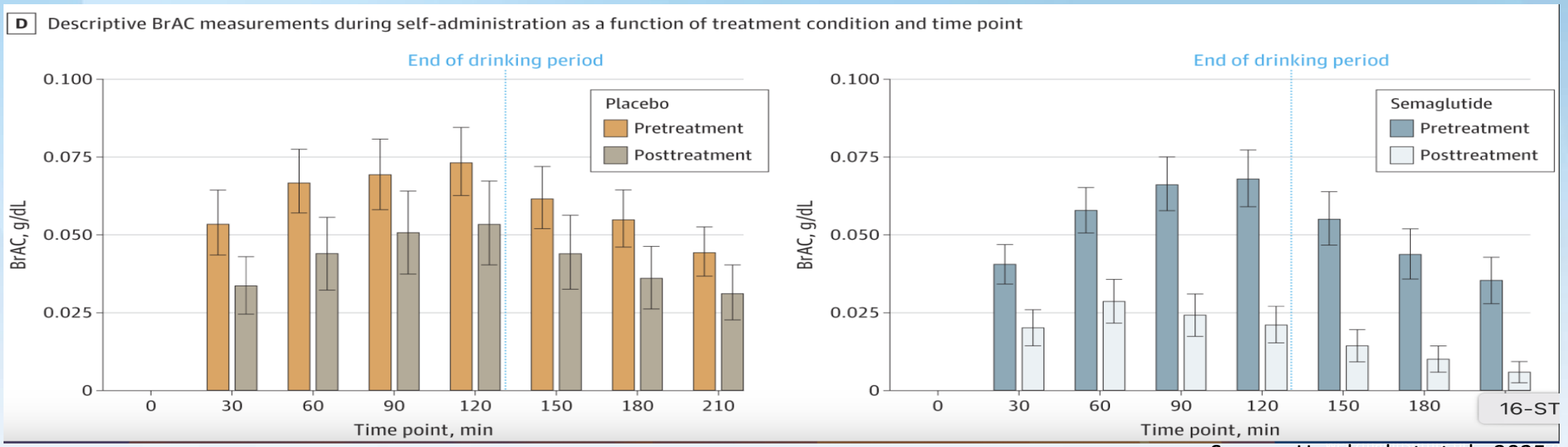
Table. Pretreatment Characteristics by Treatment Group for All Randomized Participants

Characteristic	Mean (SD)		
	Placebo	Semaglutide	Total
Randomized, No.	24	24	48
Sex, No.(%)			
Female	17 (71)	17 (71)	34 (71)
Male	7 (29)	7 (29)	14 (29)
Age, y	39.0 (10.9)	40.6 (10.5)	39.9 (10.6)
Race, No.(%)[a]			
Asian	2 (8)	0	2 (4)
Black/African American	4 (17)	3 (13)	7 (15)
Hawaiian/Pacific Islander	0	0	0
White	18 (75)	21 (88)	39 (81)
Other (unspecified) or multiple	0	0	0
Hispanic ethnicity, No.(%)[a]	2 (8)	2 (8)	4 (8)
AUD symptoms, *DSM-5*	4.3 (2.0)	4.1 (1.5)	4.2 (1.7)
AUDIT	14.2 (6.5)	12.7 (5.6)	13.4 (6.0)
Alcohol consumption[b]			
Drinks/calendar day	3.0 (1.7)	2.7 (1.7)	2.9 (1.7)
Drinks/drinking day	4.5 (2.5)	3.8 (1.8)	4.2 (2.2)
Drinking days	19.6 (5.5)	20.8 (6.8)	20.2 (6.1)
Heavy drinking days	9.8 (5.5)	8.4 (7.9)	9.1 (6.8)
Alcohol craving, PACS score	12.2 (6.5)	11.9 (4.7)	12.0 (5.6)
Current smoking, No.(%)[c]	7 (29)	6 (25)	13 (27)
Cigarettes per day	14.0 (13.5)	8.0 (7.7)	11.2 (11.2)
WHO risk level, No.(%)[d]			
1	5 (21)	8 (33)	13 (27)
2	10 (42)	10 (42)	20 (42)
3	7 (29)	4 (17)	11 (23)
4	2 (8)	2 (8)	4 (8)
Weight, kg	93.1 (15.1)	95.4 (20.9)	94.2 (18.1)
BMI	31.7 (4.5)	32.4 (6.7)	32.1 (5.6)

Source: Hendershot et al., 2025

Results

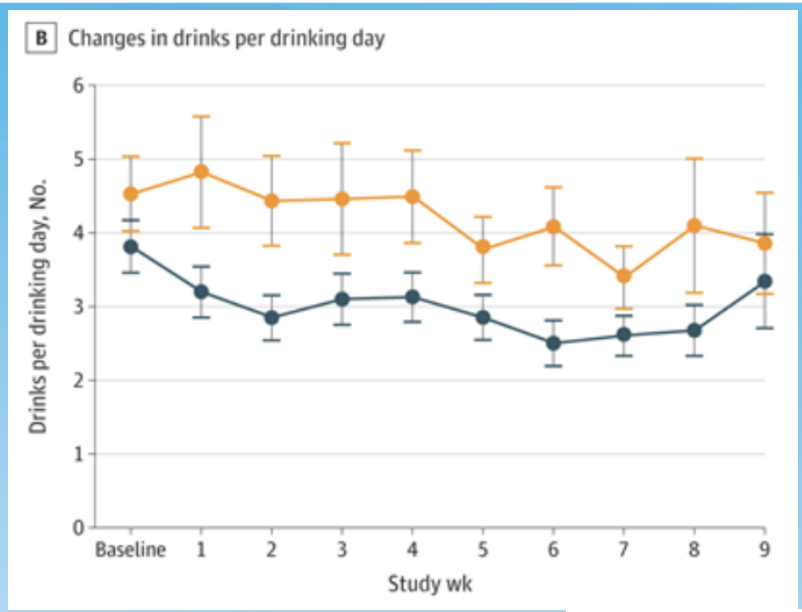
- Participants receiving semaglutide reduced post-treatment alcohol consumption (both g-ETOH and BrAC) significantly more so than participants receiving placebo (g-ETOH: β = –0.48; *P* = .01; BrAC: β = –0.46; *P* = .03).

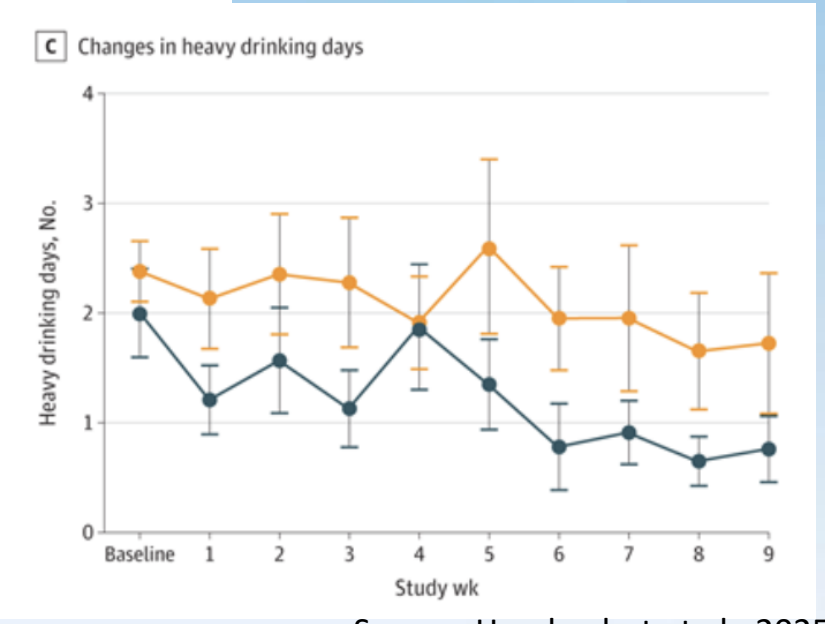


Source: Hendershot et al., 2025

Results

- Significant effect of semaglutide for drinks per drinking day (β = -0.41, p = 0.04) and cravings (β = −0.39, p = 0.01).
- Significant semaglutide x time interaction for heavy drinking days (β = 0.84, p = 0.04) and cigarette use (β = -0.10, p = 0.01).
- All small effect sizes.





Source: Hendershot et al., 2025

Results

- No significant effect for drinks per calendar day or number of drinking days.
- No serious adverse events, adverse interactions with alcohol, or treatment-related discontinuations recorded.

Conclusions

- Weekly administration of semaglutide reduced drinking among a sample of non-treatment seeking adults with AUD in laboratory settings.
- Also reduced reported drinks per drinking day and cravings and interacted with time to reduce reported heavy drinking days.
- Larger effect sizes seen in studies of other medications used to treat AUD.

Limitations

- Few methodological limitations due to RCT design, however…
  - Modest sample size.
  - Participants randomized to placebo consumed more alcohol and had higher AUDIT score at baseline.
  - Weekly consumption was self-reported.
  - Limited generalizability – participants were non-treatment seeking, high BMI, had moderate AUD.

Implications for Practice: GLP-1

- GLP-1 receptor agonists are currently FDA approved for Diabetes, Weight loss, Sleep apnea
- GLP-1 receptor agonists are not yet FDA approved for AUD. They are investigational, but promising.
- Contraindications include personal or family history of medullary thyroid carcinoma, Multiple Endocrine Neoplasia syndrome type 2, and history of pancreatitis.
- Common side effects include nausea, vomiting, and diarrhea, which may affect adherence and require proactive management.
- Cost, Cost, Cost…

Poll:

Q1 - What type of insurance is most common in your practice population?

- Medicare Managed Care
- Medicaid Managed Care
- Uninsured
- Commercial

Q2 - Do you have a access to a 340B pharmacy?

- Yes
- No
- Unsure
- N/A

Insurance Coverage

- Most state Medicaid programs cover FDA-approved medications for AUD (naltrexone, acamprosate, disulfiram) due to the federal requirement to cover mental health and substance use disorder services under Medicaid Alternative Benefit Plans (ABPs).
- Injectable extended-release naltrexone (Vivitrol) is often covered but may require PA due to high cost.
- Medicare Part D plans cover oral naltrexone, acamprosate, and disulfiram.
- Injectable naltrexone (Vivitrol) is often covered under Part B if administered in a physician's office or clinic, but this depends on the setting.

Cost Summary- MAUD

Medication	Typical Dose	Average Cash Price (Monthly)	Notes
Naltrexone (oral)	50 mg daily	$20–$60	Generic; widely available; often <$10 with discount programs
Naltrexone (injection)	380 mg IM every 4 weeks (Vivitrol®)	$1,200–$1,500	High cost; usually billed under medical benefit; may require PA
Acamprosate	666 mg TID (1980 mg/day)	$100–$250	Generic; 3x/day dosing can affect adherence
Disulfiram	250 mg daily	$40–$100	Generic; inexpensive; adherence often a challenge
Gabapentin	900–1800 mg/day	$10–$30	Generic; usually inexpensive; **off-label** for AUD
Topiramate	100 mg BID (up to 200 mg/day)	$20–$60	Generic; **off-label** for AUD; often covered due to other indications
Baclofen	15–60 mg/day	$20–$40	Generic; **off-label**; low cost

Case 1: Follow up

- WG was not interested in full abstinence, but was contemplative about taking a medication that might help him reduce his drinking. He is already prescribed gabapentin for diabetic peripheral neuropathy, and reports some subjective benefit from it in reducing evening cravings.
- After discussing treatment options, he expressed interest in trying oral naltrexone, but was not open to the injectable formulation. We reviewed risks and benefits, and planned to initiate therapy with close monitoring of liver function and drinking patterns.

Case 2: follow up

- Following her hospitalization for acute alcohol hepatitis, TJ expressed significant fear about the progression of her liver disease and demonstrated a readiness to consider abstinence for the first time. Her partner, who has five years of sobriety, expressed a strong willingness to support her recovery, including helping with medication adherence and accountability.
- During a shared decision-making discussion, we reviewed pharmacologic options for alcohol use disorder. While disulfiram was initially considered due to the potential benefits of external accountability and aversion conditioning, we ultimately agreed to initiate oral naltrexone, given:
  - Her motivation for abstinence
  - Her preference to avoid the daily commitment and risk associated with disulfiram
  - The fact that her liver disease was classified as Child-Pugh Class A, which does not constitute an absolute contraindication to naltrexone use
- We agreed to monitor liver function tests closely and assess treatment response and tolerability over the coming weeks, with the option to re-evaluate or consider alternative treatments if needed.

Questions?

Feel free to unmute or put your questions in the chat!

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