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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!

We will begin the session shortly.

*Please keep your microphones on **mute** for now to avoid background noise.*

You are muted if there is a line across your microphone icon.

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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 Summer 2026!

Session #1:

Modern Screening and Evolving Treatment Strategies

May 28, 2026

EW1

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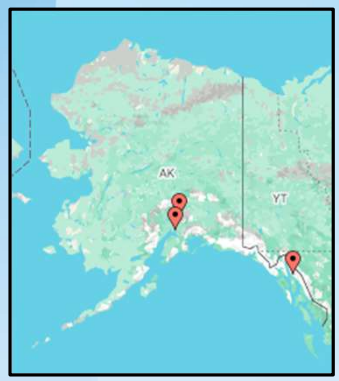
inspiring primary care innovation

Our Learning Community

246 participants across 41 States, and 3 Countries



Slide 3

EW1 UPDATE

Warshauer, Emma, 2026-05-27T12:37:57.606

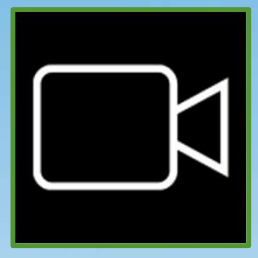
Technology: Your Zoom window

Sound

Stay on mute while others are speaking or presenting to avoid background noise

Chat

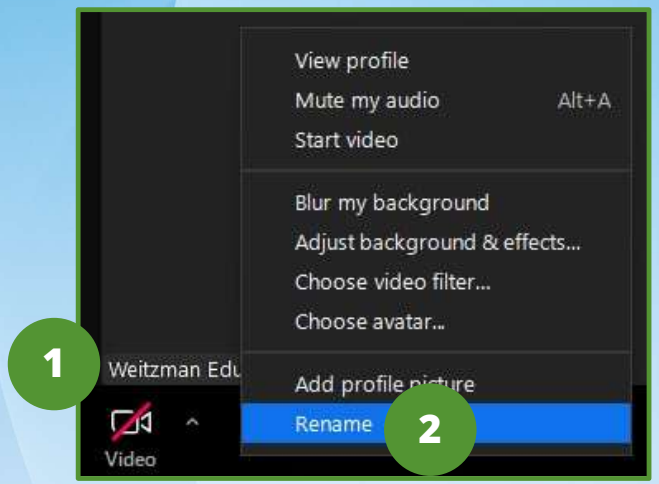
Use the chat function to share comments, questions, relevant resources, and engage with faculty and your fellow learners



Camera

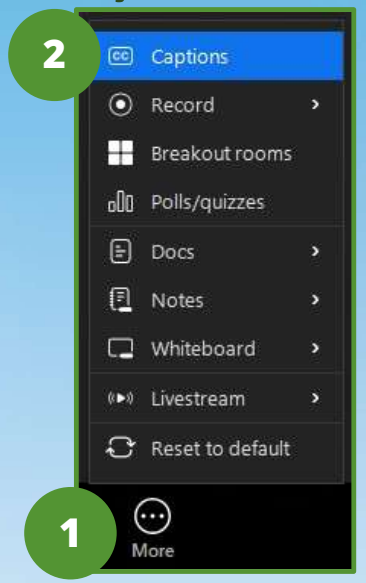
If possible, share your camera with us

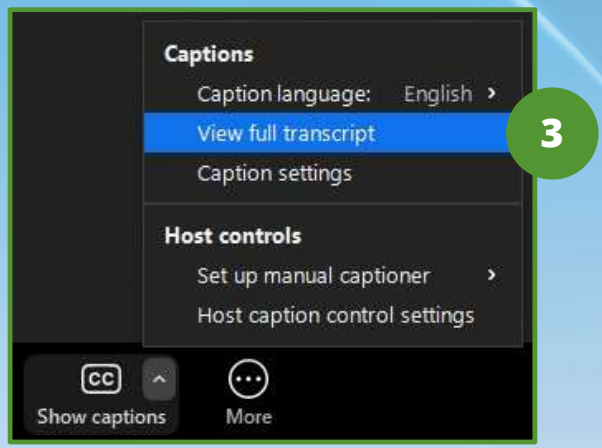
Technology: Your Zoom window, continued



Change your name

1. Right click your name in the lower left hand corner of your Zoom window.
2. Select “Rename”.





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1. If “Show Captions” does not appear in the bottom toolbar, select “More”.
2. Select “Captions”.
3. Select the carrot and then select “View full transcript”.

Continuing Education Credits

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).

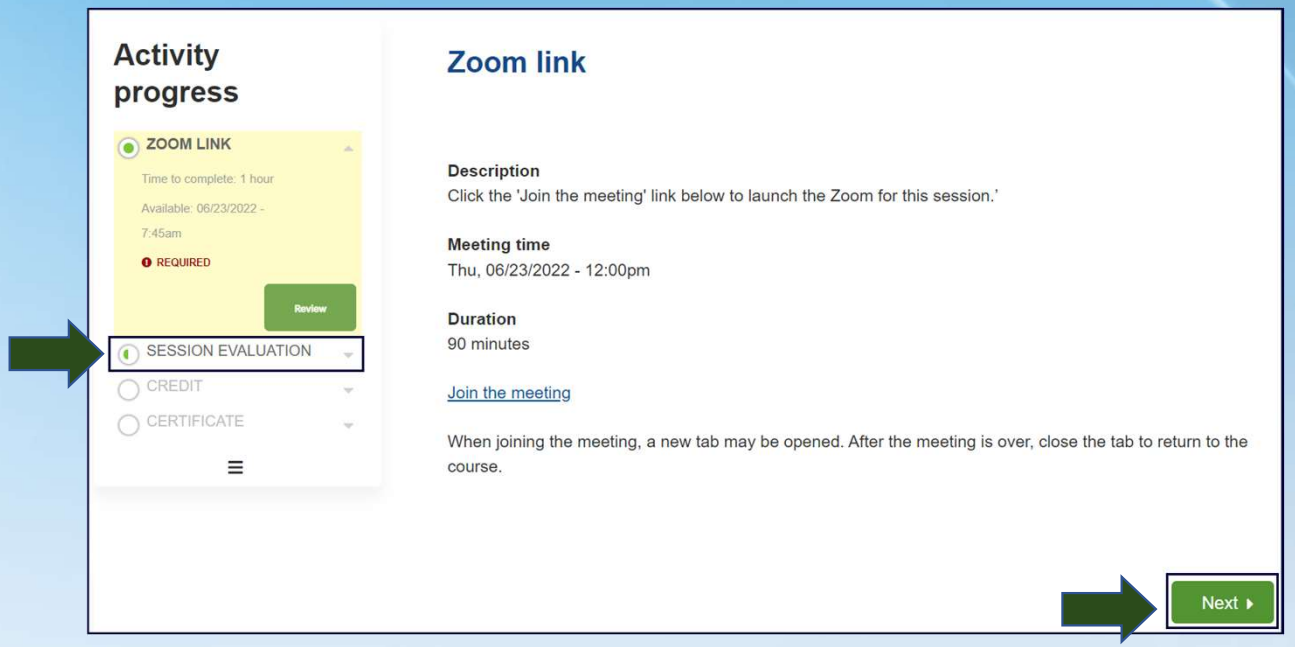
Please complete the post session survey and claim your post-session certificate on the WeP after today's session. **Please note: Pharmacists must claim credits within two weeks following today's session or we will not be able to award ACPE credits.**

You will be able to claim a comprehensive certificate on the WeP at the end of the series, July 9, 2026.

Program logistics post-session

Completing the session evaluation and claiming your CME/CE credit

After the live session has ended, **select the Next button or Session Evaluation** in the left-hand navigation bar.



Program logistics post-session

Completing the session evaluation and claiming your CME/CE credit

1. Complete the questions in the session evaluation
2. Select the **Submit** button at the bottom of the evaluation.
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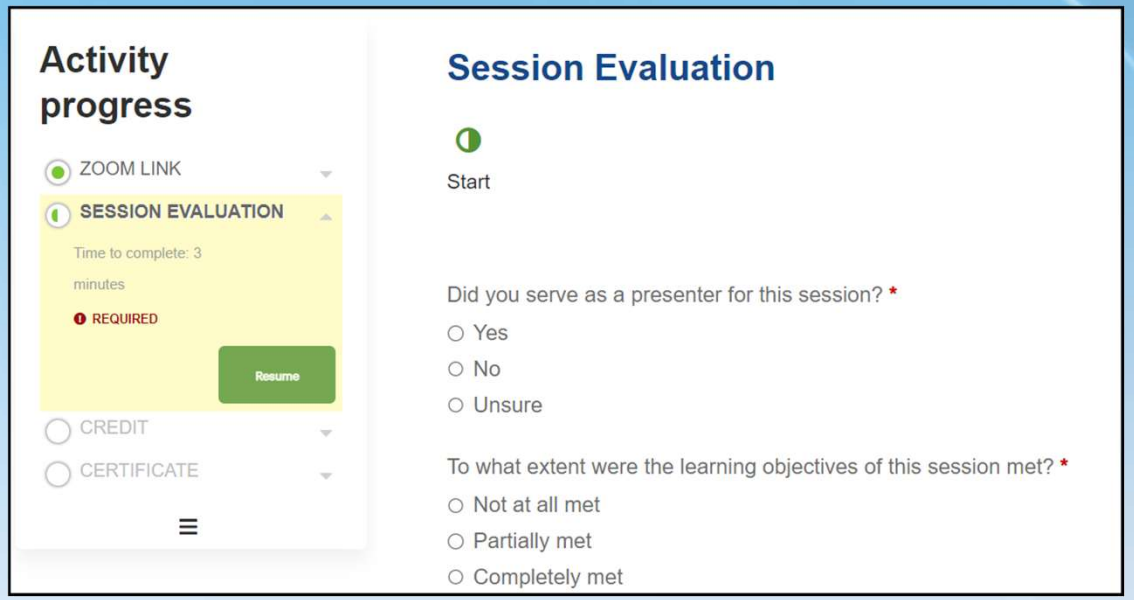

Accessing session recordings and materials

1. Return to the **Overview tab** of the live activity, *Weitzman Science to Practice: Alcohol Use Disorder – Modern Screening and Evolving Treatment Strategies (May 28, 2026)*
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.

Disclosures

- With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the faculty listed above or other activity planners and any ineligible company in the past 24 months which would be considered a relevant financial relationship.
- The views expressed in this presentation are those of the faculty and may not reflect official policy of Moses Weitzman Health System.
- We are obligated to disclose any products which are off-label, unlabeled, experimental, and/or under investigation (not FDA approved) and any limitations on the information that are presented, such as data that are preliminary or that represent ongoing research, interim analyses, and/or unsupported opinion.

All Are Welcome

MOSES/WEITZMAN
Health System

The Weitzman Institute wants to hear from FQHC healthcare providers and staff about their knowledge and opinions on HPV self-sampling for cervical cancer screening.

Your feedback will directly shape an implementation guide designed to bring this screening option to community health centers.

Scan here to take our survey!

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FREE E-LEARNING SERIES

Applying Research to Practice to Improve Alcohol Use Disorder Care

The first module, *Evaluating Research Findings for Practicing Clinicians* (1.0 CME/CE), is available now, with more modules to follow.

START LEARNING TODAY!

- **Free, self-paced education activity!**
- **Gain insights from an expert on alcohol use disorder research**
- **Strengthen your ability to critically evaluate peer-reviewed literature**
- **Reinforce knowledge through knowledge checks**

Weitzman Science to Practice Faculty

Elizabeth Salisbury-Afshar, MD, MPH

Jack Todd Wahrenberger, MD, MPH

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

Weitzman Science to Practice: Alcohol Use Disorder

Modern Screening and Evolving Treatment Strategies

Elizabeth Salisbury-Afshar, MD, MPH, and J. Todd Wahrenberger, MD, MPH

May 28, 2026

Learning objectives

By the end of the Science to Practice series, participants will be able to…

1. Apply best practices derived from peer-reviewed literature into practice within safety net settings.
2. Describe the steps involved in assessing peer-reviewed literature and their implications for determining validity.
3. Infer how peer-reviewed literature contributes to the evidence base behind clinical guidelines.

Opening Polls

- How often is alcohol screening performed in your practice using a validated tool?
  - Routinely
  - Sometimes
  - Rarely
  - Unsure
- Do you feel comfortable performing a brief intervention for unhealthy alcohol use?
  - Yes
  - No

Pragmatic considerations

1. This is not very glamorous work – would you rather be a fire marshal or a fire fighter?
2. Screening can be a schedule wrecker in a busy practice – “open up a can of worms”
3. Prevention is not a revenue generator - primary care is volume driven in many markets
4. My patient might get upset and not return for care

(Johnson et al., 2010); (Williams et al., 2016)

Why Alcohol Screening Feels Different

Traditional medical concerns:

- patient usually identifies the problem
- patient seeks relief
- clinician and patient share the agenda

Unhealthy alcohol use:

- insight may be limited
- ambivalence is common
- behavior may feel adaptive
- stigma and shame interfere
- alcohol may function as coping

SBIRT requires behavioral and relational skills in addition to medical knowledge

Case Study 1

Background:

- 52-year-old employed male presents for follow-up of:
  - hypertension
  - insomnia
  - obesity
  - elevated liver enzymes
  - worsening depression and anxiety
- Social history:
  - "Drinks socially."
  - No prior alcohol diagnosis documented.
- **Question: Would unhealthy alcohol use be identified without systematic screening?**

Risky use, unhealthy drinking, and alcohol use disorder

A SPECTRUM

- **Risky** use of alcohol means that you consume amounts that increase the likelihood of health consequences (injury, interpersonal problems, medical consequences etc.)
- **Unhealthy** alcohol use (UAU)
  - Use amounts that risk consequences
  - Use has already resulted in consequences (problem use, misuse, hazardous use)
  - Some features of DSM-5 Alcohol Use Disorder
- **Alcohol Use Disorder** (mild, moderate and severe)

Alcohol Use Disorder DSM-5

(Early, sustained, controlled environment)

A problematic pattern of alcohol use leading to significant impairment or distress, with at least 2 of the following in a 12-month period:

1. Drinking more or longer than intended
2. Unsuccessful efforts to cut down or control use
3. Spending excessive time obtaining, using, or recovering from alcohol
4. Craving or strong urge to drink
5. Failure to fulfill major obligations (work, school, home)
6. Continued use despite social or interpersonal problems
7. Giving up important activities due to alcohol use
8. Drinking in hazardous situations
9. Continued use despite physical or psychological harm
10. Tolerance (need more to get same effect)
11. Withdrawal symptoms or drinking to avoid withdrawal

Severity Levels

- **Mild: 2-3 symptoms**
- **Moderate: 4-5 symptoms**
- **Severe: 6+ symptoms**

Why screen for alcohol use?

Unhealthy alcohol use is one of the most common causes of preventable death. From 2020-2021, an estimated **178,000 alcohol-attributable deaths occurred annually in the US. Alcohol associated liver disease mortality has increased significantly post COVID**

Unhealthy alcohol use is found in **28% of adults in the US. Alcohol Use Disorder** is found in **13% of adults in the US.**

- Without screening, unhealthy alcohol use goes unrecognized
- Screening when combined with brief interventions has been shown to reduce complications in unhealthy alcohol use
- Screening helps as the first step to identify AUD
- Alcohol use during pregnancy is also one of the major preventable causes of birth defects and developmental disabilities

Esser MB et al. MMWR 2022;71:409–413.
CDC ARDI (2023 update).
White AM et al. JAMA 2022.

US Preventive Services Task Force (USPSTF) Recommendations

All adults (age 18 and older including pregnant persons) in primary care be screened to identify unhealthy alcohol use, AND that those with unhealthy use receive a brief counseling intervention: Grade B

What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

(Curry et al., 2018)

- **What screen do we use?**
- **What about just screening?** (Not effective)
- **Frequency?** (Annual)
- **12-17 age range?** (No amount is safe!)
- **What is a brief intervention?** (Not clearly defined)
- **Benefits?** (Yes) **Harms?** (No)

Why Primary Care Matters

Primary care often sees patients:

- before cirrhosis
- before pancreatitis
- before legal problems
- before job loss
- before family collapse
- before recurrent detox admissions

Alcohol use contributes to:

- depression
- anxiety
- hypertension
- sleep disorders
- liver disease
- trauma
- chronic disease burden

Primary care is often the earliest intervention point

Screening tools

Single Alcohol Screening Question (SASQ)

AUDIT-C

AUDIT

CAGE

CARET (older populations)

T-ACE (pregnancy)

CRAFFT (adolescents)

The best recommendation is to keep it simple and consistent

(Curry et al., 2018)

SBIRT:
Screening, Brief Intervention, Referral to Treatment

Brief Intervention:

- motivational interviewing approach
- nonjudgmental discussion
- increase awareness
- explore readiness for change

Referral to Treatment:

- stepped care approach
- not every patient needs specialty addiction treatment

What Does SBIRT Look Like Operationally?

Example workflow:

- MA administers AUDIT-C annually
- Positive screen flags provider
- Provider spends 3–5 minutes on brief intervention
- Assess withdrawal risk if severe use suspected
- Arrange follow-up
- Consider behavioral health referral or MAUD

SBIRT succeeds or fails operationally

Real-World Barriers

Patient Barriers	Clinician Barriers	System Barriers
• Stigma • Work obligations • Childcare • Transportation • Ambivalence • Normalization of drinking	• Time pressure • Discomfort with topic • Uncertainty about MAUD • Limited training	• Fragmented treatment systems • Referral limitations • Staffing shortages • EHR/workflow limitations

Practice Facilitation to Address Unhealthy Alcohol Use in Primary Care

Huffstetler et al

JAMA Health Forum

August 2024

Study Design

- Cluster Randomized Clinical Trial
- 76 Virginia primary care practices
- Intervention: Practice facilitation
- Control: Delayed intervention
- Key Point: The practice — not the patient — was randomized
- Reason: Workflow contamination would otherwise occur

What Was the Intervention?

Not simply physician education

Intervention included:

- practice facilitators
- workflow redesign
- QI teams
- motivational interviewing training
- EHR support tools
- audit and feedback
- referral mapping
- implementation support

This was an operational intervention

Implementation science in real-world primary care

Seven High-Leverage Changes

Practice facilitation focused on:

- building QI teams
- workflow assessment
- clinician education
- standardized screening
- standardized counseling
- referral connections
- measurement and feedback

The intervention targeted systems and workflows

Why Cluster Randomization?

The intervention changed:

- workflows
- rooming processes
- documentation systems
- team behavior

Patients inside the same clinic are not independent

Mixed-effects models accounted for clustering within practices

This is why the study design matched the intervention

Main Results

- Validated screening improved dramatically
- Intervention group:
  2.1% → 35.5%
- Control:
  0.4% → 1.4%
- Brief intervention also improved significantly
- Referral and medication treatment changed much less

Why Did Screening Improve More Than Treatment?

Screening easier to operationalize:

- questionnaires
- rooming workflows
- EHR prompts

Treatment harder because of:

- stigma
- patient readiness
- clinician confidence
- workforce shortages
- fragmented systems
- access barriers

This mirrors real-world primary care experience

Important Limitations

Study began during the COVID pandemic

Only 76 practices recruited instead of planned 125

Other limitations:

- volunteer practices
- documentation-based outcomes
- relatively short follow-up
- modest MAUD uptake
- self-report limitations

Important Point: Implementation studies are heavily affected by operational disruption

Case Study 1 – Follow up

AUDIT-C positive

Further discussion revealed:

- nightly alcohol use
- escalating tolerance
- worsening sleep
- worsening depression
- relationship strain

Patient initially ambivalent about change

Brief intervention initiated

Follow-up became longitudinal rather than episodic

Key Takeaways

- UAU is common and frequently missed
- Primary care is often the earliest intervention point
- SBIRT is not simply a counseling technique
- SBIRT is an implementation challenge
- Screening is easier than treatment engagement
- MAUD remains underutilized despite strong evidence
- Integrated care systems matter

Improving Screening is only the beginning!

Many clinicians still feel uncertain about:

- medications
- treatment pathways
- patient engagement
- longitudinal management

Next: How primary care can more confidently use Medications for Alcohol Use Disorder (MAUD)

Pharmacotherapy for Alcohol Use Disorder

McPheeters et al

JAMA

November 2023

Case Study 2

Background: Severe AUD

35-year-old man who comes to your office for a first visit- his main request is to get a medication that will help with alcohol cravings.

- He started drinking as a child, but use escalated in his teenage years
- Alcohol has caused many problems in his life, including multiple DWIs and past legal consequences including incarceration. (Meets DSM 5 criteria for severe AUD)
- He's used drugs in the past, with the most recent being crack cocaine- but feels like alcohol is the main problem.
- A few months ago he was driving while intoxicated and got a 4th DWI, he spent some time in jail and had mild withdrawal while there (no medical intervention needed)

Case Study 2 - Continued

Background Continued:

- Since then, he's been living in a sober living facility and is engaging in outpatient addiction treatment services. He continues to have cravings daily but hasn't had any return to use.
- He anticipates having prison time and would like to show the judge he's, "doing everything right," including maintaining abstinence.
- Past psychiatric diagnoses (per patient report): depression, anxiety, PTSD, "borderline" and panic disorder. He notes he has over a decade of experiencing "hearing voices" on a daily basis. Acknowledges these get worse with cocaine use but are present even during long periods of abstinence. Has tried numerous psych meds in past (multiple SSRIs, mirtazapine, Zoloft, lamotrigine) and reports AH persist.
- Past Medical history (per patient report): hypertension, sciatic pain
- He's never tried naltrexone or acamprosate but has received gabapentin the past and prefers to take that medication. He says he also has sciatica and anxiety and feels it helps with all 3 of these problems.

Key Clinical Question

- For adults with AUD who want to maintain abstinence and do not have a history of severe alcohol withdrawal, does gabapentin reduce return to drinking or heavy drinking?

JAMA | Original Investigation

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

Melissa McPheeters, PhD, MPH; Elizabeth A. O'Connor, PhD; Sean Riley, MSc, MA; Sara M. Kennedy, MPH; Christiane Voisin, MSLS; Kaitlin Kuznacic, PharmD; Cory P. Coffey, PharmD; Mark D. Edlund, MD, PhD; Georgiy Bobashev, PhD; Daniel E. Jonas, MD, MPH

Why this article?

- Is a 2023 JAMA systematic review and meta-analysis
- Includes 118 clinical trials and 20,976 participants
- Compares FDA-approved medications and commonly used off-label medications for AUD
- Directly informs medication choices in outpatient primary care / behavioral health settings

McPheeters et al. JAMA 2023;330(17):1653–1665

Medications for Alcohol Use Disorder

Mediation	FDA-Approved	First-Line
Oral Naltrexone	X	X
Acamprosate	X	X
Disulfiram	X	
Injectable Naltrexone	X	
Baclofen		
Gabapentin		
Topiramate		

McPheeters et al. JAMA 2023;330(17):1653–1665

What is a Systematic Review?

1

Search

Use a planned search strategy across databases

2

Select

Apply predefined inclusion/exclusion criteria

3

Appraise

Assess risk of bias in individual studies

4

Grade

Rate strength of evidence across the body of studies

Key point: the review process should be explicit and reproducible, so readers can judge how trustworthy the conclusion is.

What is a meta-analysis?

A statistical method for combining similar studies

Individual studies

Study A

Study B

Study C

Pooled estimate

One summary result
with uncertainty

Helps distinguish signal from noise

Methods for this review

- Searched major databases for studies of adults with AUD
- Included randomized clinical trials of at least 12 weeks for efficacy outcomes
- Focused on alcohol consumption, health outcomes, and harms
- Used two reviewers for study selection, data extraction, and risk-of-bias assessment
- Graded strength of evidence using risk of bias, consistency, directness, and precision

Why it matters clinically
The methods tell us whether the evidence is strong enough to change practice — or only strong enough to discuss uncertainty.

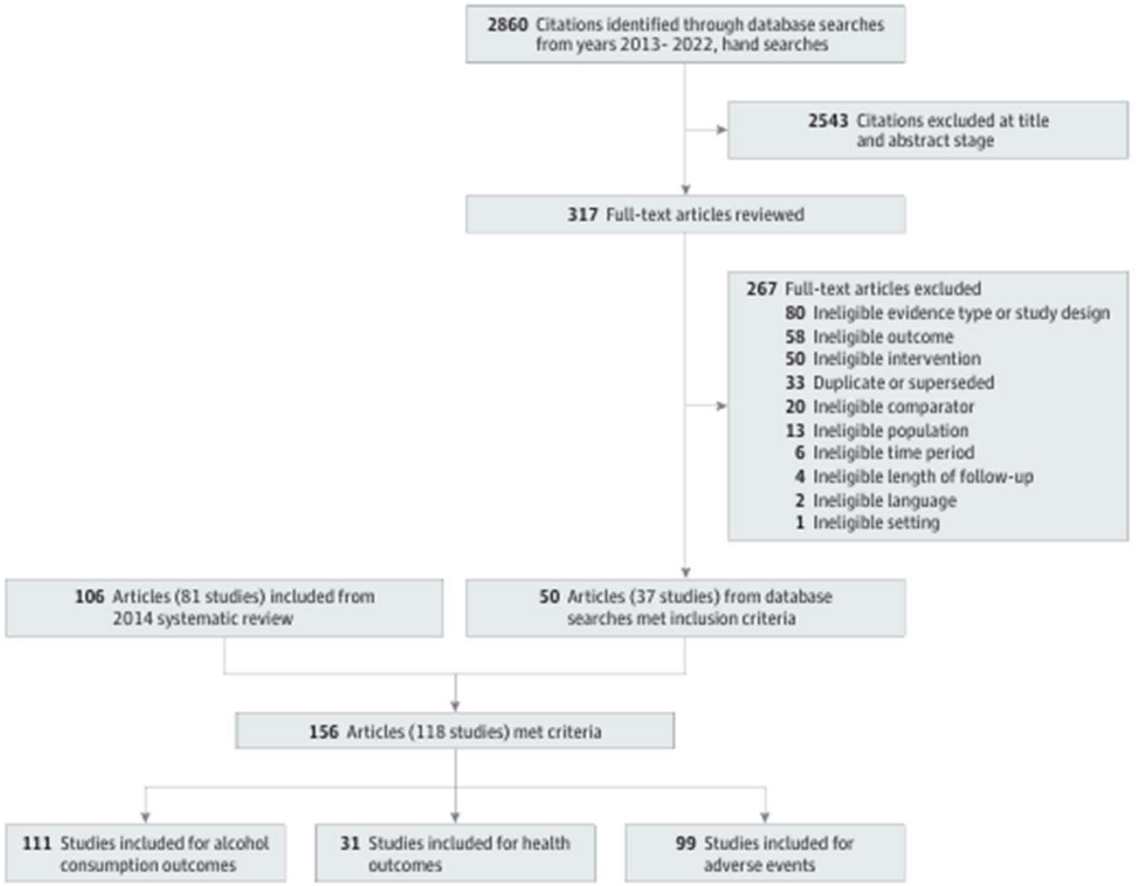
McPheeters et al. JAMA 2023;330(17):1653–1665

Outcomes Studied:

- Return to any drinking
- Return to heavy drinking
- Percentage of drinking days
- Percentage of heavy drinking days
- Drinks per drinking day
- Motor vehicle crashes or injuries
- Quality of life or function
- Mortality

McPheeters et al. JAMA 2023;330(17):1653–1665

Figure 1. Study Identification and Review for Medications Used in the Treatment of Alcohol Use Disorder



McPheeters et al. JAMA 2023;330(17):1653–1665

Strength of Evidence

The authors rated strength of evidence across four domains:

Risk of bias

Were the included studies designed and conducted in ways that reduce systematic error?

Directness

Do the studies directly answer the clinical question, with relevant patients, interventions, comparators, and outcomes?

Consistency

Do studies point in the same direction, or are results conflicting?

Precision

Are the estimates narrow enough to be clinically useful, or too uncertain?

Grades used in the article: high, moderate, low, or insufficient.

McPheeters et al. JAMA 2023;330(17):1653–1665

How to read the results

Translate statistical outputs into clinical interpretation

Term	Plain-language meaning	Clinical question
Return to any drinking	Any alcohol use after treatment starts	Does the medication support abstinence?
Return to heavy drinking	Return to high-risk drinking levels (≥4 drinks per day for women & ≥5 drinks per day for men)	Does the medication reduce high risk drinking?
Strength of evidence	How confident we are in the body of studies	Should this change practice or prompt caution?
Confidence interval	Range of plausible true effects	Is the result precise enough to trust?
Statistical significance	Whether the CI crosses the no-effect line	Could the result be due to chance?

McPheeters et al. JAMA 2023;330(17):1653–1665

What did the article find about first line medications?

Acamprosate and oral naltrexone had the strongest evidence

Acamprosate

- Moderate strength of evidence
- Reduced return to any drinking vs placebo
- Not associated with reduced return to heavy drinking
- NNT ≈ 11 to prevent one return to any drinking

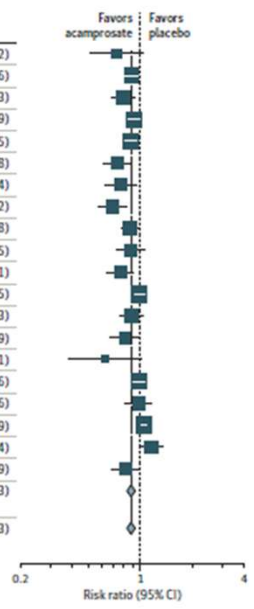
Oral naltrexone 50 mg/day

- Moderate strength of evidence
- Reduced return to any drinking vs placebo
- Reduced return to heavy drinking vs placebo
- NNT ≈ 18 for any drinking; ≈ 11 for heavy drinking

McPheeters et al. JAMA 2023;330(17):1653–1665

Figure 2. Return to Any Drinking, Acamprosate vs Placebo

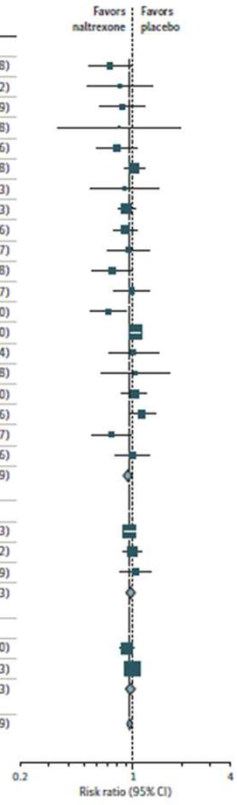
Source	Duration, wk	No./total No. (%) Acamprosate	Placebo	Risk ratio (95% CI)
Lhuintre et al,[43] 1985	13	22/42 (52.4)	31/43 (72.1)	0.73 (0.52-1.02)
Lhuintre et al,[44] 1990	12	208/279 (74.6)	245/291 (84.2)	0.89 (0.81-0.96)
Pelc et al,[56] 1992	26	42/55 (76.4)	45/47 (95.7)	0.80 (0.68-0.93)
Paille et al,[55] 1995	51	294/361 (81.4)	157/177 (88.7)	0.92 (0.85-0.99)
Whitworth et al,[65] 1996	52	183/224 (81.7)	208/224 (92.9)	0.88 (0.82-0.95)
Sass et al,[61] 1996	48	75/136 (55.1)	102/136 (75.0)	0.74 (0.61-0.88)
Poldrugo,[60] 1997	26	63/122 (51.6)	84/124 (67.7)	0.76 (0.62-0.94)
Pelc et al,[57] 1997	13	74/126 (58.7)	53/62 (85.5)	0.69 (0.57-0.82)
Geerlings et al,[32] 1997	26	96/128 (75.0)	116/134 (86.6)	0.87 (0.77-0.98)
Besson et al,[24] 1998	51	41/55 (74.5)	47/55 (85.5)	0.87 (0.72-1.05)
Tempesta et al,[62] 2000	26	87/164 (53.0)	115/166 (69.3)	0.77 (0.64-0.91)
Chick et al,[26] 2000	24	254/289 (87.9)	260/292 (89.0)	0.99 (0.93-1.05)
Gual and Lehert,[33] 2001	26	92/141 (65.2)	109/147 (74.1)	0.88 (0.75-1.03)
Kiefer et al,[37] 2003	12	30/40 (75.0)	37/40 (92.5)	0.81 (0.66-0.99)
Baltieri and De Andrade,[21] 2004	12	15/40 (37.5)	21/35 (60.0)	0.63 (0.39-1.01)
Anton et al,[17] 2005	16	244/303 (80.5)	254/309 (82.2)	0.98 (0.91-1.06)
Morley et al,[48] 2006	12	44/55 (80.0)	50/61 (82.0)	0.98 (0.82-1.16)
Mason et al,[46] 2006	24	328/341 (96.2)	240/260 (92.3)	1.04 (1.00-1.09)
Berger et al,[23] 2013	12	48/51 (94.1)	40/49 (81.6)	1.15 (0.99-1.34)
Higuchi et al,[35] 2015	24	86/163 (52.8)	105/164 (64.0)	0.82 (0.68-0.99)
Heterogeneity: $\tau^2 = 0.01$, $I^2 = 77.64\%$, $H^2 = 4.47$ Test of $\theta_i = \theta_j$: $Q(19) = 84.97$, $P < .001$				0.88 (0.83-0.93)
Overall Heterogeneity: $\tau^2 = 0.01$, $I^2 = 77.64\%$, $H^2 = 4.47$ Test of group differences: $Q_b(0) = 0.00$				0.88 (0.83-0.93)



Return to any Drinking, Acamprosate vs Placebo
Risk Ratio= 0.88 (95% CI 0.83-0.93)

Figure 4. Return to Any Drinking, Naltrexone vs Placebo

Source	Duration, wk	No./total No. (%) Naltrexone	Placebo	Risk ratio (95% CI)
Naltrexone, 50 mg/d oral				
O'Malley et al,[50] 1992	12	27/52 (51.9)	38/52 (73.1)	0.72 (0.53-0.98)
Volpicelli et al,[63] 1995	12	21/54 (38.9)	21/45 (46.7)	0.83 (0.53-1.32)
Volpicelli et al,[64] 1997	12	27/48 (56.3)	32/49 (65.3)	0.86 (0.62-1.19)
Oslin et al,[54] 1997	12	6/21 (28.6)	8/23 (34.8)	0.82 (0.34-1.98)
Anton et al,[18] 1999	12	36/68 (52.9)	42/63 (66.7)	0.79 (0.60-1.06)
Chick et al,[27] 2000	12	70/85 (82.4)	64/79 (81.0)	1.02 (0.88-1.18)
Lee et al,[42] 2001	12	19/35 (54.3)	11/18 (61.1)	0.89 (0.55-1.43)
Krystal et al,[40] 2001	12	255/418 (61.0)	140/209 (67.0)	0.91 (0.81-1.03)
Morris et al,[49] 2001	12	43/55 (78.2)	49/56 (87.5)	0.89 (0.75-1.06)
Gastpar et al,[31] 2002	12	41/84 (48.8)	45/87 (51.7)	0.94 (0.70-1.27)
Ahmadi and Ahmadi,[15] 2002	36	32/58 (55.2)	43/58 (74.1)	0.74 (0.56-0.98)
Guardia et al,[34] 2002	12	53/101 (52.5)	54/101 (53.5)	0.98 (0.76-1.27)
Kiefer et al,[37] 2003	12	26/40 (65.0)	37/40 (92.5)	0.70 (0.55-0.90)
Balldin et al,[20] 2003	24	55/56 (98.2)	59/62 (95.2)	1.03 (0.97-1.10)
Killeen et al,[38] 2004	12	30/51 (58.8)	21/36 (58.3)	1.01 (0.70-1.44)
Petrakis et al,[58] 2005	12	21/59 (35.6)	22/64 (34.4)	1.04 (0.64-1.68)
Morley et al,[48] 2006	12	44/53 (83.0)	50/61 (82.0)	1.01 (0.86-1.20)
O'Malley et al,[52] 2007	12	49/57 (86.0)	38/50 (76.0)	1.13 (0.94-1.36)
O'Malley et al,[51] 2008	16	22/34 (64.7)	30/34 (88.2)	0.73 (0.56-0.97)
Baltieri et al,[22] 2008	12	35/49 (71.4)	39/54 (72.2)	0.99 (0.78-1.26)
Heterogeneity: $\tau^2 = 0.01$, $I^2 = 35.07\%$, $H^2 = 1.54$ Test of $\theta_i = \theta_j$: $Q(19) = 29.26$, $P = .06$				0.93 (0.87-0.99)
Naltrexone, 100 mg/d oral				
Anton et al,[19] 2006	16	241/309 (78.0)	254/309 (82.2)	0.95 (0.88-1.03)
Oslin et al,[53] 2008	24	95/120 (79.2)	96/120 (80.0)	0.99 (0.87-1.12)
Pettinati et al,[59] 2010	14	39/49 (79.6)	30/39 (76.9)	1.03 (0.83-1.29)
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta_i = \theta_j$: $Q(2) = 0.70$, $P = .70$				0.97 (0.91-1.03)
Naltrexone, injection				
Kranzler et al,[39] 2004	12	130/158 (82.3)	141/157 (89.8)	0.92 (0.84-1.00)
Garbutt et al,[30] 2005	24	388/415 (93.5)	198/209 (94.7)	0.99 (0.95-1.03)
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 54.45\%$, $H^2 = 2.20$ Test of $\theta_i = \theta_j$: $Q(1) = 2.20$, $P = .14$				0.96 (0.90-1.03)
Overall Heterogeneity: $\tau^2 = 0.00$, $I^2 = 25.82\%$, $H^2 = 1.35$ Test of group differences: $Q_b(2) = 0.99$, $P = .61$				0.95 (0.92-0.99)



"Overall" refers to pooled estimate for all forms of naltrexone (50 mg/d oral, 100 mg/d oral, and injection).

Return to any Drinking, Naltrexone vs Placebo
Risk Ratio= 0.95 (95% CI 0.92-0.99)

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Gabapentin-Specific Findings

Evidence base

3 trials

Only 3 clinical trials reported return-to-drinking outcomes for gabapentin.

Efficacy

- Return to any drinking: not significantly reduced
- Return to heavy drinking: reported reduction, but low strength of evidence
- No NNT calculated because evidence was not at least moderate strength

Harms

- Dizziness increased vs placebo
- Cognitive dysfunction increased vs placebo
- Monitor sedation, functioning, and safety

Interpretation for clinicians: gabapentin can be discussed, especially when patient-specific factors matter, but the evidence is weaker than for naltrexone or acamprosate.

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Table. Summary of Findings and Strength of Evidence From Trials Assessing Efficacy of Medications With at Least Low Strength of Evidence for Benefit for Alcohol Use Disorder[a]

					Naltrexone				
	Acamprosate	Baclofen	Disulfiram	Gabapentin	50 mg/d, oral	100 mg/d, oral	Injection	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
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
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
Motor vehicle crashes or injuries									
No. of studies	0[e]	0	0	0				0	2
No. of participants	0	0	0	0				0	541
Results effect size (95% CI)[b]									Reduced risk

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Table. Summary of Findings and Strength of Evidence From Trials Assessing Efficacy of Medications With at Least Low Strength of Evidence for Benefit for Alcohol Use Disorder[a] (continued)

	Acamprosate	Baclofen	Disulfiram	Gabapentin	Naltrexone 50 mg/d, oral	Naltrexone 100 mg/d, oral	Naltrexone Injection	Naltrexone Any dose	Topiramate
Strength of evidence	Insufficient	Insufficient	Insufficient	Insufficient				Insufficient	Low
Quality of life or function									
No. of studies	1	2	0	0				5	2
No. of participants	612[f]	384[g]	0	0				1844[h]	118[i]
Results effect size (95% CI)[b]	No significant difference[j]	No significant difference						Some conflicting results[k]	No significant difference
Strength of evidence	Insufficient	Low (no effect)	Insufficient	Insufficient				Insufficient	Low (no effect)
Mortality									
No. of studies	8	4	0	0				6	3
No. of participants	2677	660	0	0				1738	507
Results effect size (95% CI)[b]	7 events (acamprosate) vs 6 events (placebo)	8 baclofen vs 3 placebo						1 event (naltrexone) vs 2 events (placebo)	Not reported
Strength of evidence	Insufficient	Insufficient	Insufficient	Insufficient				Insufficient	Insufficient

Abbreviations: RR, risk ratio; WMD, weighted mean difference.

[a] Blank cells indicate data not applicable. Strength of evidence was not rated for naltrexone by dose. Heavy drinking days was defined as ≥4 drinks/d for women and ≥5 drinks/d for men.

[b] Negative effect sizes favor intervention over placebo/control.

[c] Lack of entry for number needed to treat indicates that the relative risk (95% CI) was not statistically significant, so the investigators did not calculate a number needed to treat or the effect measure was not one that allows direct calculation of number needed to treat (eg, WMD).

[d] One study contained 2 treatment groups included in the meta-analysis.[79]

[e] Results were not reported for each treatment group separately, but there were no clinically significant differences across treatment groups.

[f] Quality of life and functioning were assessed with the World Health Organization Quality of Life (WHOQOL) and 12-item Short-Form Health Survey (SF-12) version 2 physical and mental health scores.

[g] Quality of life and functioning were assessed with the Quality of Life Enjoyment and Satisfaction Questionnaire and the 36-item Short Form Health Survey (SF-36).

[h] Each trial used a different measure to assess quality of life and functioning, including the Short Inventory of Problems, SF-36, WHOQOL, SF-12 version 2 physical and mental health scores, Drinker Inventory of Consequences, and SF-12.

[i] Quality of life was assessed with the SF-36.

[j] Results were not reported for each treatment group separately, but there were no clinically significant differences across treatment groups.

[k] One study rated as having unclear risk of bias reported that 1 patient in the placebo group died by "accident." No other details on the cause or nature of the accident were provided.[44] That study also reported 1 injury in the acamprosate group and 2 in the placebo group. Another study, rated as having high risk of bias, reported a "traffic accident" in the acamprosate group.[80]

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Harms Associated with Pharmacotherapies

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

IE indicates insufficient evidence; NA, not assessed. This figure includes all drugs with a rating of at least low strength of evidence for adverse events for at least 1 outcome. All doses of naltrexone were assessed together.

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Strengths and limitations

- Strengths:
  - Rigorously and transparently conducted systematic review using a registered protocol with 2 reviewers
  - Assessed risk of bias and graded strength of evidence (makes results more trustworthy than a narrative review or single trial)
  - Large body of evidence overall (118 studies in total across all medications)

- Limitations:
  - Only 3 clinical trials included with gabapentin.
  - Doesn't help as much for more complex patients with multiple psychiatric comorbidities- evidence can be applied, but imperfectly.
  - Health outcomes were under-reported in in many studies (i.e. quality of life, overall functioning).

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Applying the Findings to the Case

What we can say to the patient:

"Gabapentin may help some people, and I hear that it helped you before. The best overall evidence for AUD medications is stronger for naltrexone and acamprosate. Gabapentin has less certain evidence and can cause dizziness or cognitive side effects, so we should make a careful plan and monitor closely."

Clinical decision points:

- Offer naltrexone and/or acamprosate as evidence-supported first-line options
- Consider gabapentin's possible benefits in helping with anxiety and sciatic pain
- Assess psychiatric symptoms, cocaine use risk, sedation, cognition, misuse/diversion risk, and renal function
- Define follow-up outcomes: cravings, abstinence, heavy drinking, side effects, functioning, and safety

Case Study 2 - Follow up

- Day of intake: Patient declined trial of naltrexone or acamprosate- only wanted to try gabapentin and wanted to start at 900mg 3-4 times daily.
  - We agreed on 300mg three times a day with a 1 week follow-up.
- 1 week follow up: Continued anxiety/hallucinations and intermittent cravings- Gabapentin dose was increased to 600mg three times a day one week later. Patient declined naltrexone or acamprosate again, saying he wouldn't take them anyway.
- 3 week follow up: Continued anxiety/hallucinations- saw psychiatry who prescribed duloxetine, clonidine and naltrexone; continued gabapentin

Key Points from Both Cases

- SBIRT is an implementation challenge that requires focused effort.
- Screening is easier than treatment engagement.
- MAUD remains underutilized despite strong evidence.
- Systematic reviews and meta-analyses are helpful in giving a synopsis of the available literature.
- Naltrexone and Acamprosate are first line medications for treatment of alcohol use disorder.
- Gabapentin may reduce return to heavy drinking, but the quality of evidence is low.
- Patient preference and co-occurring diagnoses should be considered during discussions related to pharmacotherapies.

Questions?

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