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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

TREATMENT CONSIDERATIONS FOR COMORBID ALCOHOL USE DISORDER AND OPIOID USE DISORDER

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UW Medicine
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Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

OBJECTIVES

- Review prevalence of alcohol use disorders in patients with opioid use disorders
- Explain the impact that MOUD has on alcohol consumption
- Discuss who could benefit from medications for alcohol use disorder
- Identify what medications are used for alcohol use disorder
- Develop an understanding of what to consider when using medications for alcohol use disorder in the context of opioid use disorder

PREVALENCE OF CO-OCCURRING AUD IN PATIENTS WITH OUD

WHY DOES IT MATTER?

Greater severity of alcohol dependence

Higher rates of psychiatric comorbidities

Worse treatment outcomes

~15%

of opioid overdose deaths involved alcohol (2017)

Pikovsky M, Peacock A, Larney S, Larance B, Conroy E, Nelson E, Degenhardt L. Alcohol use disorder and associated physical health complications and treatment amongst individuals with and without opioid dependence: A case-control study. Drug Alcohol Depend. 2018 Jul 1;188:304-310. doi: 10.1016/j.drugalcdep.2018.04.016. Epub 2018 May 21. PMID: 29807218.

Tori ME, Larochelle MR, Naimi TS. Alcohol or Benzodiazepine Co-involvement With Opioid Overdose Deaths in the United States, 1999-2017. JAMA Netw Open. 2020;3(4):e202361. doi:10.1001/jamanetworkopen.2020.2361

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PREVALENCE OF CO-OCCURRING AUD IN PATIENTS WITH OUD

- 27%
  - Based on a systematic review of 194 studies and 77,212 participants
  - 2nd most common behind cocaine at 30.5%

- Bidirectional
  - Individuals with AUD had a **5.24 times the odds of concurrent OUD** vs those without any substance use disorder

Santo T Jr, Gisev N, Campbell G, Colledge-Frisby S, Wilson J, Tran LT, Lynch M, Martino-Burke D, Taylor S, Degenhardt L. Prevalence of comorbid substance use disorders among people with opioid use disorder: A systematic review & meta-analysis. Int J Drug Policy. 2024 Jun;128:104434. doi: 10.1016/j.drugpo.2024.104434. Epub 2024 Apr 26. PMID: 38677160.
Harton MR, Adams ZW, Parker MA. Associations of alcohol use disorder, cannabis use disorder, and nicotine dependence with concurrent opioid use disorder in U.S. adults. Exp Clin Psychopharmacol. 2023 Dec;31(6):998-1004. doi: 10.1037/pha0000649. Epub 2023 May 11. PMID: 37166911.

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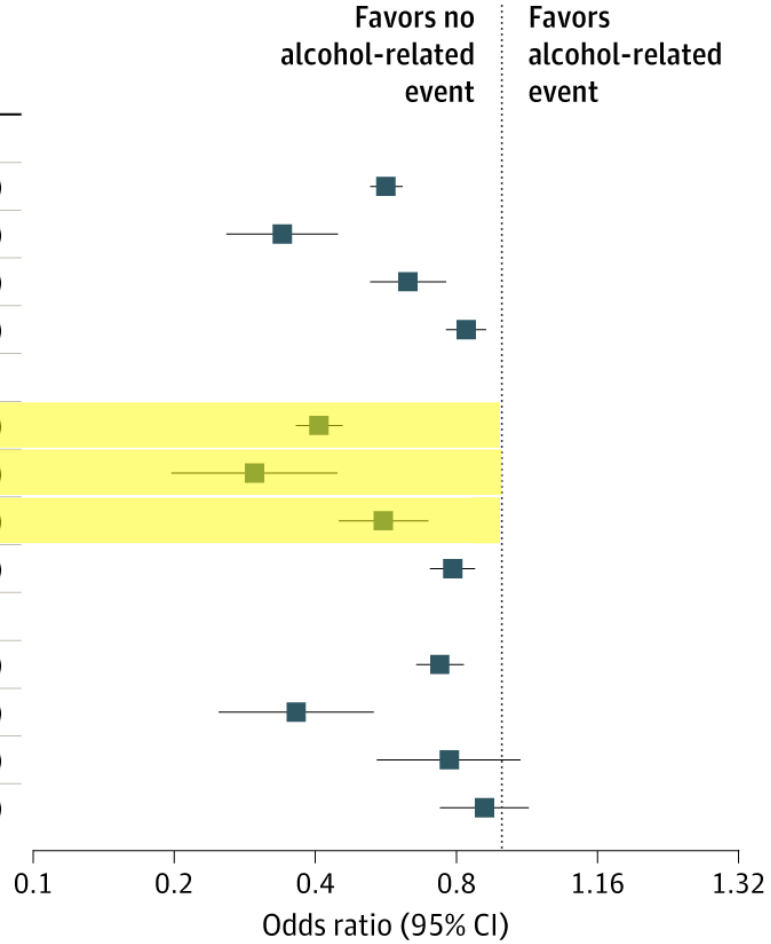
WHAT IS THE IMPACT OF MOUD ON ALCOHOL USE?

- **Reduction** in Alcohol-Related Acute Events: Falls, Injuries, Poisonings

Group	Odds ratio (95% CI)
All participants	
Buprenorphine	0.57 (0.52-0.61)
Methadone	0.34 (0.26-0.45)
Naltrexone extended release	0.63 (0.52-0.76)
Naltrexone oral	0.84 (0.76-0.93)
Participants with recent AUD claim	
Buprenorphine	0.41 (0.36-0.46)
Methadone	0.30 (0.20-0.45)
Naltrexone extended release	0.56 (0.45-0.70)
Naltrexone oral	0.79 (0.70-0.88)
Participants without recent AUD claim	
Buprenorphine	0.74 (0.66-0.83)
Methadone	0.36 (0.25-0.53)
Naltrexone extended release	0.77 (0.54-1.10)
Naltrexone oral	0.92 (0.74-1.14)



- Case-control cohort study of 13,335 individuals
- From prescription claim data and alcohol-related admissions. 2006-2016.

Xu KY, Presnall N, Mintz CM, et al. Association of Opioid Use Disorder Treatment With Alcohol-Related Acute Events. JAMA Netw Open. 2021;4(2):e210061. doi:10.1001/jamanetworkopen.2021.0061

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DOES MOUD IMPACT ALCOHOL CONSUMPTION?

Open-label randomized trial • 12 months • 218 heroin-dependent patients with comorbid alcohol dependence

Methadone
80–200 mg/day

Buprenorphine
8–32 mg/day

KEY FINDINGS

- Both drugs reduced heroin use and addiction severity (ASI)
- Both suppressed alcohol use — but the **highest dose of buprenorphine (32 mg) outperformed the highest dose of methadone (200 mg)**
  - lower alcohol craving, fewer drinks/day, and lower ASI alcohol subscale

First clinical evidence that high-dose (32mg) buprenorphine may suppress ethanol intake in heroin addicts with alcohol dependence.

Nava F, Manzato E, Leonardi C, Lucchini A. Opioid maintenance therapy suppresses alcohol intake in heroin addicts with alcohol dependence: preliminary results of an open randomized study. Prog Neuropsychopharmacol Biol Psychiatry. 2008 Dec 12;32(8):1867-72. doi: 10.1016/j.pnpbp.2008.08.019. Epub 2008 Sep 4. PMID: 18801404.

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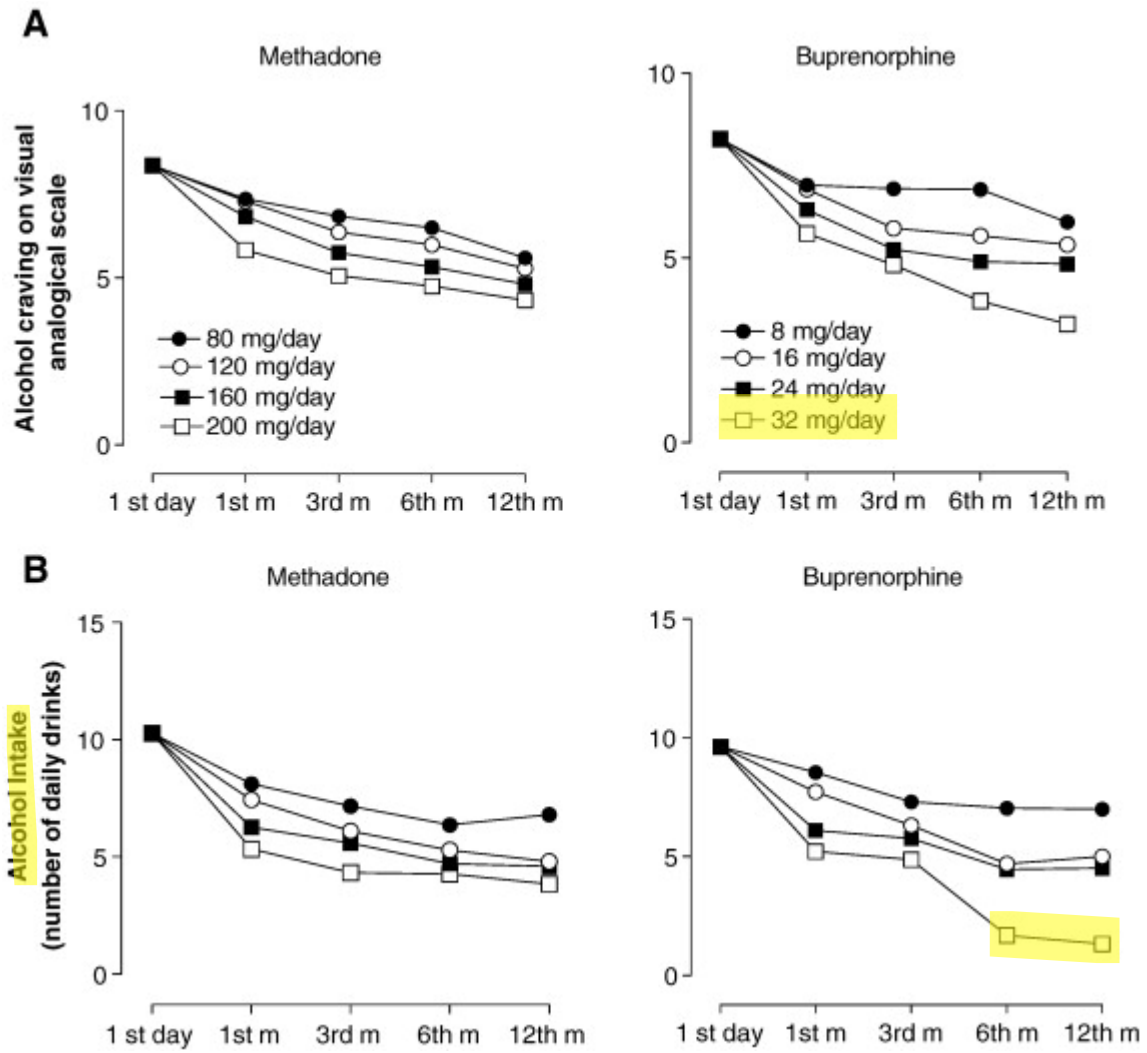

HOW TO SCREEN FOR ALCOHOL USE DISORDER IN OUD

SCREENING TOOL
AUDIT-C or AUDIT

FREQUENCY
Yearly (?) — no clear evidence base

With higher baseline prevalence, are more frequent screening intervals needed?

EVIDENCE 2015 cross-sectional survey of AUDIT scores in patients on methadone for OUD

24.4%
scored 8–15 on AUDIT (hazardous use)

12.6%
scored >15 on AUDIT (likely use disorder)

r = 0.187
Longer time on methadone → higher AUDIT score (P=0.039)

Moussas G, Fanouraki I, Pachi A, Asomatou A, Drylli O, Paschalakis G, Tselebis A, Giotakis K, Bratis D, Dermatis G, Malliori M. Comorbid Psychopathology and Alcohol Use Patterns among Methadone Maintenance Treatment Patients. J Addict. 2015;2015:197652. doi: 10.1155/2015/197652. Epub 2015 Mar 23. PMID: 25878919; PMCID: PMC4386644.

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BRIEF INTERVENTIONS FOR RISKY DRINKING IN MOUD?

Yes, it can help

Design

- Double-blind RCT, parallel group (SBI vs. screening only), **India**
- On buprenorphine 3+ months; AUDIT 7–20 (8–14 hazardous, 15+ likely dependence)

Brief intervention: one 20-min session

- Personalized, normative feedback on alcohol with buprenorphine and with HCV
- Stage-of-change–specific MI to shift drinking behavior

Results

Outcome	Intervention	Control
Shifted to low-risk drinking	**64%**	4%
Days abstinent / 3 months	**6.4 → 21.7**	5.9 → 7.7
Non-prescription opioid use	**Decreased**	—
Buprenorphine adherence	**Better**	—

Gupta, S., Pillai, R. R., & Ghosh, A. (2026). Efficacy of Screening and Brief Intervention for Alcohol Misuse in Opioid Agonist Maintenance Treatment: A Randomized Clinical Trial. *Journal of Psychoactive Drugs*, *58*(2), 171–181. https://doi-org.offcampus.lib.washington.edu/10.1080/02791072.2024.2428139

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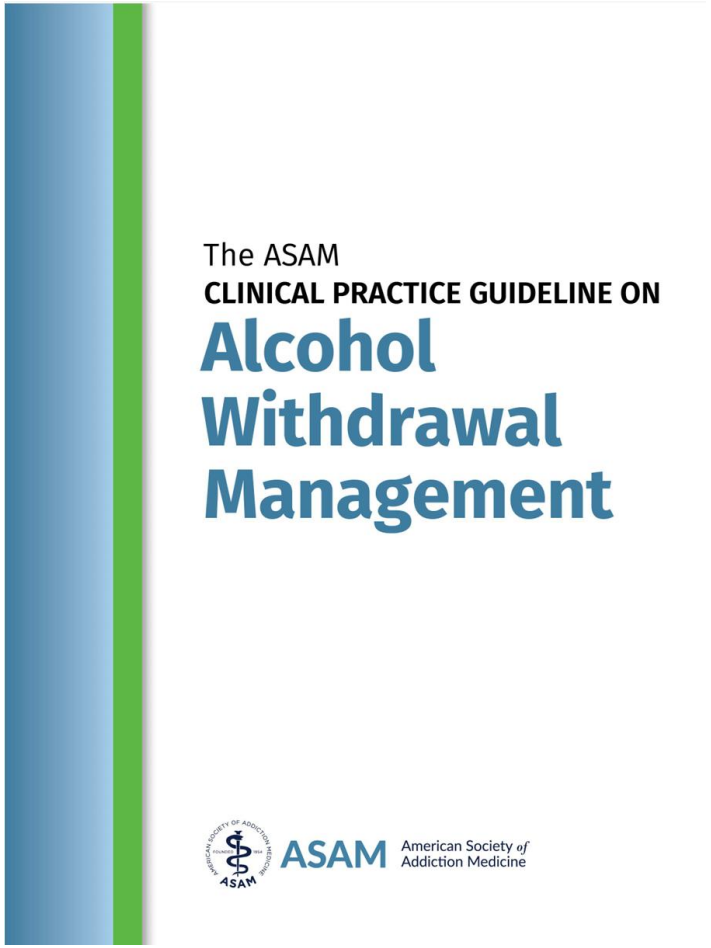
BRIEF INTERVENTIONS FOR RISKY DRINKING IN MOUD?

- **No, it does not matter**
- RCT BI vs Gen Health Education only. **China**.
- On Methadone
- Brief Intervention
  - Based on WHO BI Intervention Manual
  - 5-15 min
- **Results**
  - AUDIT scores decreased in both groups
  - **No significant difference between groups**

Gong Y, Zhang L, Long J, Wu Q, Zhang J, Bao J, Du J, Du Z. Feasibility of a Brief Intervention to Decrease Harmful Alcohol Use Among Methadone Maintenance Treatment Clients in Shanghai: A Randomized Controlled Trial. J Addict Med. 2023 May-Jun 01;17(3):294-299. doi: 10.1097/ADM.0000000000001101. Epub 2022 Oct 27. PMID: 37267171.

CONSIDERATIONS FOR CO-OCCURRING OUD AND AUD?

- 2020 ASAM Guidelines on treating Opioid Use Disorder
  - Patients with active co-occurring alcohol use disorder **may need a higher level of care** than an office-based setting
  - Those who are drinking but DO NOT have a use disorder, should be carefully monitored



https://www.asam.org/quality-care/clinical-guidelines/alcohol-withdrawal-management-guideline

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TREATMENT FORKS

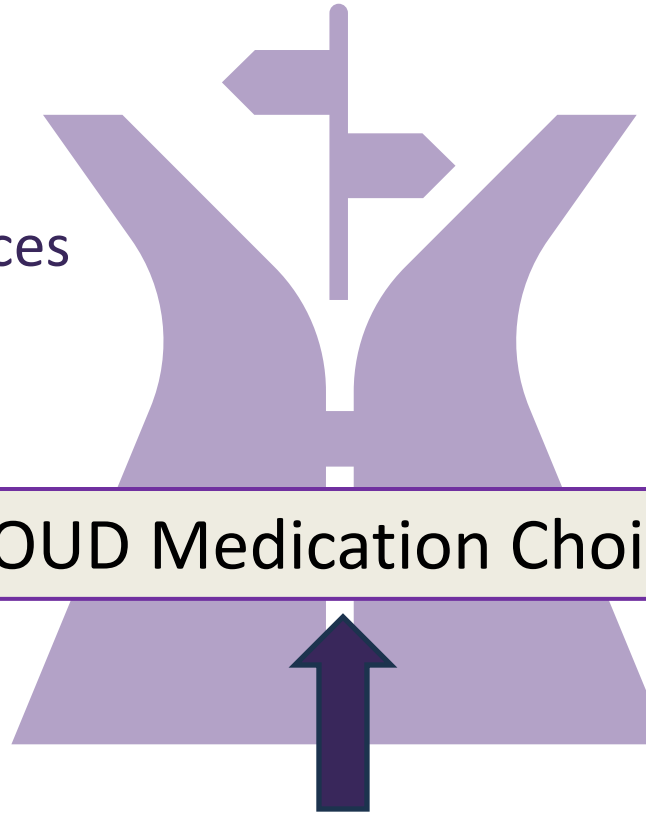
SHARED DECISION MAKING

Simultaneous Treatment

- **Recommended**
- Higher level of care may be needed at start
  - Detox from both substances

Sequential Treatment

- An untreated substance will impact a treated substance
- May be more acceptable for the patient



MOUD Medication Choice

Start Here

NOT in treatment and actively using both opioids and alcohol

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TREATMENT FORKS

SHARED DECISION MAKING

Simultaneous Treatment

- Recommended
- Higher level of care may be needed
  - Detox from both substances

Sequential Treatment

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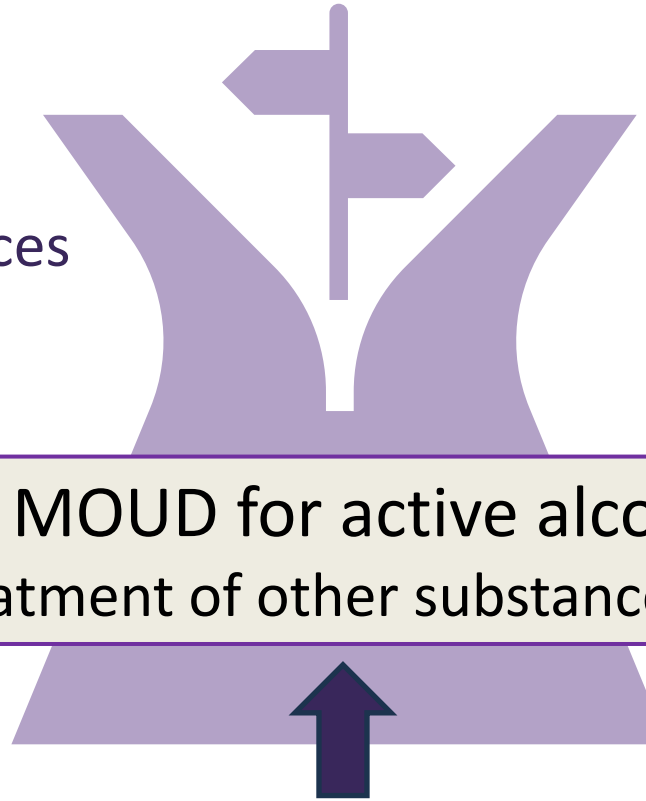

Don’t withhold MOUD for active alcohol use disorder

Start treatment of other substance (alcohol)

Start Here

In treatment for one substance, active use of the other substance

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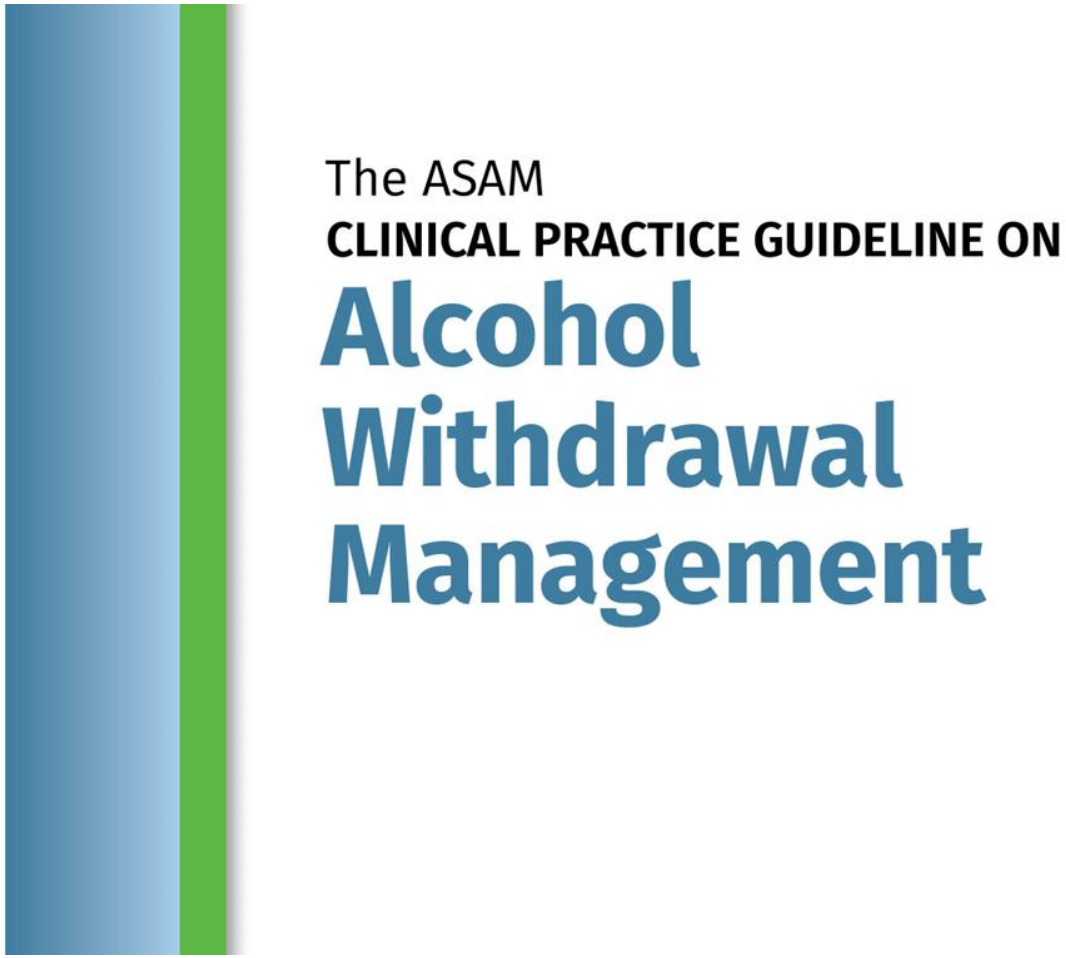
ALCOHOL WITHDRAWAL MANAGEMENT IN OUD



- **2020 ASAM Guidelines on treating alcohol withdrawal**
  - For patients with concomitant alcohol withdrawal and opioid use disorder, stabilize opioid use disorder (e.g. with methadone or buprenorphine) **concomitantly** with treating alcohol withdrawal.

- **Where** should a patient have their alcohol withdrawal and buprenorphine induction started at the same time?
  - **Best done in a medically supervised facility**
  - Outpatient management is challenging
    - Patient: Will need support person to help keep plan straight
    - Provider: Hard to know what is exactly happening

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ALCOHOL USE DISORDER MEDICATION CONSIDERATIONS IN CO-OCCURRING OUD AND AUD

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WHO SHOULD BE OFFERED MEDICATIONS FOR ALCOHOL USE DISORDER?

Answer: everyone with an alcohol use disorder

- People do better when medications are added to the treatment plan

Minozzi S, La Rosa GR, Salis F, Camposeragna A, Saulle R, Leggio L, Agabio R. Combined pharmacological and psychosocial interventions for alcohol use disorder. Cochrane Database of Systematic Reviews 2025, Issue 3. Art. No.: CD015673. DOI: 10.1002/14651858.CD015673.pub2. Accessed 23 April 2026.c

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ORAL NALTREXONE: NOT AN OPTION FOR OUD

How It Works

- **Opioid receptor blocker**
- Blocks the release of dopamine in the reward pathway. Reduces the rewarding effects of alcohol.
- Modifies the hypothalamic-pituitary axis to suppress alcohol intake

How It Helps

- Helps with relapse prevention
- Reduces frequency and quantity of alcohol consumption
- Reduces alcohol craving
- Reduces health care utilization and cost

Prescribing: 50mg daily

- Can titrate up to 100mg daily , if needed
- Can start while still drinking

Side Effects: abdominal pain, nausea, headaches

Lab monitoring: liver enzymes at 1 month and 3-6 months

Pregnancy: benefits may outweigh risks

Potential Reasons Not to Use:

- Liver Impairment
- Opioid Use

McPheeters M, O'Connor EA, Riley S, Kennedy SM, Voisin C, Kuznacic K, Coffey CP, Edlund MD, Bobashev G, Jonas DE. Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis. JAMA. 2023 Nov 7;330(17):1653-1665. doi: 10.1001/jama.2023.19761. Erratum in: JAMA. 2024 Oct 2. doi: 10.1001/jama.2024.11331. PMID: 37934220; PMCID: PMC10630900.
Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, Gastfriend DR, Hosking JD, Johnson BA, LoCastro JS, Longabaugh R, Mason BJ, Mattson ME, Miller WR, Pettinati HM, Randall CL, Swift R, Weiss RD, Williams LD, Zweben A; COMBINE Study Research Group. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA. 2006 May 3;295(17):2003-17. doi: 10.1001/jama.295.17.2003. PMID: 16670409.

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EX RELEASE IM NALTREXONE

Oral Vs IM Naltrexone

ADOPT Trial

- **Similar effect on reducing heavy drinking days**
- **Similar effect on reduced use of healthcare**

Adherence: IM Advantage

- Treatment persistence better at 3 months (OR 1.43) and 6 months (OR 1.96)

Prescribing: 380mg every 4 weeks

- Consider oral test dose before starting if patient has opioid history

Side Effects: similar to oral and injection site reactions

Lab Monitoring: similar to oral

Pregnancy: reassuring case studies

Other Notes:

- Poor adherence
- If abstinence is not the goal

Magane KM, Dukes KA, Fielman S, et al. Oral vs Extended-Release Injectable Naltrexone for Hospitalized Patients With Alcohol Use Disorder: A Randomized Clinical Trial. JAMA Intern Med. 2025;185(6):635–645. doi:10.1001/jamainternmed.2025.0522
Elmosalamy A, Sirohi A, Moustafa A, Masoud O, Hassett LC, Kolla BP, Singh B. Extended-release naltrexone versus oral naltrexone for substance use disorders: A systematic review and meta-analysis. Drug Alcohol Depend. 2025 Sep 1;274:112789. doi: 10.1016/j.drugalcdep.2025.112789. Epub 2025 Jul 7. PMID: 40660643; PMCID: PMC12289340.

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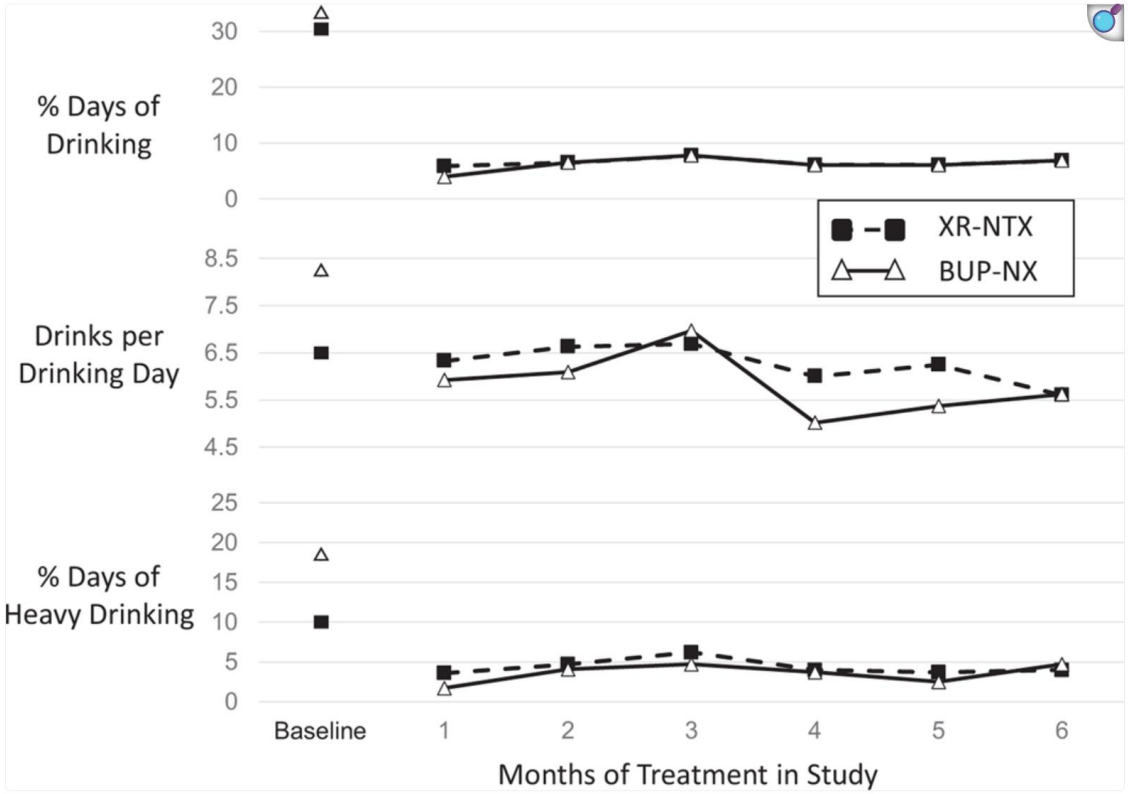
IS XR-NALTREXONE THE BEST OPTION FOR CO-OCCURRING OUD AND AUD?

- X:BOT Original Trial
  - XR-Naltrexone vs Bup-Nal SL
  - Randomized
  - Patients first detoxified
  - 6 month follow-up, **weekly visits**

- Secondary Analysis Results (N=474)
  - Limitations: Floor-effects
  - 21% had a mod-sev AUD

Results: No significant differences in drinking reductions between groups



Drinking outcomes for each of 6 months of treatment with extended release naltrexone (XR-NTX) or buprenorphine-naloxone (BUP-NX). Data are observed means for the subsample of *n* = 179 patients—unadjusted for any statistical model parameters

Roache JD, Pavlicova M, Campbell A, Choo TH, Peavy M, Kermack AS, Nunes EV Jr, Rotrosen J. Is extended release naltrexone superior to buprenorphine-naloxone to reduce drinking among outpatients receiving treatment for opioid use disorder? A secondary analysis of the CTN X:BOT trial. Alcohol Clin Exp Res. 2021 Dec;45(12):2569-2578. doi: 10.1111/acer.14729. Epub 2021 Nov 23. PMID: 34698397; PMCID: PMC8722377.

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IS EX RELEASE IM NALTREXONE THE BEST OPTION FOR CO-OCCURRING OUD AND AUD?

Observational comparative-effectiveness study • US MarketScan claims, 2011–2016 • 179,280 adults with OUD (methadone excluded)

UNDER-TREATMENT

70.4%

of patients with co-occurring SUD received no MOUD (vs 52.7% without)

TREATMENT STEERING

RR 0.55

lower odds of starting buprenorphine with co-occurring SUD — while naltrexone rose (oral RR 1.95)

OVERDOSE PROTECTION

OR 0.56

fewer drug-related poisonings on **buprenorphine**; oral naltrexone showed none, oral and ER none for nonopioid poisonings

Bottom line: patients with polysubstance use are steered toward naltrexone and away from buprenorphine — despite buprenorphine's protective association against drug-related poisoning.

Xu KY, Mintz CM, Presnall N, Bierut LJ, Grucza RA. Comparative Effectiveness Associated With Buprenorphine and Naltrexone in Opioid Use Disorder and Co-occurring Polysubstance Use. JAMA Netw Open. 2022;5(5):e2211363. doi:10.1001/jamanetworkopen.2022.11363

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XR-NALTREXONE: A TRADEOFF-NOT A FREE LUNCH

Compared with XR-naltrexone, buprenorphine showed:

Better retention in treatment

Patients stayed engaged in care longer on buprenorphine.

Fewer nonfatal overdoses

Lower incidence of nonfatal overdose during treatment.

Ross RK, Nunes EV, Olfson M, Shulman M, Krawczyk N, Stuart EA, Rudolph KE. Comparative effectiveness of extended-release naltrexone and sublingual buprenorphine for treatment of opioid use disorder among Medicaid patients. Addiction. 2024 Nov;119(11):1975-1986. doi: 10.1111/add.16630. Epub 2024 Aug 5. PMID: 39099417; PMCID: PMC11479822.
Hsu HE, Lodi S, Yan S, et al. Buprenorphine-Naloxone vs Extended-Release Naltrexone Following Opioid Withdrawal Treatment. JAMA Netw Open. 2026;9(7):e2623280. doi:10.1001/jamanetworkopen.2026.23280
Ajazi EM, Dasgupta N, Marshall SW, Monaco J, Howard AG, Preisser JS, Schwartz TA. Revisiting the X:BOT Naltrexone Clinical Trial Using a Comprehensive Survival Analysis. J Addict Med. 2022 Jul-Aug 01;16(4):440-446. doi: 10.1097/ADM.0000000000000931. PMID: 35960214.

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ACAMPROSATE: NOT STUDIED IN OUD

How It Works

- Modulation NMDA receptor transmission and GABA transmission
- Decrease glutamate during alcohol withdrawal
- Increase beta-endorphin

How It Helps

- Effective in maintaining abstinence in individuals who were recently withdrawn from alcohol use. (OR 1.86)
- Protracted withdrawal?
- Use NOT well supported in patients who are not yet abstinent

Prescribing: 666mg three times a day

- Dose adjust for moderate renal impairment

Side Effects: diarrhea, nervousness, fatigue

Lab monitoring: none needed

Pregnancy: very limited data, maybe better for pain control

Warnings:

- **Do not use** in severe renal impairment

McPheeters M, O'Connor EA, Riley S, Kennedy SM, Voisin C, Kuznacic K, Coffey CP, Edlund MD, Bobashev G, Jonas DE. Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis. JAMA. 2023 Nov 7;330(17):1653-1665. doi: 10.1001/jama.2023.19761. Erratum in: JAMA. 2024 Oct 2. doi: 10.1001/jama.2024.11331. PMID: 37934220; PMCID: PMC10630900.
Cheng HY, McGuinness LA, Elbers RG, MacArthur GJ, Taylor A, McAleenan A, Dawson S, López-López JA, Higgins JPT, Cowlishaw S, Lingford-Hughes A, Hickman M, Kessler D. Treatment interventions to maintain abstinence from alcohol in primary care: systematic review and network meta-analysis. BMJ. 2020 Nov 25;371:m3934. doi: 10.1136/bmj.m3934. PMID: 33239318; PMCID: PMC7687021.
Kalk, N.J. and Lingford-Hughes, A.R. (2014), The clinical pharmacology of acamprosate. Br J Clin Pharmacol, 77: 315-323. https://doi-org.offcampus.lib.washington.edu/10.1111/bcp.12070
Kelty E, Tran D, Lavin T, Preen DB, Hulse G, Havard A. Prevalence and safety of acamprosate use in pregnant alcohol-dependent women in New South Wales, Australia. Addiction. 2019 Feb;114(2):206-215. doi: 10.1111/add.14429. Epub 2018 Sep 21. PMID: 30152012.

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- Use NOT well supported in patients who are not yet abstinent

Reasons to Consider in OUD

- **No medication interactions with methadone or buprenorphine.**
- **Safe to use in liver disease.**

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DISULFIRAM

How It Works

- Threat of “Disulfiram Reaction”
- Blocks the enzymatic breakdown of alcohol→increase levels of acetaldehyde
- Within 10-30min: sweating, headaches, low blood pressure, flushing, nausea, vomiting, palpitations

How It Helps

- Unsupervised dosing: not effective?
- Supervised dosing: effective
- Maintaining abstinence
- Reduced heavy drinking days

Prescribing: 250-500mg daily

- Start after 48 hours of abstinence
- Educate patients on “hidden” forms of alcohol

Side Effects: metallic taste, fatigue, headache

Lab monitoring: liver enzymes every 6 months

Pregnancy: safety not established, some reports are ok, (risk/benefits)

Warnings:

- Avoid in significant to decompensated liver disease
- Avoid in significant heart disease
- Psychosis (risk/benefit)
- Seizures (risk/benefit)

Bahji A, Bach P, Danilewitz M, Crockford D, Devoe DJ, El-Guebaly N, Saitz R. Pharmacotherapies for Adults With Alcohol Use Disorders: A Systematic Review and Network Meta-analysis. J Addict Med. 2022 Nov-Dec 01;16(6):630-638. doi: 10.1097/ADM.0000000000000992. PMID: 35653782; PMCID: PMC10010623.
https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=07abe950-3565-418c-8086-b804406a8c87

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DISULFIRAM IN OUD

How It Works

- Studied in patients on methadone, N=29
- 300mg qday Combined with methadone daily dose
- Well tolerated, 50% retention at 6 months
- Low alcohol use, other drug use did not change

How to Use

- Unsupervised dosing: not effective?
- **Supervised dosing: effective**
- Avoid in severe myocardial disease, severe hepatic dysfunction, and psychosis

Reasons to Consider in OUD

- **No significant medication interactions with methadone or buprenorphine.**
- **Has evidence for effectiveness in patients with OUD on methadone**
  - N=29, German Methadone Clinic
  - Results
    - Half finished
    - Levels of other drug use did not change

Specka M, Heilmann M, Lieb B, Scherbaum N. Use of disulfiram for alcohol relapse prevention in patients in opioid maintenance treatment. Clin Neuropharmacol. 2014 Nov-Dec;37(6):161-5. doi: 10.1097/WNF.0000000000000050. PMID: 25384073
VA SUD Practice Guideline. https://www.healthquality.va.gov/guidelines/mh/sud/

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TOPIRAMATE

How It Works

- Modulates dopamine reward pathway
- Enhances inhibitory GABA
- Moderates the effect of chronic alcohol consumption on neural excitability, reducing inner tension and discomfort

How It Helps

- Higher rates of abstinence
- Reduces heavy drinking
- One small study showed a greater effect than naltrexone on drinks per day and heavy drinking days

Prescribing: Start 25mg daily; Target dose is 200-300mg divided.

- 5-6 week titration needed
- Do not stop abruptly → rebound seizures

Side Effects: cognitive/memory impairment, paresthesia

Lab monitoring: none needed

Pregnancy: small but increased risk for birth defects and learning delays, may make birth control less effective at doses over 200mg

Warnings:

- Dose adjustments needed in renal and liver impairment

Morley KC, Kranzler HR, Luquin N, Jamshidi N, Adams C, Montebello M, Tremonti C, Dali G, Logge W, Baillie A, Teesson M, Trent R, Haber PS. Topiramate Versus Naltrexone for Alcohol Use Disorder: A Genotype-Stratified Double-Blind Randomized Controlled Trial. Am J Psychiatry. 2024 May 1;181(5):403-411. doi: 10.1176/appi.ajp.20230666. PMID: 38706338.
Blodgett JC, Del Re AC, Maisel NC, Finney JW. A meta-analysis of topiramate's effects for individuals with alcohol use disorders. Alcohol Clin Exp Res. 2014 Jun;38(6):1481-8. doi: 10.1111/acer.12411. Epub 2014 May 5. PMID: 24796492; PMCID: PMC4047180.

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TOPIRAMATE IN OUD (FOR COCAINE)

How It Works

- Modulates dopamine reward pathway
- Enhances inhibitory GABA
- Moderates the effect of chronic alcohol consumption on neural excitability, reducing inner tension and discomfort

How It Helps

- Was not helpful for cocaine abstinence

Considerations in OUD

- **Interactions: CNS depression**
- **Cognitive Impairment**

Umbricht A, DeFulio A, Winstanley EL, Tompkins DA, Peirce J, Mintzer MZ, Strain EC, Bigelow GE. Topiramate for cocaine dependence during methadone maintenance treatment: a randomized controlled trial. Drug Alcohol Depend. 2014 Jul 1;140:92-100. doi: 10.1016/j.drugalcdep.2014.03.033. Epub 2014 Apr 16. PMID: 24814607; PMCID: PMC4431633.

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CAN MEDICATIONS HELP WITH CONTROLLED DRINKING?

Source: Palpacuer C. et al. (2018) — Network meta-analysis, 32 RCTs

⚠ 26/32 RCTs high bias risk

★ CLEAR WINNER

Topiramate

Superior on every outcome measured

Reduced total alcohol consumption, fewer heavy drinking days, and more non-drinking days vs. placebo, naltrexone, and acamprosate.

TOTAL CONSUMPTION

& Heavy Drinking Days

Nalmefene · Topiramate · Baclofen

vs. Placebo, Naltrexone, Acamprosate

NON-DRINKING DAYS

Increased frequency

Topiramate

Stood alone on this outcome

HEAD-TO-HEAD

Indirect drug comparison

Topiramate

Superior on all measures

✓ **SAFETY (between drugs)**

No difference in mortality or serious adverse effects

⚠ **TOLERABILITY**

More withdrawals & adverse effects with Nalmefene

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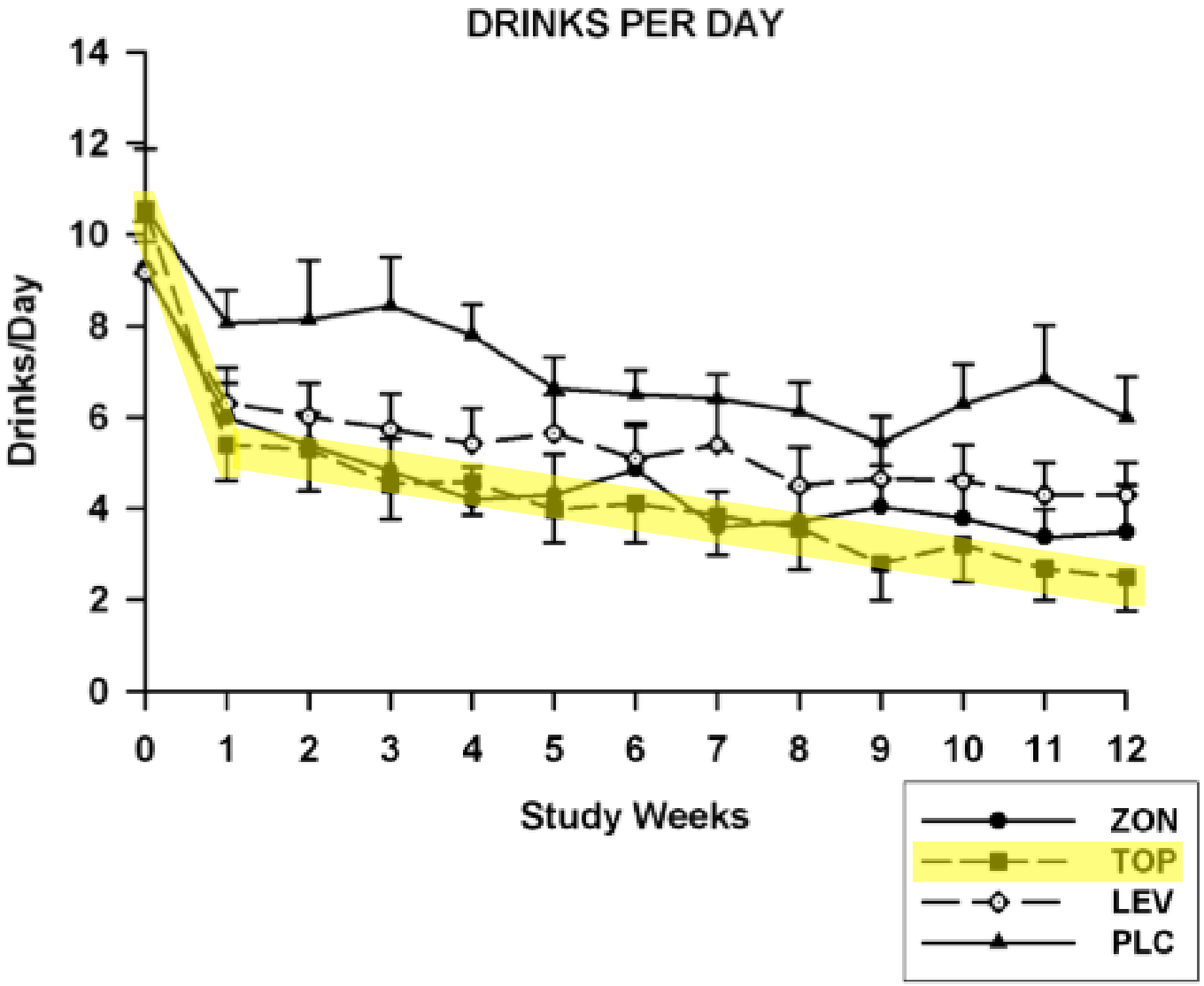
TOPIRAMATE AND CONTROLLED DRINKING



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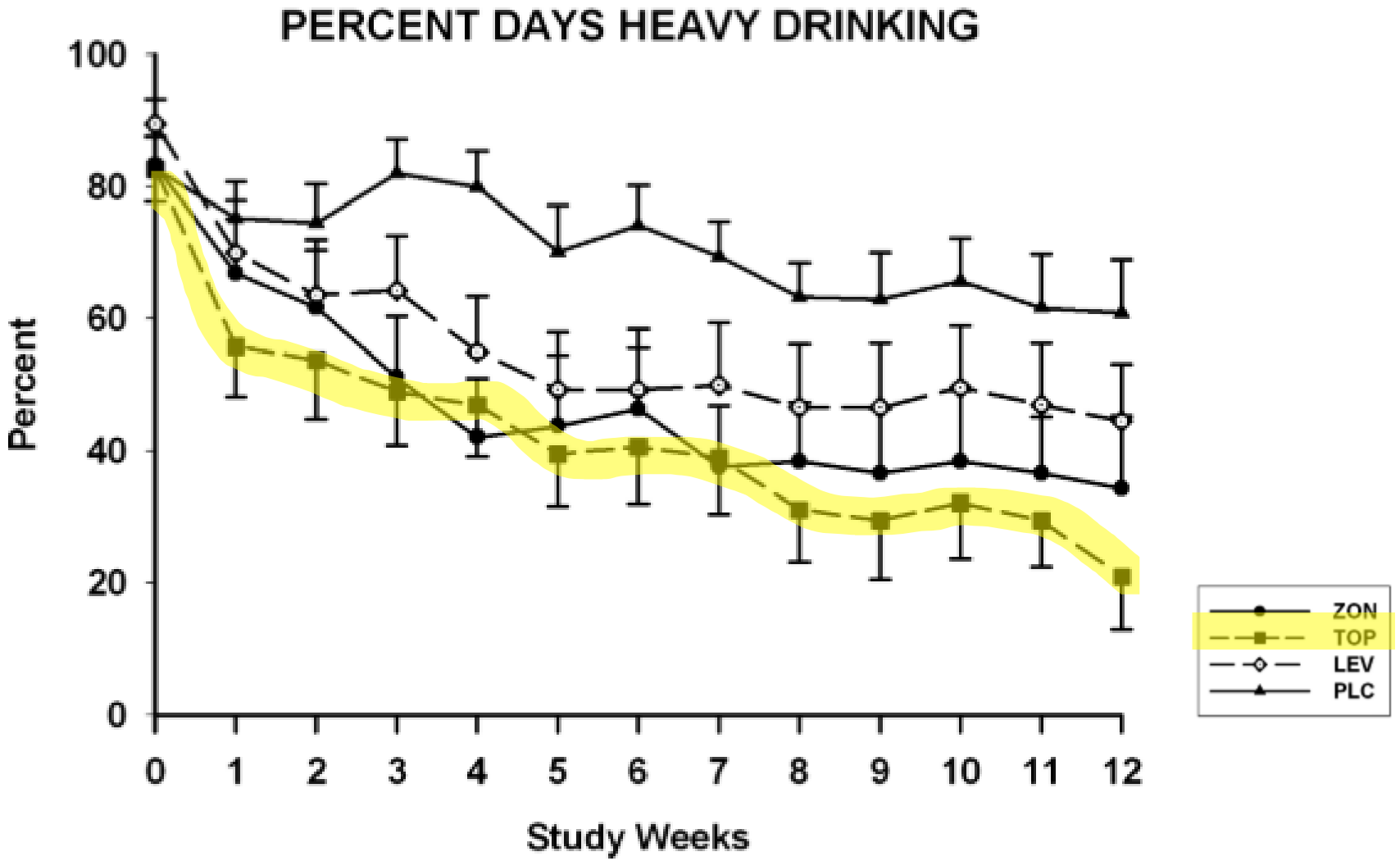
TOPIRAMATE AND CONTROLLED DRINKING



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TOPIRAMATE AND CONTROLLED DRINKING

PRIMARY OUTCOME — REDUCTION IN DRINKING

DRINKING DAYS / WEEK

BEFORE → AFTER

90% → 50%

▼ −40 pts

DRINKS PER DAY

BEFORE → AFTER

10 → 4

▼ −60%

HEAVY DRINKING DAYS / WK

BEFORE → AFTER

80% → 30%

▼ −50 pts

✓ **ADDITIONAL EFFICACY** Reduced cravings · Lower GGT at end of study

SAFETY — NEUROTOXICITY (TOPIRAMATE & ZONISAMIDE)

⚠ **COGNITIVE IMPACT**

Reduced verbal fluency, verbal working memory, and visual memory — most notable in the final 2 weeks of the study.

✓ **PRESERVED**

No effect on executive function.

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TREATING AUD IN THE OUD CONTEXT

1. Start and stabilize meds for OUD
   - Shared Decision Making for MOUD
2. Baseline Liver and Kidney function tests
3. Abstinence vs Controlled Drinking?

MOUD: Bup or Methadone

Abstinence AUD Meds

- Topiramate
- Acamprosate (kidney)
- Disulfiram (liver)

MOUD: Bup or Methadone

Controlled Drinking AUD Meds

- Topiramate
- Acamprosate (kidney)

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PSYCHOSOCIAL SUPPORT FOR AUD AND OUD?

Contingency Management

- Systematic review of **74 RCTs** of CM for substance use
- **23 studies** tested CM for increasing abstinence from 2 or more drugs

Incentives for verified abstinence — one of the most consistently effective psychosocial treatments for substance use.

70%

of those studies (16 of 23) showed increased abstinence at end of treatment

Bolívar HA, Klemperer EM, Coleman SRM, DeSarno M, Skelly JM, Higgins ST. Contingency Management for Patients Receiving Medication for Opioid Use Disorder: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2021;78(10):1092–1102. doi:10.1001/jamapsychiatry.2021.1969

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EVIDENCE GAP: PSYCHOSOCIAL SUPPORTS FOR CO-OCCURRING OUD AND AUD

- **Engage in evidence-based approaches for AUD**
  - 12 Step facilitation
  - CBT
  - Community Reinforcement

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SUMMARY

- Treat both simultaneously
- Do not withhold MOUD even if actively drinking
- IM Naltrexone is not the overwhelming choice for treatment. Buprenorphine and Methadone have some advantages.
- Options for medications for AUD can vary depending on patient goals and MOUD
- CM has the best extrapolated data for psychosocial support, but otherwise focus on psychosocial supports for AUD

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