Medications for Alcohol Use Disorder

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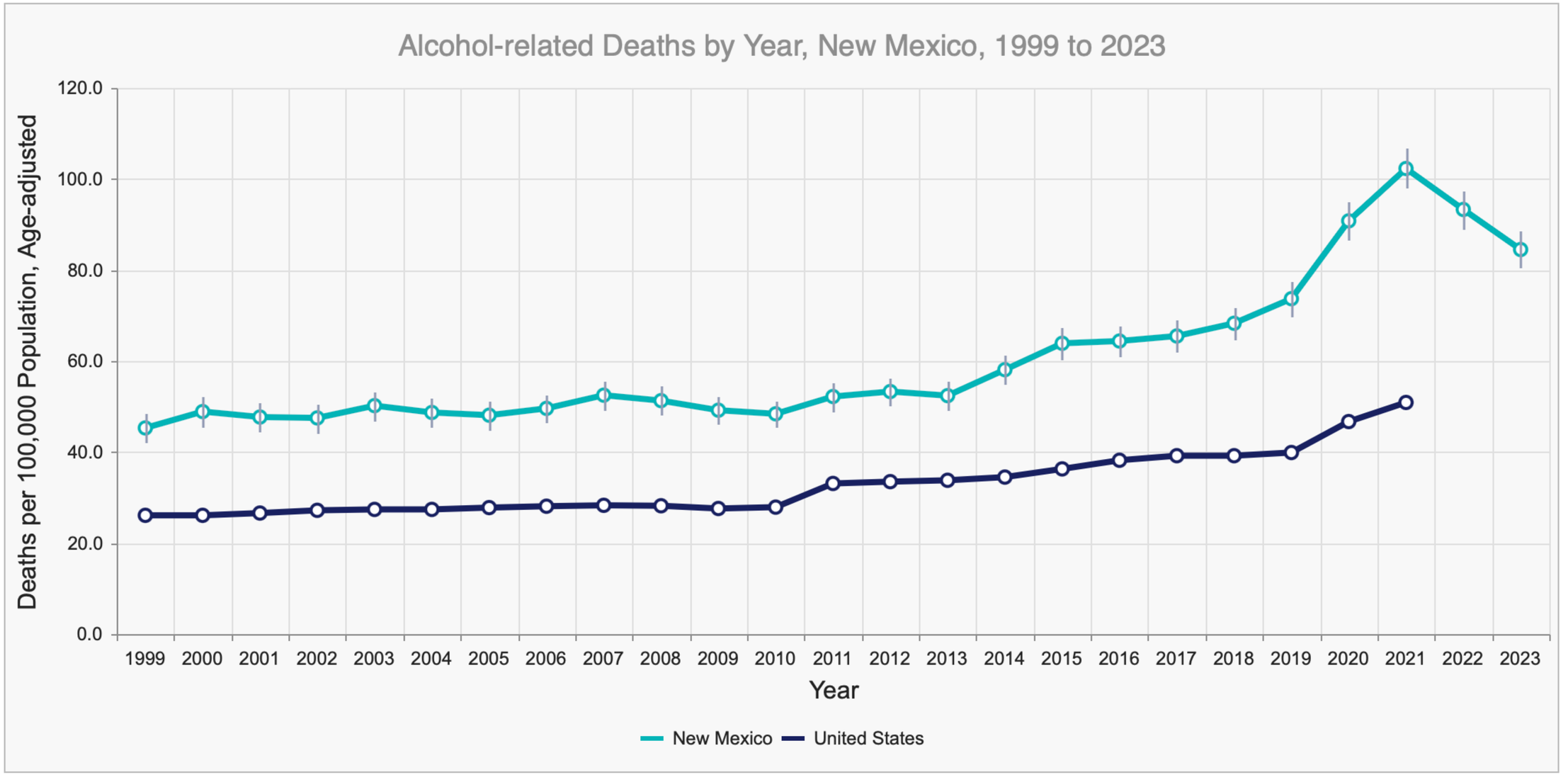
Disclosures

Nothing to disclose

Learning Objectives

At the conclusion of this activity, participants should be able to:

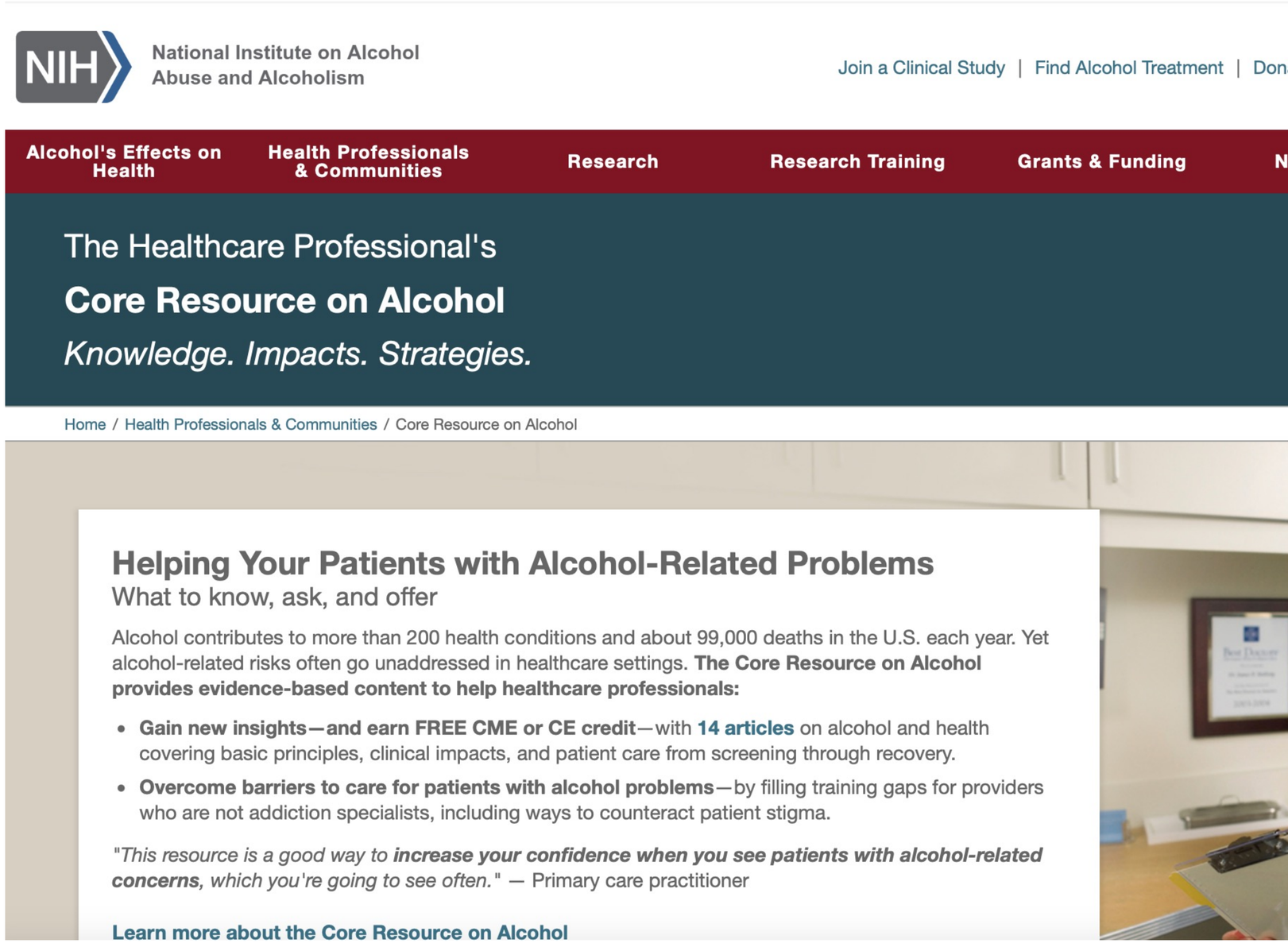
- Identify the FDA-approved and off-label medications for alcohol use disorder.
- Apply treatments to appropriate cases.



https://ibis.doh.nm.gov/indicator/view/AlcoholRelatedDth.Year.NM_US.html

The Healthcare Professional's Core Resource on Alcohol

https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol



NIAAA single item screening question

“How many times in the past year have you had (4 for women, 5 for men) or more drinks in a day?”

A response of one or more warrants follow-up.

NIAAA has additional resources for screening tools that may be appropriate for adolescents and people from diverse backgrounds

AUDIT-C (consumption)

Each question is worth 0-4 points
Positive Screen: 4 points or more for men
3 points or more for women

1. **How often do you have a drink containing alcohol?**
   - ☐ Never
   - ☐ Monthly or less
   - ☐ 2-4 times a month
   - ☐ 2-3 times a week
   - ☐ 4 or more times a week

2. **How many standard drinks containing alcohol do you have on a typical day?**
   - ☐ 1 or 2
   - ☐ 3 to 4
   - ☐ 5 to 6
   - ☐ 7 to 9
   - ☐ 10 or more

3. **How often do you have six or more drinks on one occasion?**
   - ☐ Daily or almost daily
   - ☐ Weekly
   - ☐ Monthly
   - ☐ Less than monthly
   - ☐ Never

Bush K, Kivlahan DR, et al (1998). The AUDIT alcohol consumption questions (AUDIT-C): An effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Arch Intern Med. 158:1789-95.

Harm Reduction for Alcohol Use

World Health Organization

	World Health Organization Drinking Risk Levels (for males)			
	Low Risk	**Medium Risk**	**High Risk**	**Very High Risk**
Drinks per day (in grams)	1 to 40 g	41 to 60 g	61 to 100 g	101+ g
Drinks per day (U.S. standard drinks, 14 grams)	0 to 3 drinks	3 to <4 drinks	4 to 7 drinks	7+ drinks
Drinks per week (U.S. standard drinks, 14 grams)	0 to 20 drinks	21 to 30 drinks	31 to 50 drinks	51+ drinks

	World Health Organization Drinking Risk Levels (for females)			
	Low Risk	**Medium Risk**	**High Risk**	**Very High Risk**
Drinks per day (in grams)	1 to 20 g	21 to 40 g	41 to 60 g	61+ g
Drinks per day (U.S. standard drinks, 14 grams)	0 to 1 drinks	2 to <3 drinks	3 to <4 drinks	4+ drinks
Drinks per week (U.S. standard drinks, 14 grams)	0 to <10 drinks	10 to <20 drinks	20 to 30 drinks	31+ drinks

84% of patients achieved one-level reductions at end of treatment, and 85% of those patients maintained that reduction at 3-year follow-up.

68% of patients achieved two-level reductions at end of treatment, and 77% of those patients maintained that reduction at 3-year follow-up.

Witkiewitz K, Falk D, Litten R, et al. Maintenance of World Health Organization Risk Drinking Level Reductions and Posttreatment Functioning Following a Large Alcohol Use Disorder Clinical Trial. *Alcohol Clinical and Experimental Research.* May 2019;43(5):979-987.

Standard Drink

A 12-ounce can of ordinary BEER

A 5-ounce glass of WINE or a 2–4-ounce glass of SHERRY

A 1.5-ounce shot of SPIRITS (whiskey, gin, rum, vodka, etc.)

1 pint of liquor ~ 8 drinks
1 fifth (1/5 gal) of liquor ~ 17 drinks
1 handle (1/2 gal) of liquor ~ 60 drinks

Coors Light = 4.3%
Budweiser = 5%
Desert Fog Hazy IPA = 6.8%
Mass Ascension IPA = 6.9%
Bosque Scotia = 8.4%

16oz glass of 6.8% IPA = 1.7 standard drinks

National Institute on Alcohol Abuse and Alcoholism:
https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking

Medications for AUD

MEDICATION	MECHANISM	SUBJECTIVE EFFECT	CIRRHOSIS *	CO-OCCURRING OUD	HOW TO START MEDICATION
Naltrexone	Mu opioid receptor antagonist	Decreases craving & Decreases euphoria	Use caution if AST/ALT are more than 5x ULN. OK if compensated cirrhosis. Avoid in decompensation.	AVOID if opioid dependent OK of no longer physiologically dependent	Can be started while patient is still drinking **50mg PO QAM, some patients increase to 100mg QAM** Most studied and most commonly used medication for alcohol use in pregnancy
Topiramate (Topamax)	Affects Glutamate and GABA transmission	Decreases craving Decreases anxiety	OK to use — — — Primarily renal excretion Hepatic dosing not defined	OK to use	Can be started while still drinking ; Can reduce anxiety Downside: Nephrolithiasis is relative contraindication Do not use in pregnancy (teratogenesis risk) **25mg PO BID x 1 week, then 50mg PO BID;** **can increase to 100mg BID**
Long-Acting Injectable Naltrexone **(Vivitrol)**	Mu opioid receptor antagonist	Decreases craving & Decreases euphoria	Use caution if AST/ALT are more than 5x ULN OK if compensated cirrhosis. Avoid in decompensation.	AVOID if opioid dependent OK of no longer physiologically dependent	Can be started while patient is still drinking **Establish PO tolerability first, then Rx 380mg IM Q4 weeks**
Acamprosate **(Campral)**	Affects Glutamate and GABA transmission	Decreases craving	OK to use — — — Primarily renal excretion No adjustment in class A or B Class C dosing not defined	OK to use	Start ASAP after withdrawal when abstinence achieved Continue even if relapse **666mg PO TID**
Disulfiram **(Antabuse)**	Acetaldehyde dehydrogenase inhibitor	Nausea, vomiting, headache and vasomotor symptoms if consuming alcohol	AVOID (Liver metabolized and hepatotoxic)	OK to use	Patient must be abstinent from alcohol This medication is for very motivated patients Most effective when given by supportive other **500mg PO QAM**
Baclofen	GABA B receptor agonist	Decreases craving Greater ratings of feeling high and intoxication after alcohol intake **	**Most studied medication for use in advanced disease.** **OK to use in AH or cirrhosis.**	Use with caution due to additive CNS depressant effects	Start 5mg TID, then increase Increase by 5mg at 3-5 day intervals **Maximum dose 15mg TID**
Gabapentin (Neurontin)	GABA receptor agonist	Decreases craving Decreased anxiety	OK to use — — — — No Adjustment	Use with caution due to additive CNS depressant and overdose risk	Can be started while still drinking Can reduce anxiety More effective when added to Naltrexone Downside: has some abuse potential **300mg - 600mg PO TID**

* ACG Clinical Guideline: Alcohol-Associated Liver Disease. *American Journal of Gastroenterology* January 2024;119(1):30-54. DOI: 10.14309/ajg.0000000000002572

** Farokhnia M, et al. Biobehavioral effects of Baclofen in anxious alcohol-dependent individuals. Translational Psychiatry. April 2019;e1108 https://doi.org/10.1038/tp.2017.71

Naltrexone History

Black Box Warning

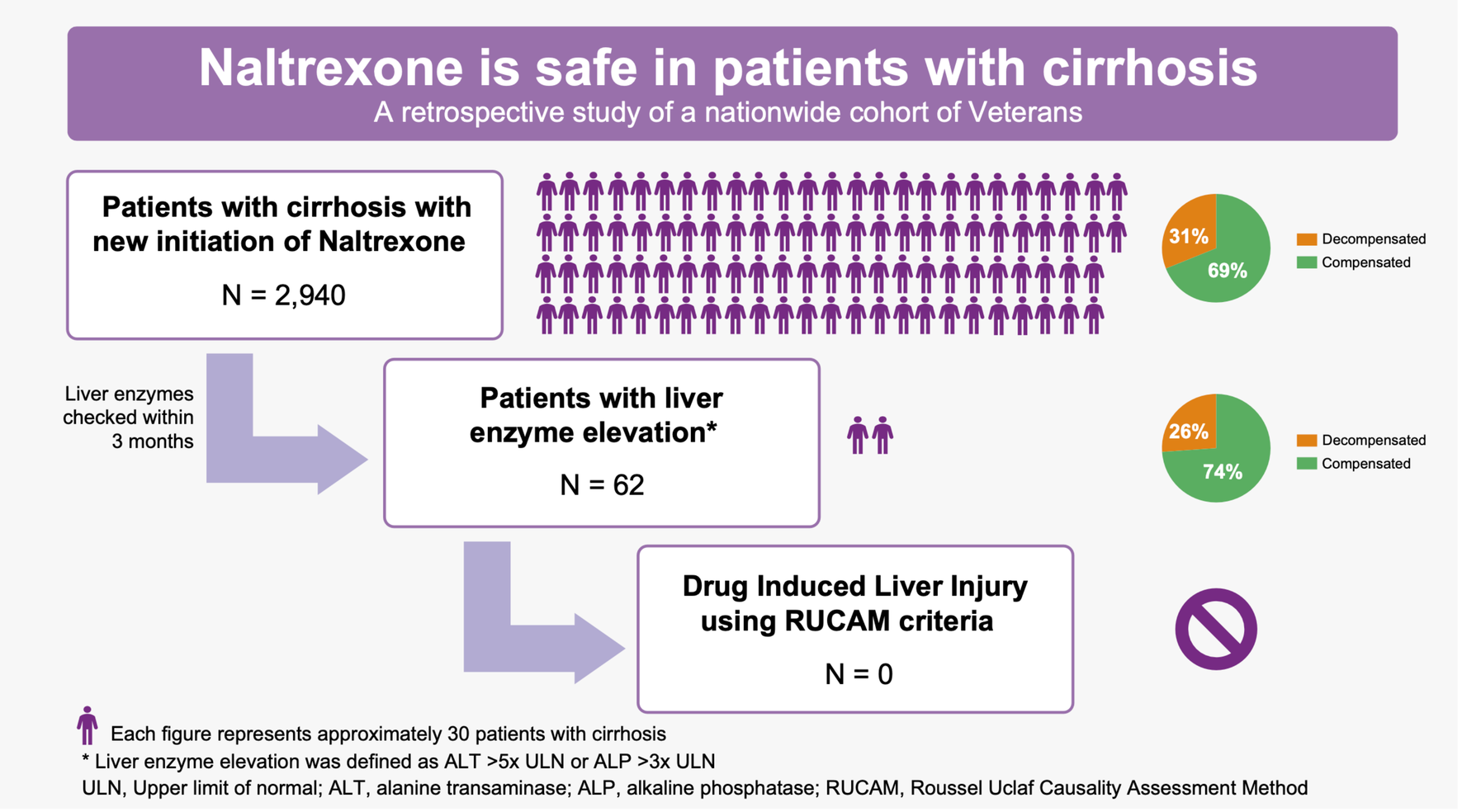
- Added in the 1980s due to asymptomatic liver transaminase elevations among patients taking high-dose naltrexone

- FDA **removed** the black box warning in 2013 due to lack of evidence of liver disease exacerbation

- American College of Gastroenterology still urges caution (in their 2024 update)

Naltrexone New Research

Does it cause transaminitis?



https://doi.org/10.1016/j.jhepr.2024.101095
Published by Elsevier B.V. on behalf of European Association for the Study of the Liver (EASL).
 JHEP Reports, 2024, 6, 1–5

Naltrexone New Research

Does it cause transaminitis?

- Largest study of Naltrexone's safety among patients with cirrhosis
- There was not a single case of drug induced liver injury
- Significant liver enzyme elevation occurred in 2%

A clear alternative cause was identified in 77% of these cases

- Median AST and ALT at follow-up decreased compared to baseline
- No deaths or new decompensations were attributed to Naltrexone

https://doi.org/10.1016/j.jhepr.2024.101095
Published by Elsevier B.V. on behalf of European Association for the Study of the Liver (EASL).

New Research for Topiramate (a repurposed medication)

Not FDA-approved for AUD

FDA-approved for seizures and migraines.
Also commonly used for weight loss (off-label).

Topiramate vs Naltrexone

Current 1st-line medication

FDA-approved for AUD

- 12-week, double-blind trial
- 147 Participants randomized to Topiramate vs Naltrexone

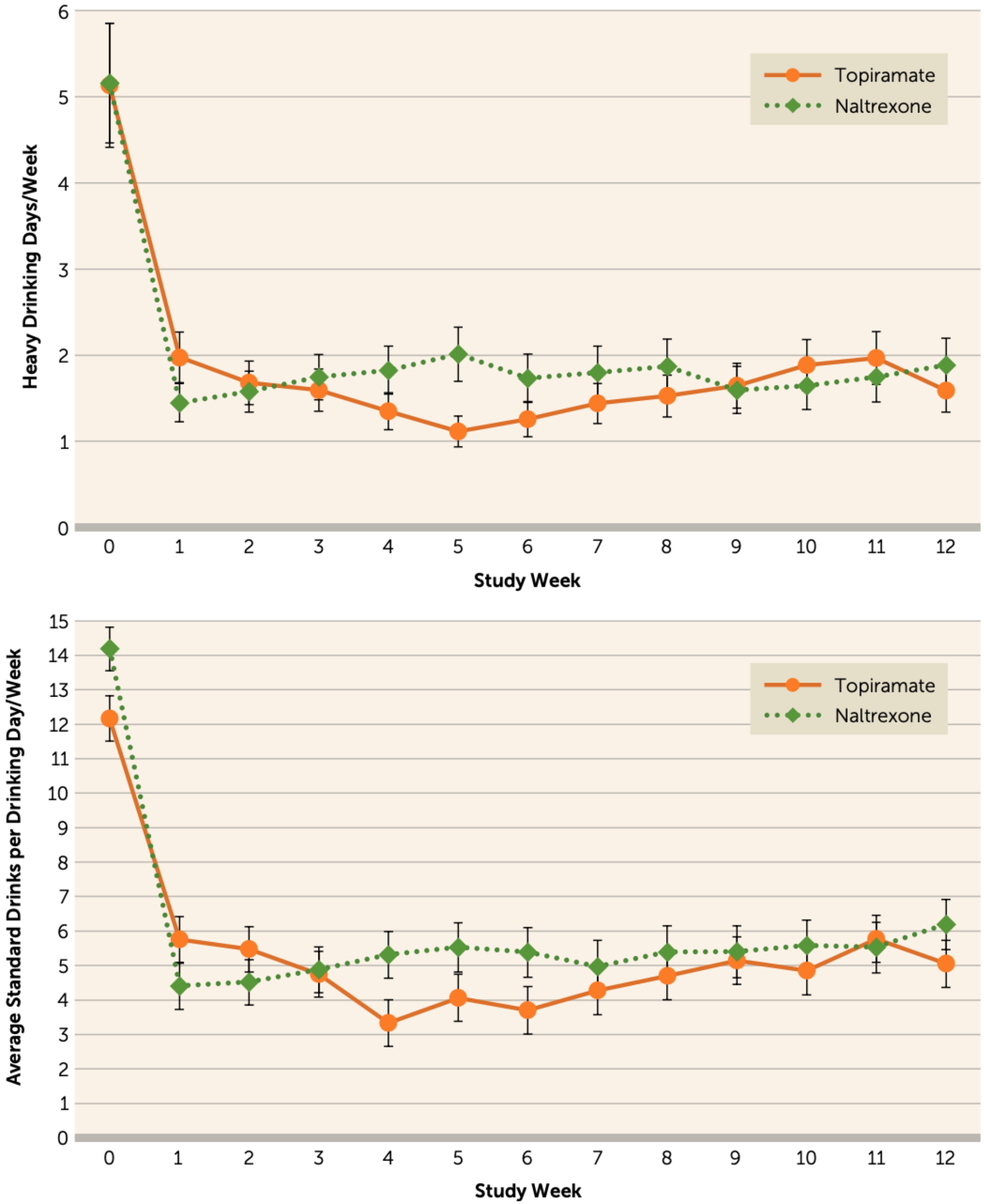
Results

1. Heavy drinking days per week: no difference
2. Topiramate led to fewer drinks per drinking day
3. Topiramate led to greater reduction in alcohol cravings and GGT level

4. Withdrawal due to side effects: Topiramate 8% Naltrexone 5%

Morley K, Kanzler H, Luquin N, et al. Topiramate Versus Naltrexone for Alcohol Use Disorder: A Genotype-Stratified Double-Blind Randomized Controlled Trial. **American Journal of Psychiatry** May 2024;181:5(403-410)

FIGURE 2. Heavy drinking days per week and average standard drinks per drinking day per week for participants treated with naltrexone or topiramate for 12 weeks (intention-to-treat analysis)[a]



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Prescribing Topiramate

- **Start 25mg BID, increase to 50mg BID after a week.**
- **Consider advancing to 100mg BID (after 2-4 weeks)**
- **Can be started while patient is still drinking.**
- **Cognitive and concentration problems more likely at doses >200mg daily.**
- **Induces metabolism of oral contraceptives at doses > 200mg daily.**
- **Teratogenic** (craniofacial defects, hypospadias).
- **Contraindicated if history of Calcium Phosphate renal stones (can recurrence)**
- **Warn about and monitor for side effects:**

Paresthesias (50%)	**Taste Change (23%)**
Decreased Appetite (20%)	**Decreased Concentration (15%)**

How is recovery defined?

Boness, Kuhlemeier, & Witkiewitz, (2022). Nonabstinent recovery from alcohol use disorder. *Psychiatric Times, 39*(5), 22-23.

- Definitions vary
- Recovery is a dynamic process, characterized by:
  - **Remission** from AUD symptoms
  - **Cessation** from heavy drinking
  - Improvements in physical health, mental health, relationships, spirituality, and other measures of well-being

Figure. **Domains and Subdomains in Definitions of Recovery From AUD**

References

- Rosner S, et al. Opioid antagonists for alcohol dependence. Cochrane Database Systematic Review, 2010
- Anton R, et al. Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence, The COMBINE Study: A randomized Controlled Trial , *JAMA* 2006; 295(17)
- Christensen C. Management of chemical dependence in pregnancy, *Clin Obstet Gynecol* 2008;51 (2): 445
- Rosner S, et al. Acamprosate for alcohol dependence. Cochrane Database Syst Rev. 2010.
- Laaksonen E, et al. A randomized, multicentre, open-label, comperative trial of disulfiram, naltrexone and acamprosate in the treatment of alcohol dependence. *Alcohol* 2008;43(1):53.
- Garbutt JC, et al. Pharmacological treatment of alcohol dependence: a systematic review of the evidence. *JAMA* 1999;281(14):1318.
- Kranzler H, et al. Naltrexone Depot for Treatment of Alcohol Dependence: A Multicenter, Randomized, Placebo-controlled Clinical Trial. *Alcoholism: Clinical and Experimental Research*. July 2004. 28(7): 1051-1059
- Mason, BJ. Gabapentin treatment for alcohol dependence: a randomized clinical trial. *JAMA Internal Med.* 2014, 174(1):70
- Anton R, et al. Gabapentin Combined with Naltrexone for the Treatment of Alcohol Dependence. *American Journal of Psychiatry* 2011;168(7):709-717
- Johnson BA, et al. Oral Topiramate for treatment of alcohol dependence: a randomized controlled trial. *Lancet* 2003; 361(9370):1677.
- Baltieri DA, et al. Comparing Topiramate with Naltrexone in treatment of alcohol dependence. *Addiction* 2008; 103(12):2035
- Batki S, et al. Topiramate Treatment of Alcohol Use Disorder in Veterans with PTSD: A Randomized Controlled Pilot Trial. *Alcoholism: Clinical and Experimental Research* 2014;38(8)

Thank you for what you do!

Q&A