Substance Use Disorders

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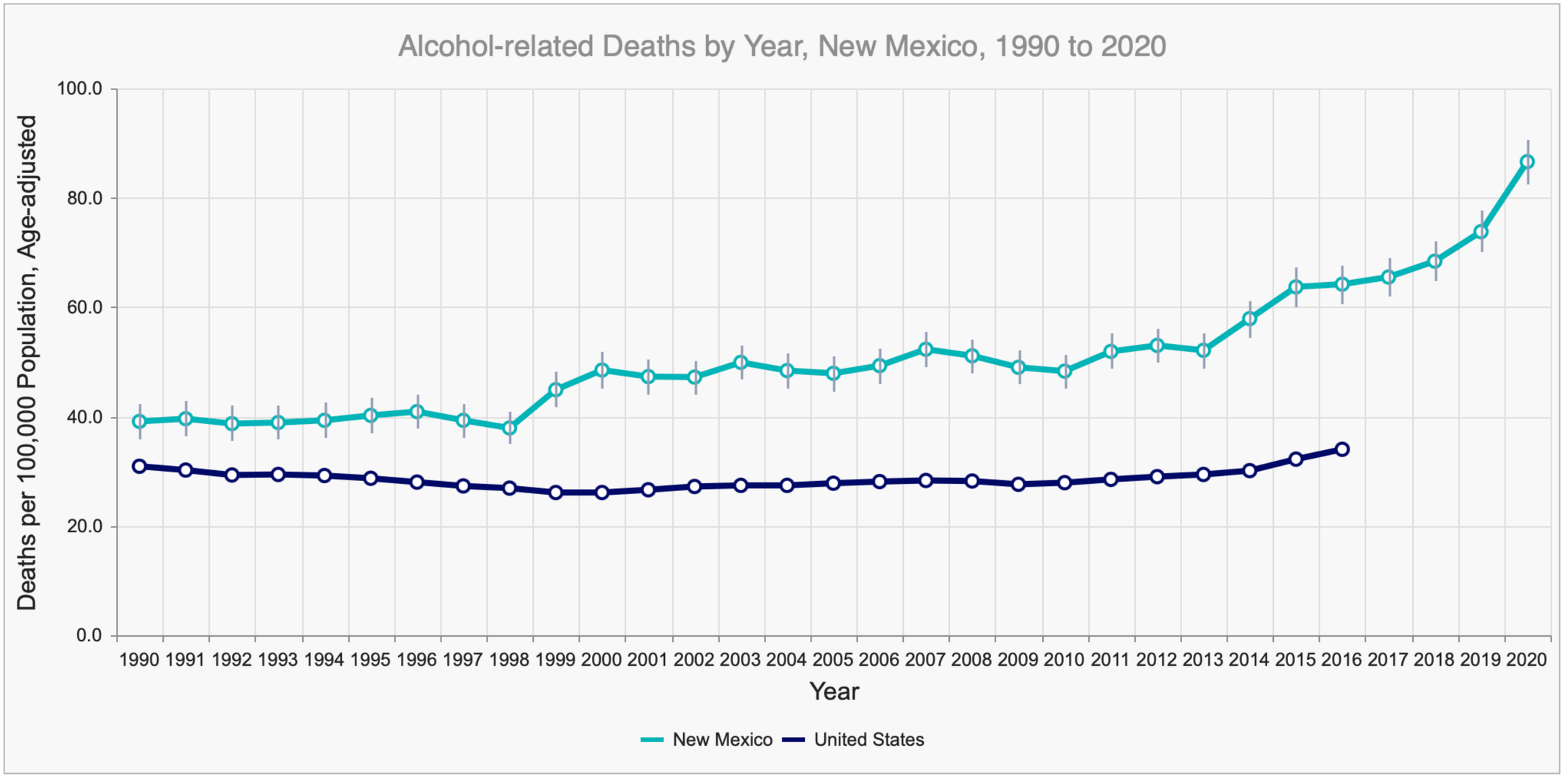
Disclosures: nothing to disclose

Learning Objectives:

- Be able to discuss new research comparing Naltrexone and Topiramate
- Be able to discuss new research regarding Nalrexone’s safety in context of cirrhosis



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

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

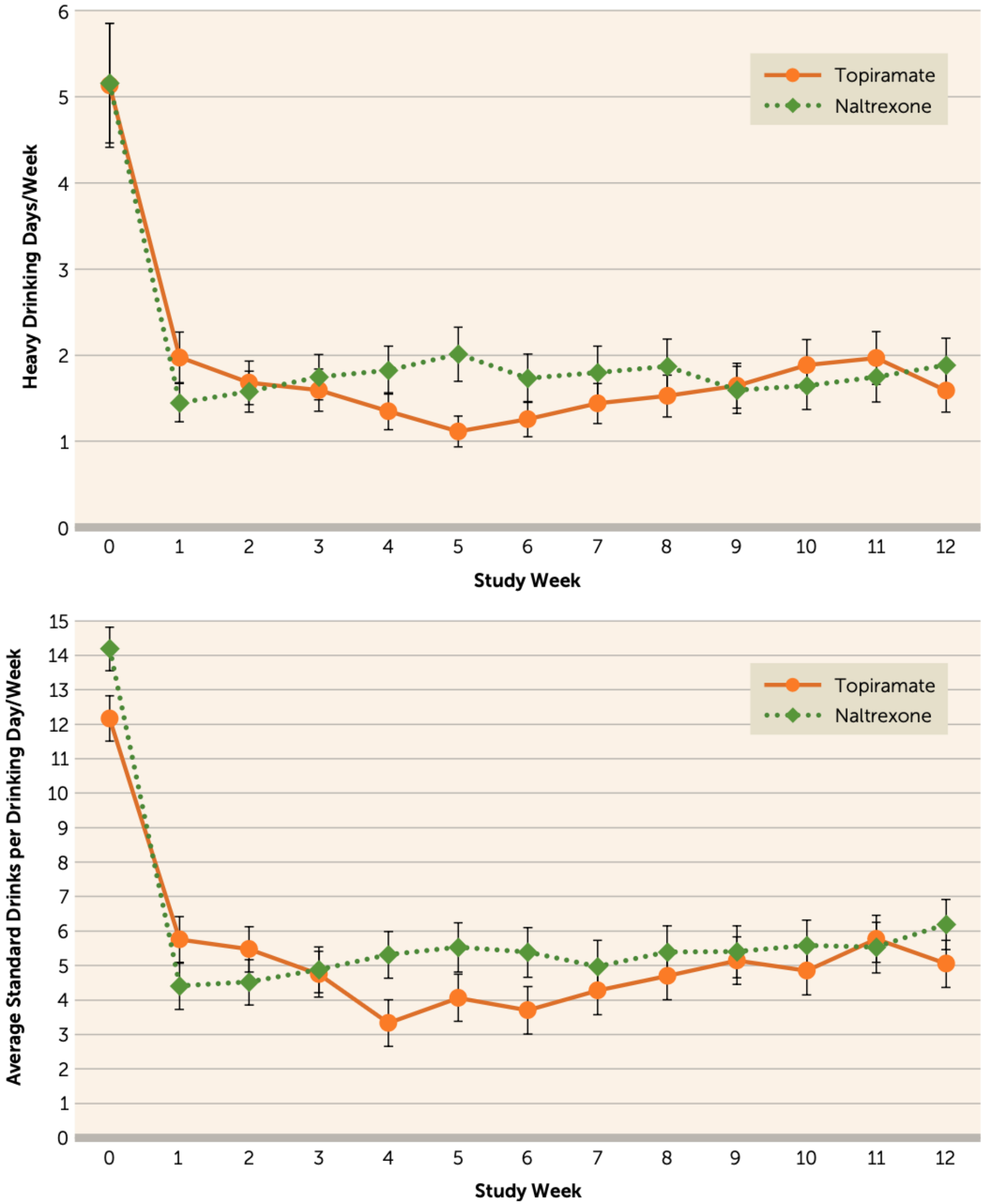
Results

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. Discontinuation due to side effects: Topiramate 8% Naltrexone 5%
   (taste disturbance, paresthesias in extremities)

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 hormonal contraception at doses > 200mg daily.**
- **Teratogenic** (craniofacial defects, hypospadias).
- **Contraindicated if history of Calcium Phosphate renal stones (can cause recurrence)**
- **Warn about and monitor for side effects:**

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

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

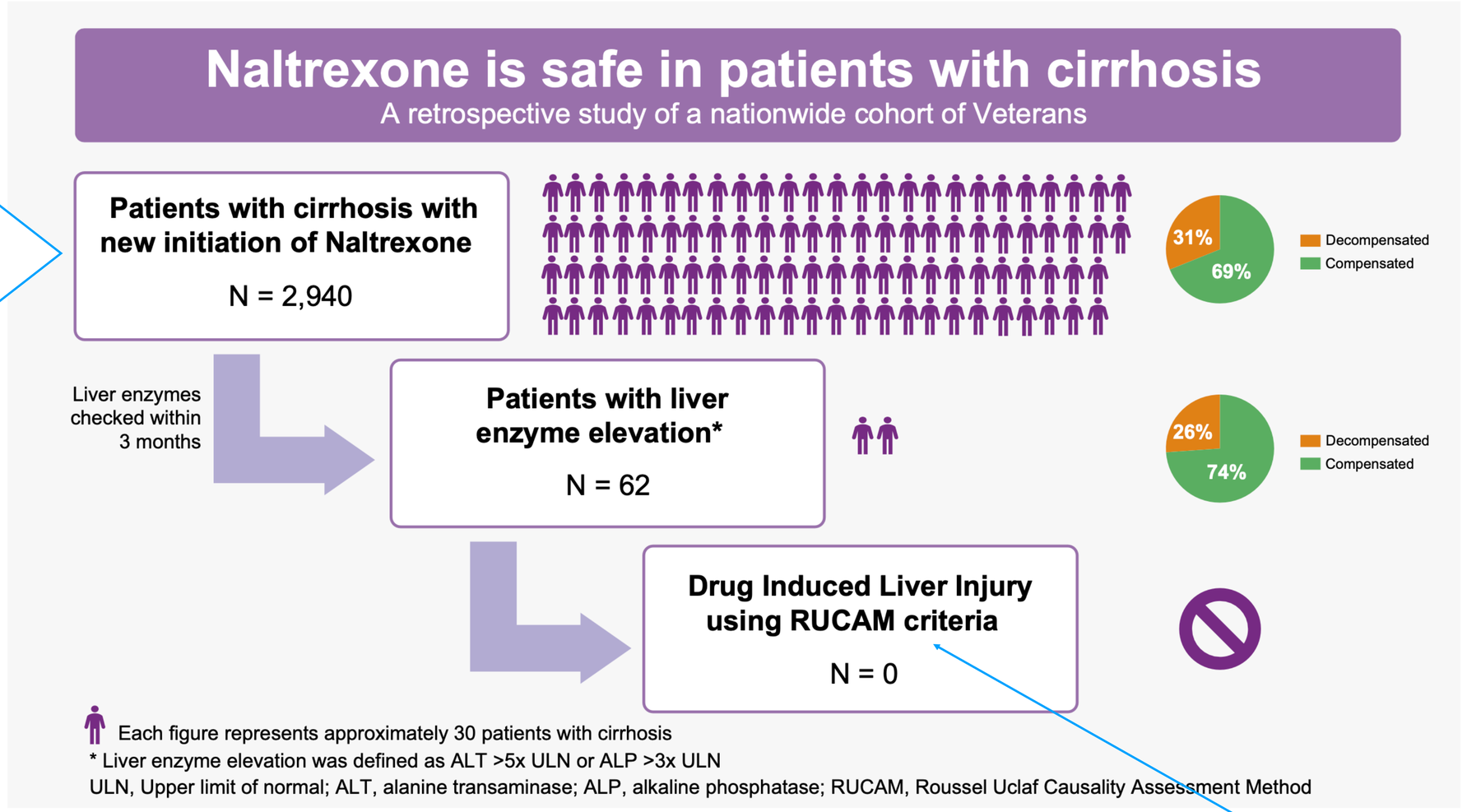
- American College of Gastroenterology still urges caution (in their 2024 update)

Naltrexone New Research

Does it cause transaminitis?

3,285 patients with Cirrhosis were started on Naltrexone

89% (n=2,940) had follow up within high risk period



Roussel Uclaf Causality Assessment Method

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

https://doi.org/10.1016/j.jhepr.2024.101095
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