Beyond CIWA: Hospital-based opportunities for improving care in AUD

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Disclosures

- None

Objectives

Describe the available medications for alcohol use disorder (MAUD), and contrast their mechanisms, indications, and practical considerations for their use

Recognize the current care gap in prescribing MAUD, including barriers to utilization and disparities in access

Apply strategies to improve outcomes through hospital-based initiation of evidence-based treatment

Mr L

- 48 yo gentleman admitted to you overnight for acute alcohol withdrawal
- PMHx includes: HTN, HLD, chronic pain
- Smokes tobacco, 1ppd

Other than treating his withdrawal, how can we alter the trajectory of his disease before he leaves the hospital?

Our urgent issue

Alcohol use as a growing problem affecting our patients

Alcohol Use Disorder (AUD) in the United States

28 million

or **1 in 10**

people ages 12 and older had AUD in 2024.

Source: 2024 NSDUH

Impact of Alcohol and Opioids in the United States

Alcohol

Past-Year Use
% of population
178,687,000
62%

Alcohol Use Disorder (AUD)
% of population
27,913,000
10%

Emergency Department Visits
4,274,523
All alcohol-related, annual average 2016-2021

Hospitalizations
1,987,498
All that list alcohol, annual average 2016-2021

527,122
Primarily for alcohol, annual average 2016-2021

Deaths*
178,307
Average annual 2020-2021 deaths

61,063 Acute (e.g., injury)
117,245 Chronic (e.g., liver disease)

Opioids

Past-Year Misuse
% of population
7,795,000
2.7%

Opioid Use Disorder (OUD)
% of population
4,822,000
1.7%

Emergency Department Visits
2,149,474
All opioid-related, annual average 2016-2021

Hospitalizations
1,400,019
All that list opioids, annual average 2016-2021

119,311
Primarily for opioids, annual average 2016-2021

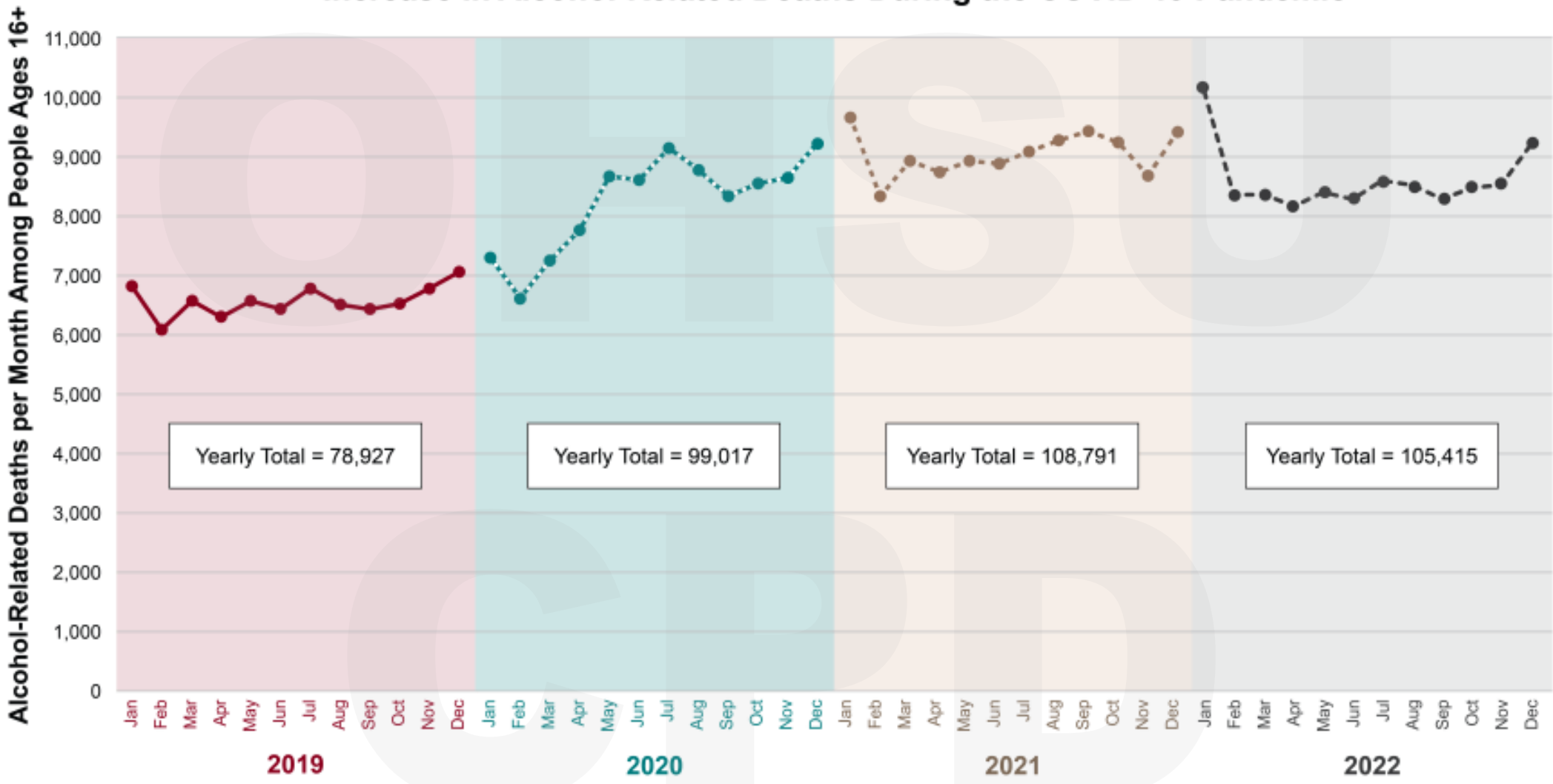
Deaths*
74,521
Average annual 2020-2021 overdose deaths

63,559 Synthetic Opioids
11,169 Heroin
14,716 Rx Opioids

Sources: 2024 NSDUH Tables 1.1A&B, 2.1A&B, 1.1A&B, 5.1A&B; 2021 HCUP-NEDS; 2020–2021 CDC ARDI; 2022 NIDA Drug Overdose Death Rates.

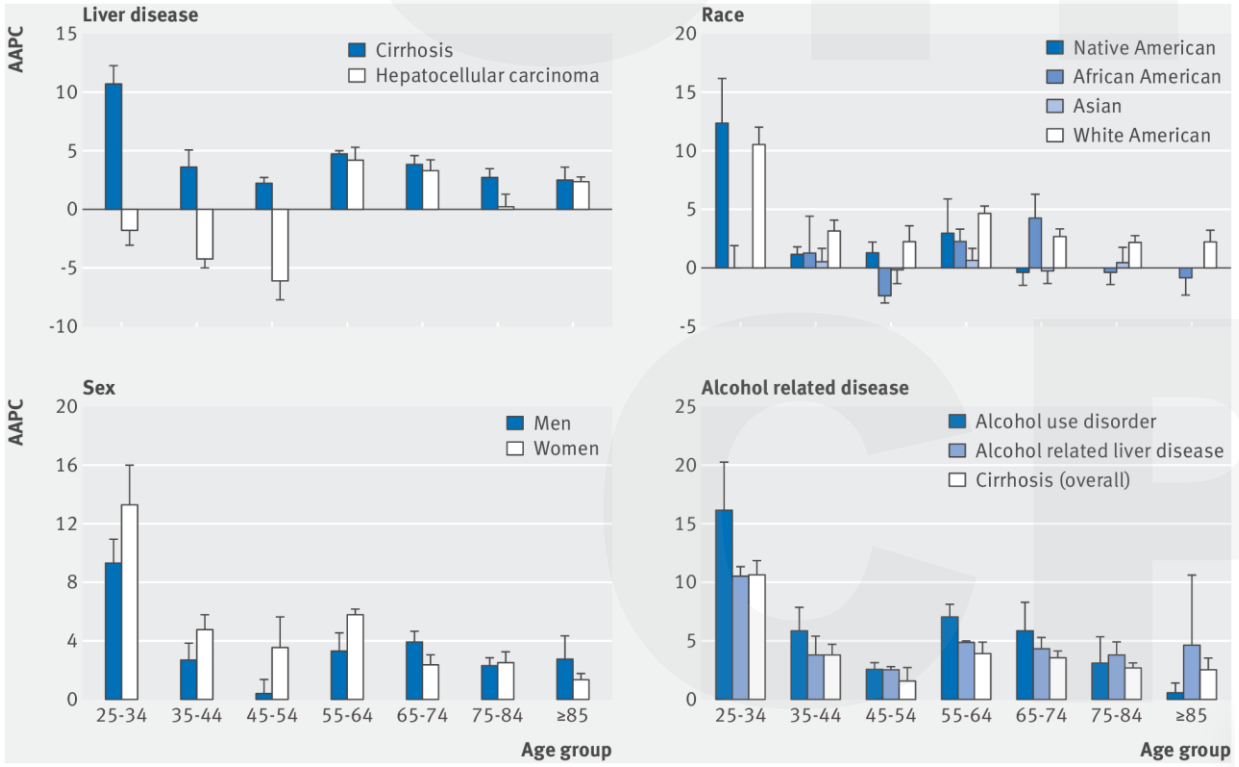
* Acute and chronic alcohol-related deaths do not add to the total due to rounding. Note that the values for the three opioid types sum to more than the total because some deaths involve multiple types of opioids.

Increase in Alcohol-Related Deaths During the COVID-19 Pandemic



Source: CDC WONDER 2024.

AUD morbidity trending fastest in youngest cohort



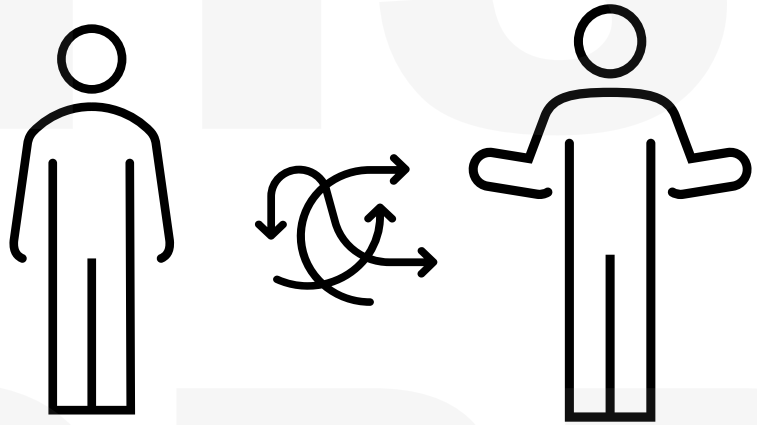
- Increasing incidence in <35
- Challenges assumptions of duration of exposure required to develop illness
- Potential causes?

Safer use strategies (Harm Reduction)

CBT and skills-based counseling

Mutual Aid (AA, SMART, Refuge Recovery, Dharma)

Counselor-led group therapy



Trained Peer Support Specialists

Residential Treatment

Meaningful / purposeful activity

Pharmacotherapy

A “Care Gap”

- <10% receive treatment
  - **<5% Rx'd MAUD**
- Non-white identity and lower SES less likely to receive medications
- **"Lack of knowledge"** the #1 barrier cited among providers and patients

Hospitalization is a vital opportunity

- "Reachable moment" with interrupt a cycle
- Start a conversation, introduce / normalize treatment
- Initiate life-saving therapy

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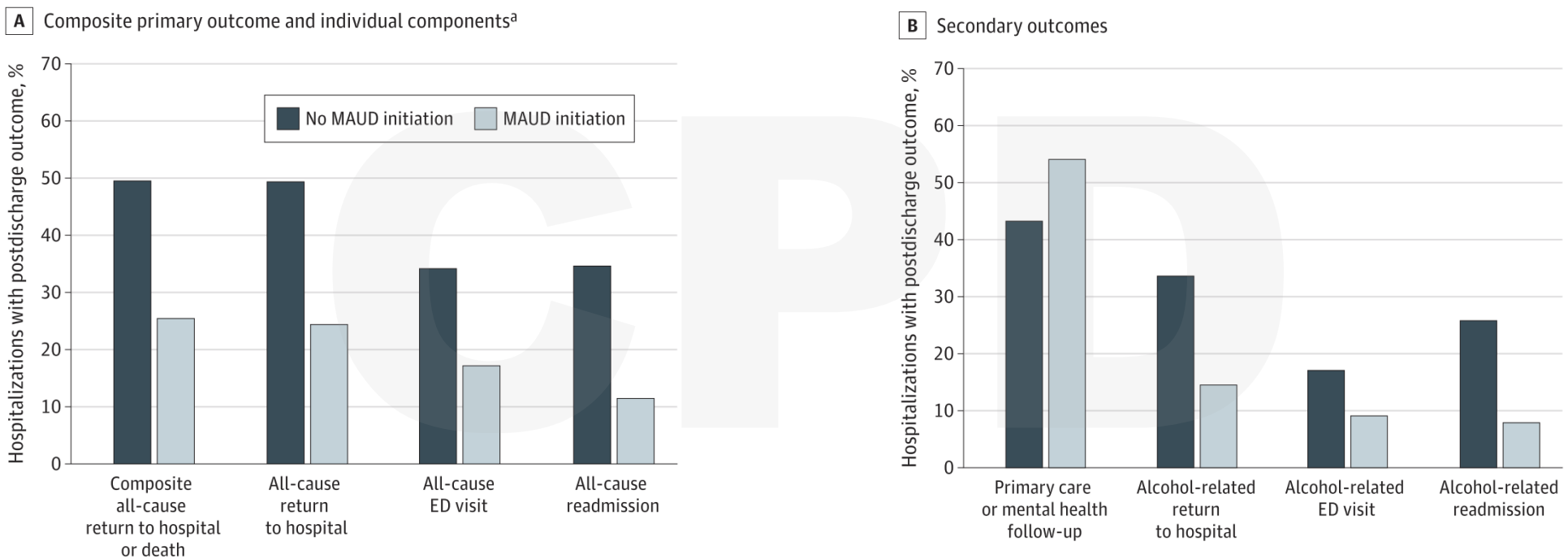
Original Investigation | Substance Use and Addiction

Outcomes After Initiation of Medications for Alcohol Use Disorder at Hospital Discharge

Eden Y. Bernstein, MD; Travis P. Baggett, MD, MPH; Shrunjal Trivedi, MPH; Shoshana J. Herzig, MD, MPH; Timothy S. Anderson, MD, MAS

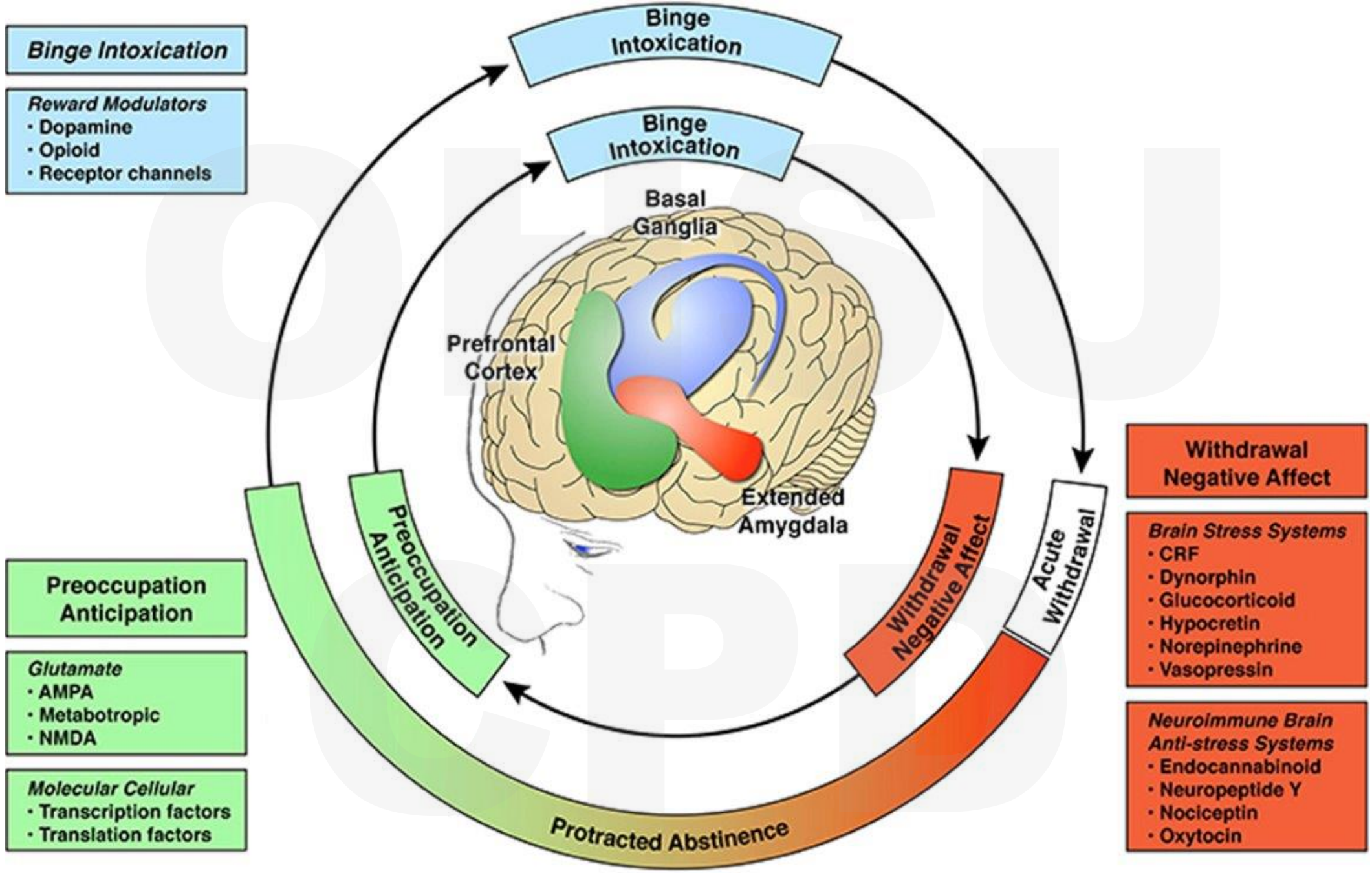


Back to Mr L

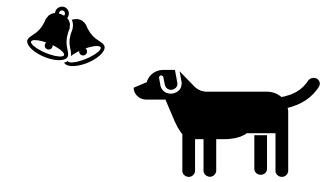
- How would you start the conversation about alcohol-use and treatment
- If he is interested, what medication would you offer and why?

Medication as treatment

Overview of MOUD options



Novel targets by stage of the alcohol use disorder cycle with corresponding clinical states. Adapted by permission from Macmillan Publishers Ltd: NEUROPSYCHOPHARMACOLOGY (Koob GF, Volkow ND. Neuropsychopharmacology 2009;35:217-38), copyright 2009.



Disulfiram

Ethanol

B-endorphins

Glutamate

GABA

Naltrexone

Acamprosate

Topiramate

Gabapentin

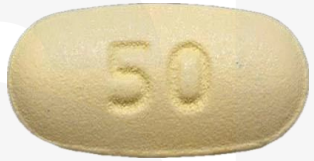
Baclofen

The *ACTION* molecule!

Dopamine

"Post-acute" withdrawal

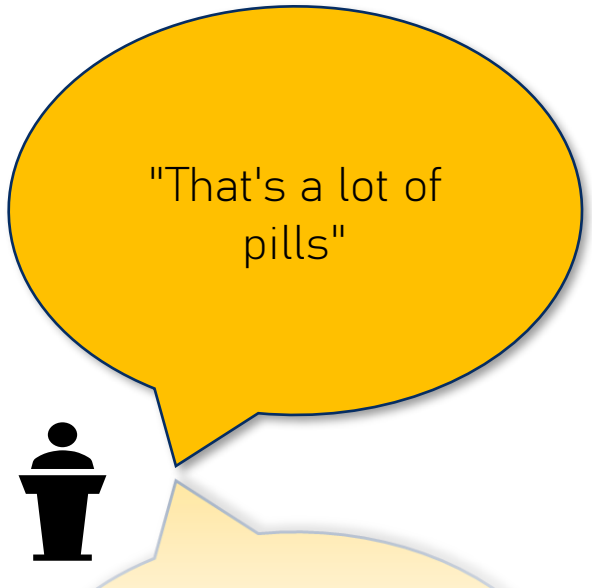
Naltrexone



- Opioid-receptor ***antagonist***
- **Once-daily** pill or **once-monthly** IM injection
- Effective to *decrease* drinking
  - NNT 11 for less heavy drinking days
  - NNT 18 to maintain abstinence
- Clinical pearl: Start at ½ dose for up to 1 week and ramp to avoid a/e (nausea)
- Shown effective across a wide range of compulsive/addiction disorders

This is the workhorse!

Acamprosate



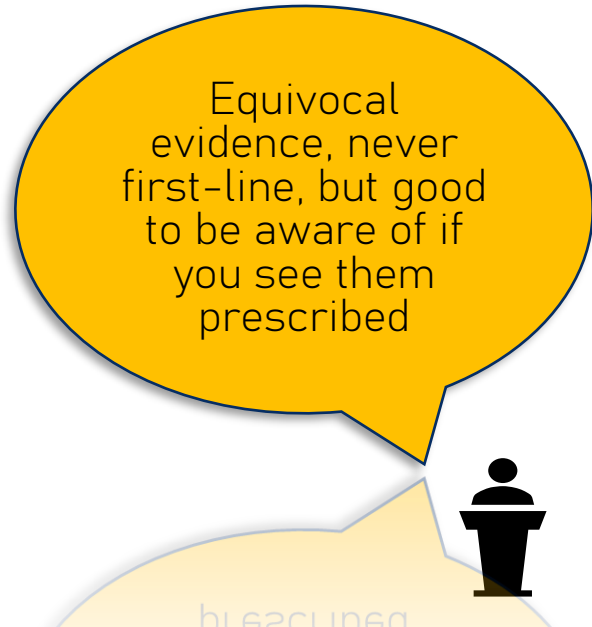
- NMDA-receptor antagonist
  - Regulates overactive *glutamate*
- Two-tablets, **three-times-daily**
- Effective only to ***maintain*** abstinence
  - Best initiated *after* stopping drinking
  - NNT of 11!
- Most common s/e diarrhea
  - Often improves with time, can decrease dose
- Role in post-acute withdrawal?

A word on disulfiram

- Aversive therapy uses classical conditioning to shape behavior
  - Aldehyde dehydrogenase inhibitor
  - Build up of **acetaldehyde = headache, nausea, malaise**
    - **"Like a hangover"**
- Highly effective in appropriately selected patients
- Risk of drug-induced liver damage
  - Avoid in any chronic liver disease
  - Monitor LFTs!

Off-label

- Gabapentin
  - Effective only those who have had significant withdrawal
    - Regulates glutaminergic system?
    - Adjunct for symptoms of acute withdrawal
  - Chronic use may increase risk of future withdrawal
- Baclofen
  - RCT of patients with cirrhosis -> maintained abstinence
  - More risk sedation, carries risk of withdrawal itself
- Topiramate
  - Effective to both decrease drinking and maintain abstinence
  - Many adverse effects



Medication	Mechanism	Typical Dose	Contraindications	Best Use Cases	Pearls
Naltrexone (PO, IM)	μ-opioid receptor antagonist → ↓ reward from alcohol	PO: 50 mg daily; IM: 380 mg q4w	Active opioid use, acute hepatitis / severe LFT elevation / *Childs-Pugh C cirrhosis*	Patients with intact liver, not on opioids	Strongest evidence; IM option aids adherence
Acamprosate	Glutamate/GABA modulation → ↓ craving, pro-abstinence	666 mg TID	Severe renal impairment (CrCl <30)	Cirrhosis, hepatic dysfunction	Pill burden is a barrier, unique mechanism
Disulfiram	Inhibits aldehyde dehydrogenase → aversive reaction with alcohol	125-250 mg daily (optional 500mg/day x1-2 week load)	Poor adherence, chronic cardiopulmonary disease, decompensated cirrhosis	Highly motivated patients	Requires close monitoring (LFTs), counseling, and buy-in
Gabapentin (off-label)	GABA analog → ↓ craving, improves sleep/anxiety	300–600 mg TID	Severe renal impairment, sedation risk	AUD + insomnia/anxiety or pain	Some RCT support; helpful adjunct (post-acute withdrawl?)
Topiramate (off-label)	Glutamate/GABA modulation	Start at 25-50mg/day, up to max 400mg daily	Cognitive side effects, renal impairment, hepatic impairment	AUD + comorbid migraines/obesity	Evidence for ↓ heavy drinking days as well as abstinence
Baclofen (off-label)	GABA-B agonist → ↓ craving	5-15mg TID	Renal impairment, sedation	Cirrhosis, unable to tolerate other MAUD	Data strongest in cirrhosis, but some increase hospitalizations with those with Childs-pugh B-C

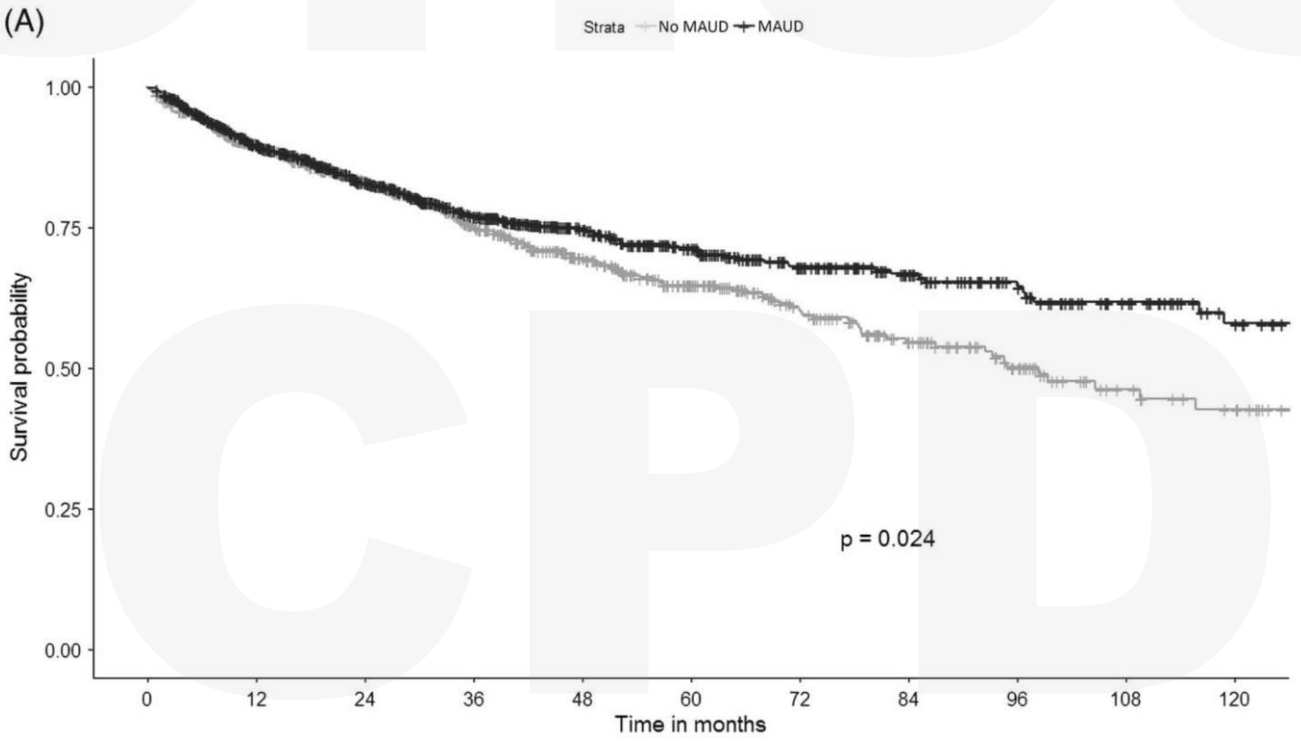
Meds for Mr L

- You choose naltrexone and initiate therapy the day prior to discharge
- How would you council Mr L on the medication choice and monitoring

MAUD in ALD

Special considerations in alcohol-related liver disease

There is a clear benefit to MAUD in ALD



Myth vs Reality: Naltrexone hepatotoxicity

ARGUMENT FOR

- Significant elevation seen only with high doses
  - >300mg day
  - Subsequent evals have not repeated findings
- Prospective analyses (*without ALD**) at typical dosing showed no significant hepatoxicity
- Retrospective analysis of those ***with ALD*** have shown safety at typical doses
- No putative hepatotoxic mechanism
  - Unclear if LFT elevation is sign of true liver injury

ARGUMENTS AGAINST

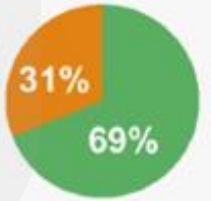
- No ***prospective*** data with advanced ALD
- Highly fragile substrate
  - Goal to avoid *potential* hepatotoxins
- Alternative options exist

Naltrexone is safe in patients with cirrhosis

A retrospective study of a nationwide cohort of Veterans

Patients with cirrhosis with new initiation of Naltrexone

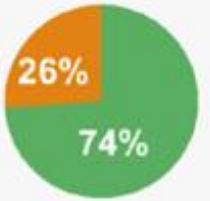
N = 2,940



Liver enzymes checked within 3 months

Patients with liver enzyme elevation*

N = 62



Drug Induced Liver Injury using RUCAM criteria

N = 0

Each figure represents approximately 30 patients with cirrhosis

* Liver enzyme elevation was defined as ALT >5x ULN or ALP >3x ULN

ULN, Upper limit of normal; ALT, alanine transaminase; ALP, alkaline phosphatase; RUCAM, Roussel Uclaf Causality Assessment Method

Naltrexone – the final word?

- At typical doses, *likely very* safe in ALD
- Consider alternatives in severe/advanced/unstable disease
  - Avoid in Childs Pugh C or worse
  - Look for confounding insults
  - Risk/benefit discussion
- Vivitrol may lower risk
  - (avoids first-pass metabolism)

Table 4. Selected Medications Commonly Associated with Elevated Liver Transaminase Levels

Antihypertensive	**Psychiatric**
Lisinopril	Bupropion (Wellbutrin)
Losartan (Cozaar)	Risperidone (Risperdal)
Antimicrobial	Selective serotonin reuptake inhibitors
Ciprofloxacin	Trazodone
Isoniazid	Valproic acid (Depakene)
Ketoconazole	**Other**
Pyrazinamide	Acarbose (Precose)
Rifampin	Amiodarone
Tetracycline	Baclofen
Chemotherapeutics	Herbal and dietary supplements
Imatinib (Gleevec)	Highly active antiretroviral therapy
Methotrexate	Omeprazole (Prilosec)
Pain relievers/anti-inflammatory	
Acetaminophen	
Allopurinol	
Aspirin	
Nonsteroidal anti-inflammatory drugs	

Information from references 25 and 28.

The horizon

Emerging therapies your patients may be asking about

Ozempic Can Curb Drinking

HEALTH

Inside One Man's Journey to Mexico for Addiction Treatment With a Psychedelic

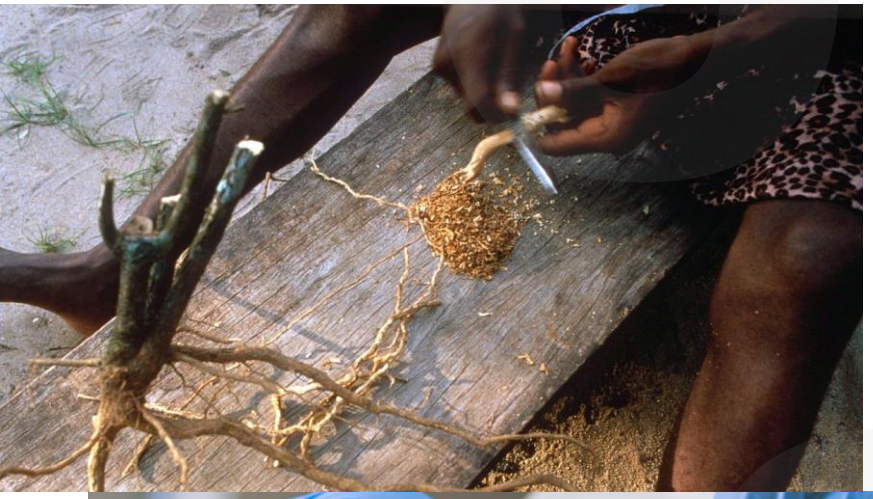
Ibogaine has been touted for its potential to erase years of addiction and withdrawal in one session. Banned in the U.S., the drug is prompting Americans to cross borders for treatment.

WILLERS T. DARENVOGT

GLP-1 agonists in the brain

- GLP-1 receptors present "motivation centers" (VTA, NAc)
  - Non-human models have CNS produced GLP-1
  - Decreased dopamine release to alcohol exposure
- Human trials have been mixed
  - Only RCT inconclusive with more drinking in normal BMI
- Social media has driven the conversation
- Phase III RCTs recruiting, expect more in a few years...

"The Last Trip" – psychedelics as cure for addiction



- Anecdotes of "life changing experiences" after single experiences are powerful, but have not been replicated
- Intensive treatment with longitudinal follow-up shows promise
  - 2, 1-day long psilocybin sessions over the course of 12 weeks of psychotherapy = significant decrease in heavy drinking days

Anecdotes are strong, data is less-so

There is patient enthusiasm for medications to treat SUD!

We should not stop looking for novel therapeutics

Take-home

AUD is common, deadly, and under-treated — you see it on your service every week.

Medications for AUD are safe, effective, and underutilized — hospitalization is the right moment to start.

Hospitalists can change the trajectory — if not you, then who?