

Management of Substance Use Disorders in the Medical Setting

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Disclosures

No relevant disclosures



Learning Objectives

By the end of this talk, the audience will:

Recognize and manage **alcohol withdrawal** and initiate evidence-based pharmacotherapy to support recovery.

Diagnose opioid use disorder and implement guideline-based **opioid agonist therapy**, and harm reduction strategies.



Learning Objective #1

Recognize and manage **alcohol withdrawal** and initiate evidence-based pharmacotherapy to support recovery.



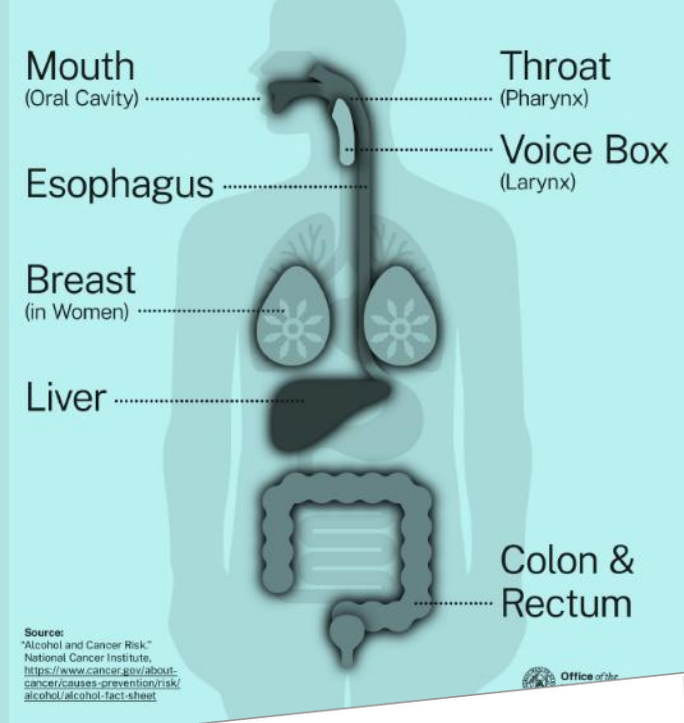
178,000

Number of **deaths** attributable to **alcohol** in 2021 (CDC)



“Alcohol Consumption is the Third Leading Preventable Cause of Cancer in the [US].”

– United States Surgeon General Dr. Vivek Murthy (January 3, 2025)



The New York Times
Surgeon General Calls for Cancer Warnings on Alcohol

Dr. Vivek Murthy's report cites studies linking alcoholic beverages to at least seven malignancies, including breast cancer. But to add warning labels, Congress would have to act.



Hospital admissions for alcohol withdrawal increased 1.8x early in the COVID-19 pandemic



JAMA
Network | **Open**[™]



Research Letter | Substance Use and Addiction

Alcohol Withdrawal Rates in Hospitalized Patients During the COVID-19 Pandemic

Ram A. Sharma, MD; Keshab Subedi, MS, MSc; Bayo M. Gbadebo, MBA; Beverly Wilson, MS; Claudine Jurkowitz, MD, MPH; Terry Horton, MD

Introduction

Coronavirus disease 2019 (COVID-19) is disrupting communities across the globe, causing physical, mental, and financial distress.¹ Economic crises have been associated with increased alcohol consumption.² Necessary public health measures may exacerbate isolation and stress, negatively impacting those who are at risk for harmful alcohol use. Increased alcohol use has been documented in the US and other countries during the pandemic, and a recent study³ has identified associated consequences. Alcohol withdrawal (AW) is a potentially dangerous complication of alcohol use disorder (AUD) in up to 8% of all hospitalized patients with AUD.⁴ AW has been suspected to worsen after the COVID-19 stay-at-home orders,⁵ but, to our knowledge, no objective data have been reported in the literature. We hypothesized that AW rates in hospitalized patients with AUD increased during the pandemic and conducted a cohort study at Christiana Care, a large, tertiary care hospital system in Newark, Delaware.

Author affiliations and article information are listed at the end of this article.



Hospitalization is a window of “iatrogenic opportunity”

5.9

days of interrupted drinking

The average admission halts alcohol use for nearly six days - the highest-risk, highest-opportunity window to intervene.

1

Stabilize

Recognize and treat withdrawal before it escalates.

2

Start treatment

Initiate naltrexone or acamprosate during the admission, not after.

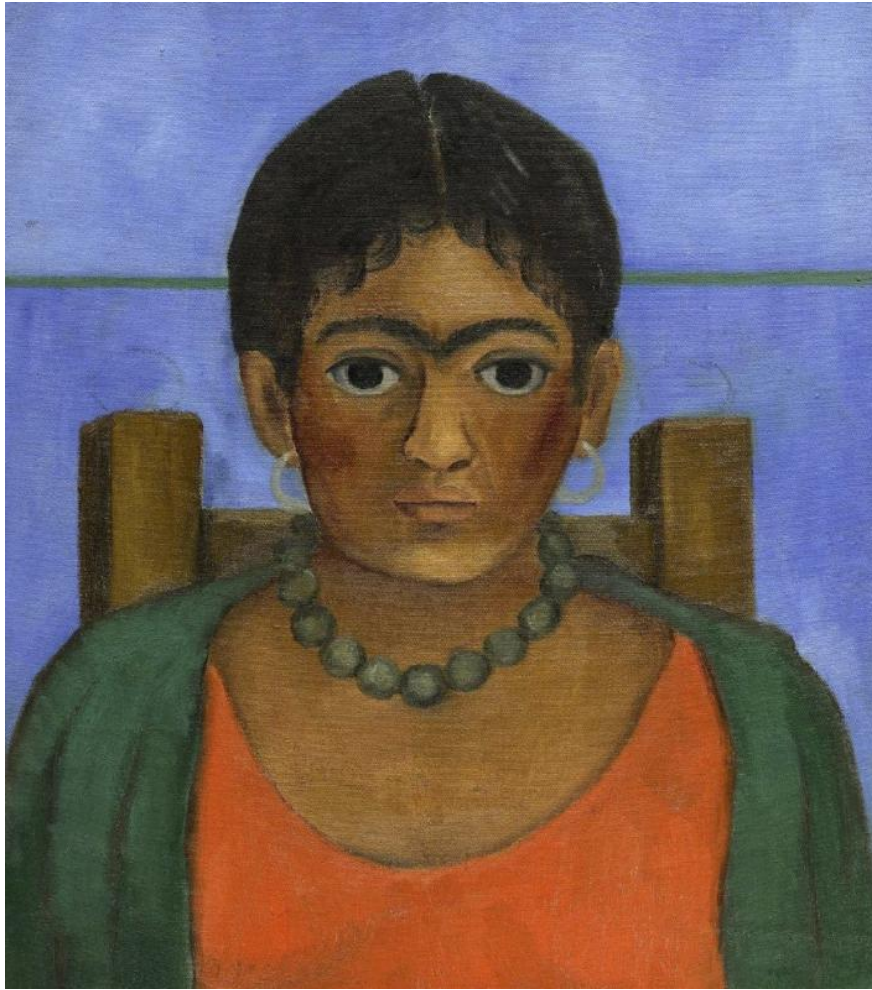
3

Link to care

Arrange follow-up and a medication supply before discharge.

Kast KA, Sidelnik SA, Nejad SH, Suzuki J. Management of alcohol withdrawal syndromes in general hospital settings. *BMJ*. 2025;388:e080461. Published 2025 Jan 8. doi:10.1136/bmj-2024-080461 (used as a source throughout this presentation), citing <https://data.oecd.org/healthcare/length-of-hospital-stay.htm#indicator-chart>





*"I tried to drown my sorrows in alcohol,
but [they] learned how to swim."
(Frida Kahlo)*

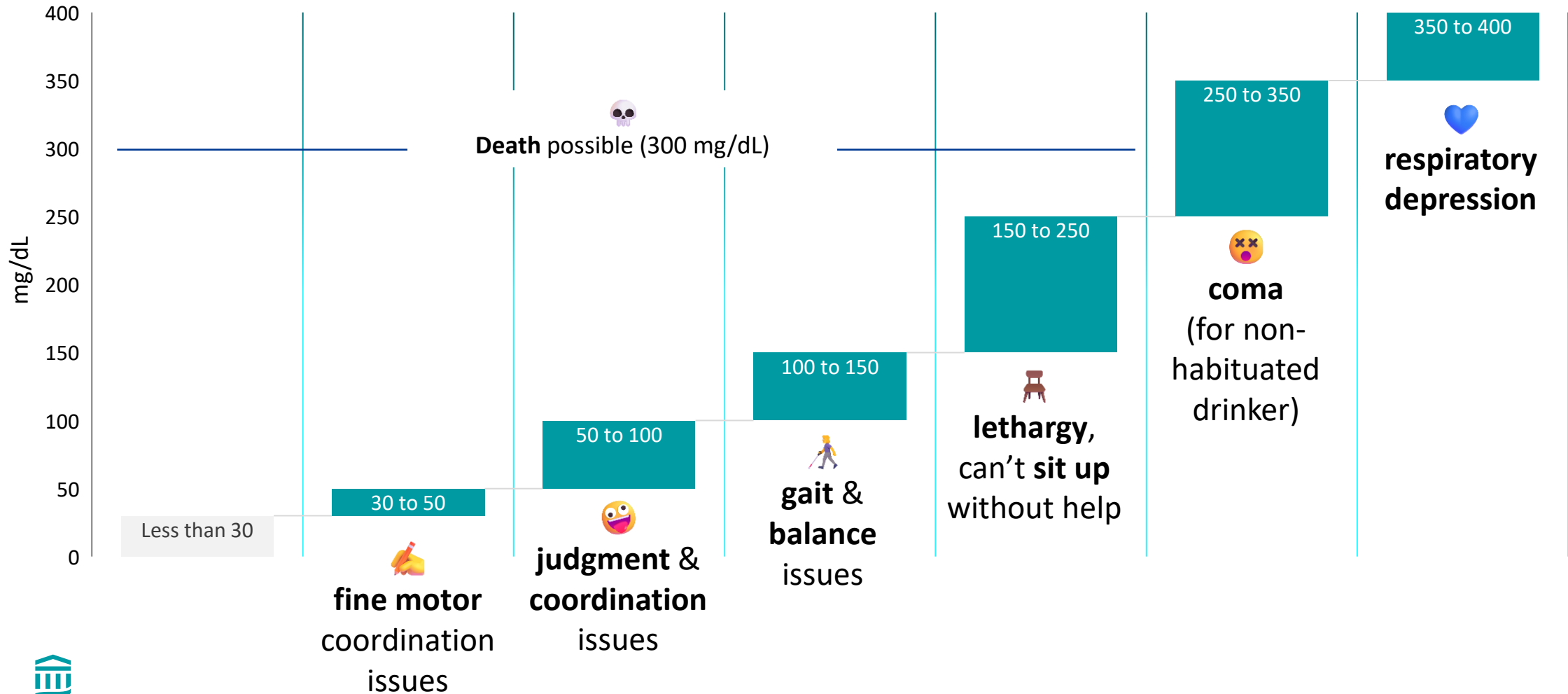
A 38-year-old woman arrives with a two-week history of daily tension-type headaches—dull, band-like pressure that worsens by evening and only partially responds to over-the-counter analgesics, and she recently received a short course of narcotic analgesics when offered for breakthrough pain. Past records are notable for her reporting a long-standing pattern of heavy weekend drinking (last AUDIT-C: 6), several recent ED visits for intoxication followed by her no-showing to outpatient PCP follow up appointments. She lives with her mother and 8-year-daughter, works intermittently as a retail manager. Her physical exam is unremarkable. Headache prophylaxis with low-dose amitriptyline is initiated, sleep hygiene is reviewed, but she declines to be referred to addiction services after discharge.

**hypothetical case vignette for teaching purposes*

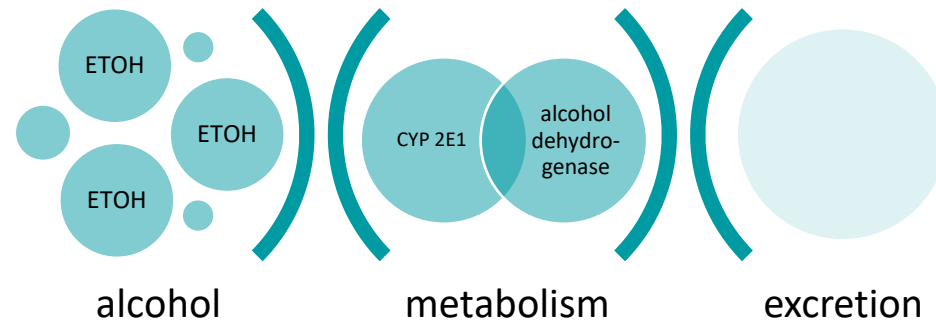


Effects of intoxication

A dose-response curve for alcohol



Alcohol elimination is zero-order - but the rate varies



Unhabituated drinker

- Falls about 15-20 mg/dL per hour
- Some sources cite 10-25 mg/dL per hour

Chronic, habituated use

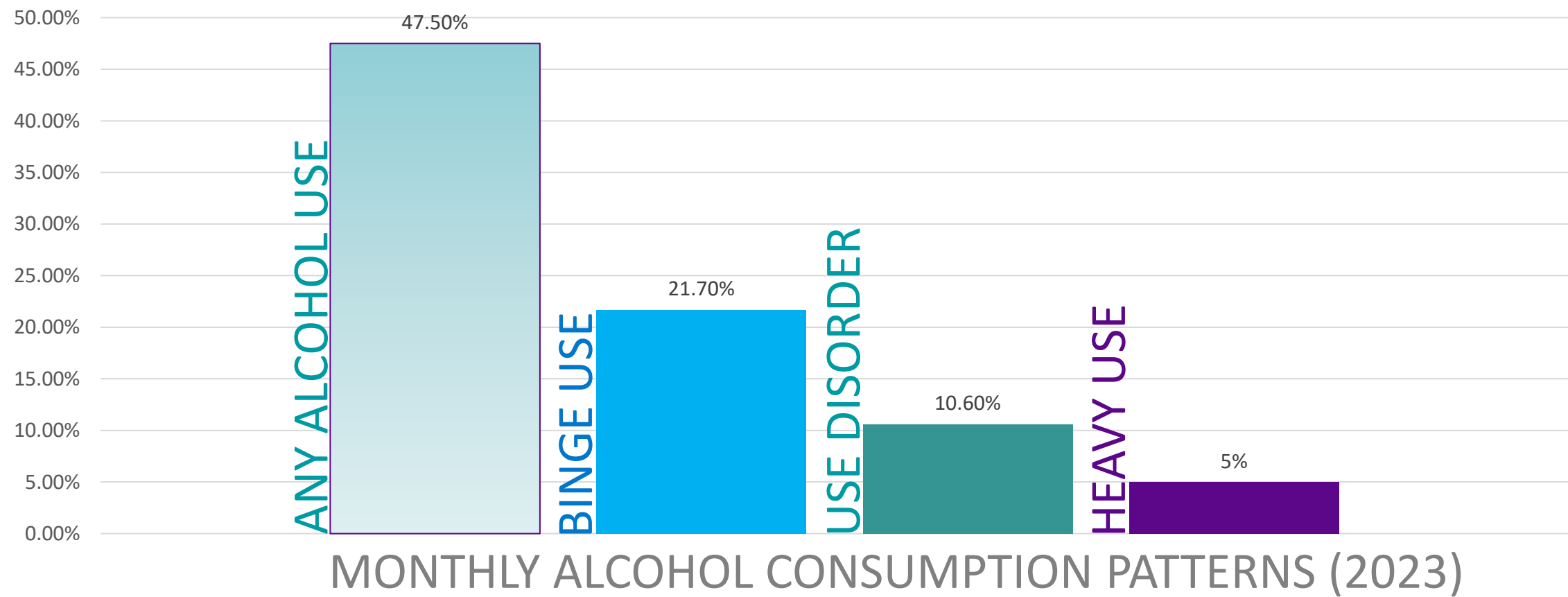
- Falls about 25-35 mg/dL per hour
- Induced metabolism clears faster

The same level means different things in different patients - impairment and symptoms track poorly with the measured concentration.

<https://pubmed.ncbi.nlm.nih.gov/1940231/>
<https://pubmed.ncbi.nlm.nih.gov/16912820/>
<https://pubmed.ncbi.nlm.nih.gov/23101976/>



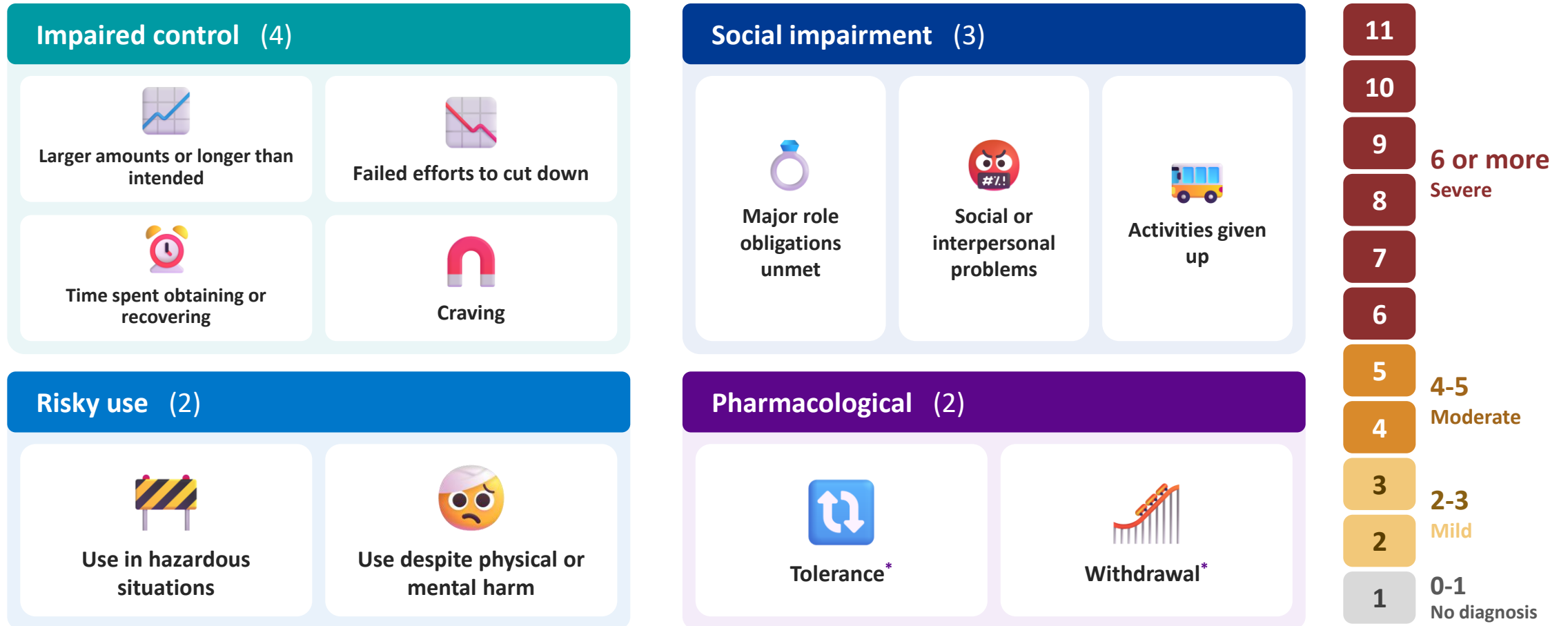
15 to 50% of persons who have an alcohol use disorder or drink heavily will develop **symptoms** of alcohol withdrawal



<https://pubmed.ncbi.nlm.nih.gov/35275407/>
<https://pubmed.ncbi.nlm.nih.gov/15706737/>



Alcohol Use Disorder | DSM-5-TR criteria



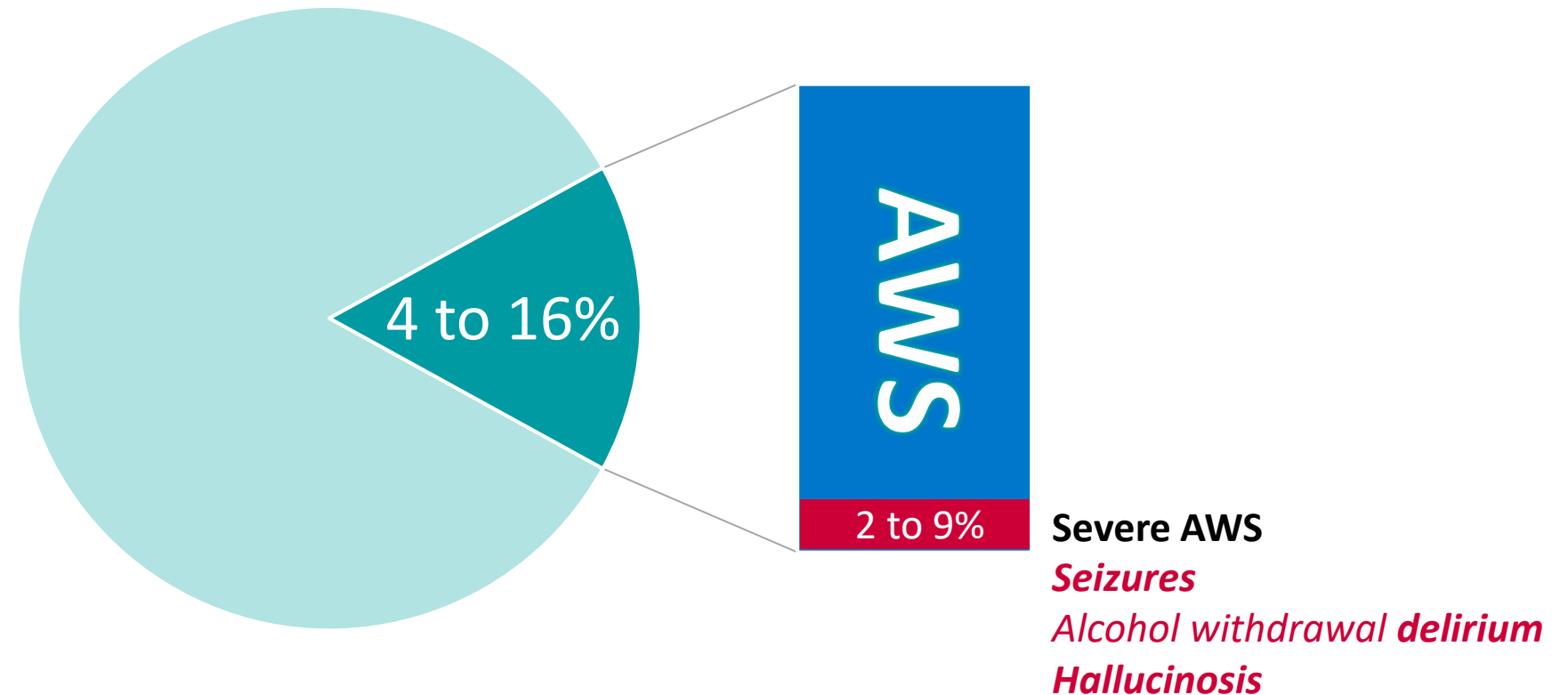
* Neither necessary nor sufficient, and they do not count when they arise during appropriate prescribed care.

Criteria met, of 11



Among all hospital admissions, **approximately 1 in 10** entail an alcohol withdrawal syndrome (AWS)

Hospital Admissions Involving an Alcohol Withdrawal Syndrome

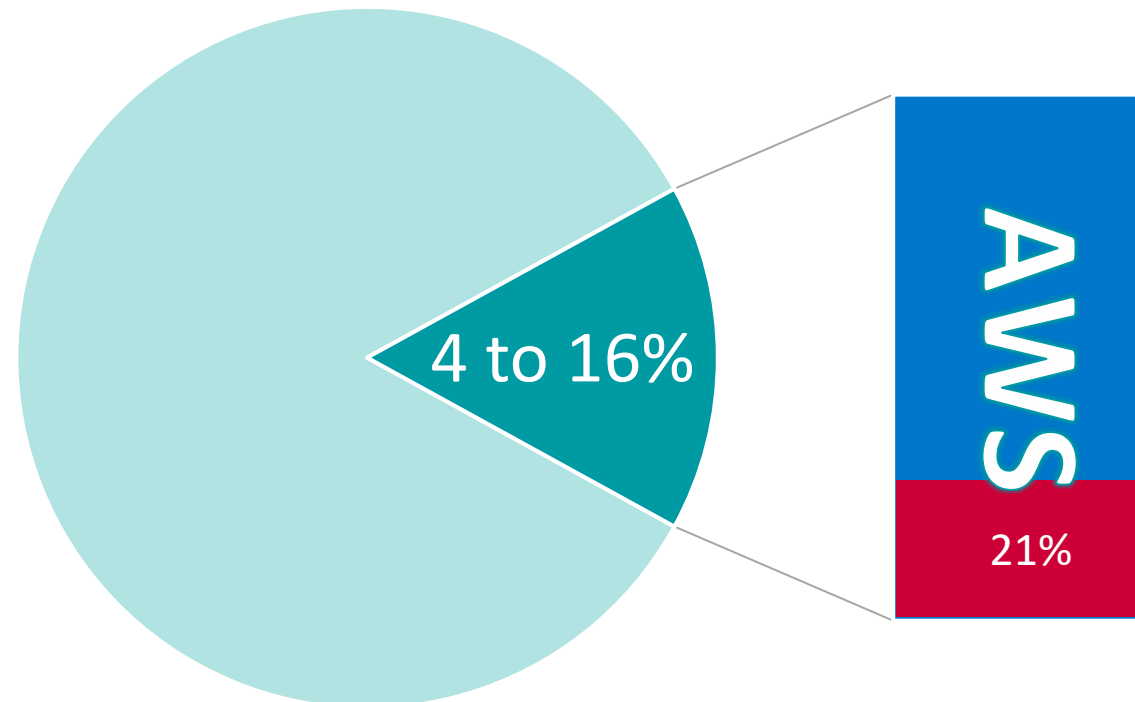


<https://pubmed.ncbi.nlm.nih.gov/31609866/>
<https://pubmed.ncbi.nlm.nih.gov/27586815/>
<https://pmc.ncbi.nlm.nih.gov/articles/PMC8522287/>



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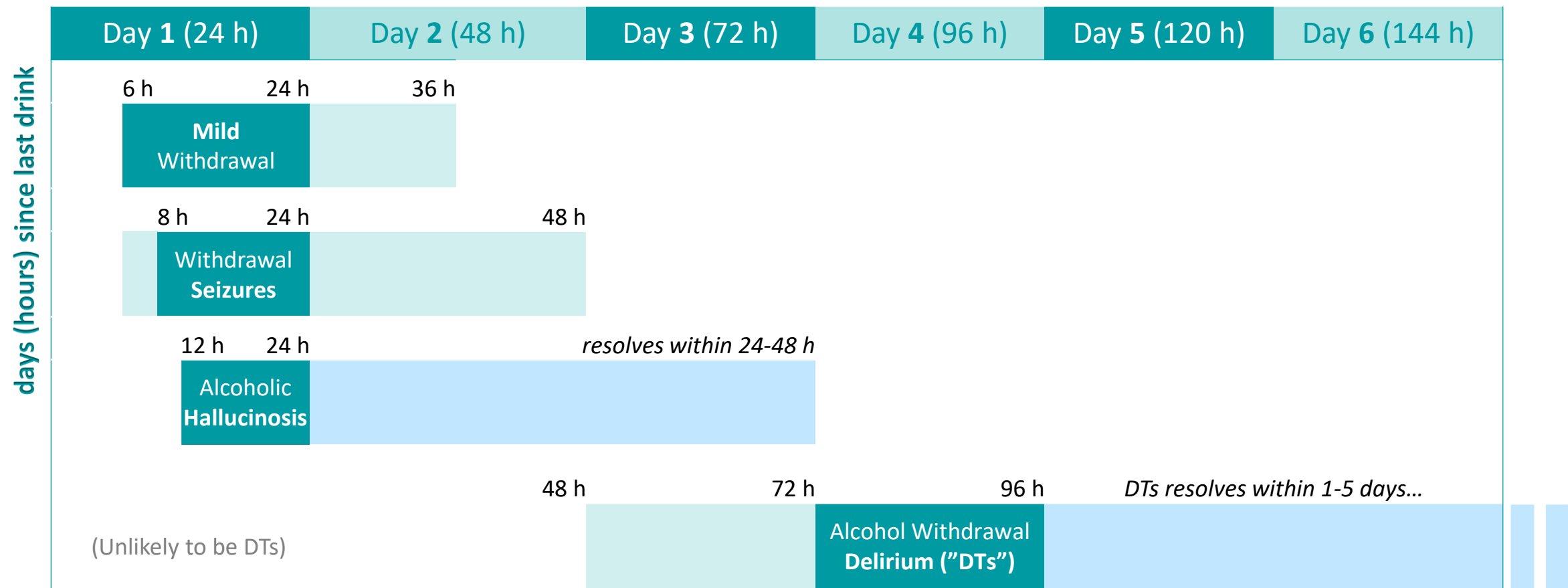


Severe AWS in the ICU
Seizures
Alcohol withdrawal delirium
(higher morbidity, 1-8% mortality)
Hallucinations

<https://pubmed.ncbi.nlm.nih.gov/31609866/>
<https://pubmed.ncbi.nlm.nih.gov/27586815/>
<https://pmc.ncbi.nlm.nih.gov/articles/PMC8522287/>



Alcohol withdrawal follows a predictable timeline - the highest-risk syndromes cluster in the first five days





DSM-5-TR Alcohol Withdrawal

Two (or more) of the following, developing within several hours to a few days after the cessation of (or reduction in) [heavy & prolonged] alcohol use....



autonomic hyperactivity



increased hand tremor



insomnia



nausea or vomiting



transient VH, TH, AH or illusions



psychomotor agitation



anxiety



generalized tonic-clonic seizures

Kindling (sensitization): if at first you don't withdraw...
what doesn't kill you may put you at higher risks for *seizures*



Combining PEth and EtG to gauge alcohol withdrawal risk

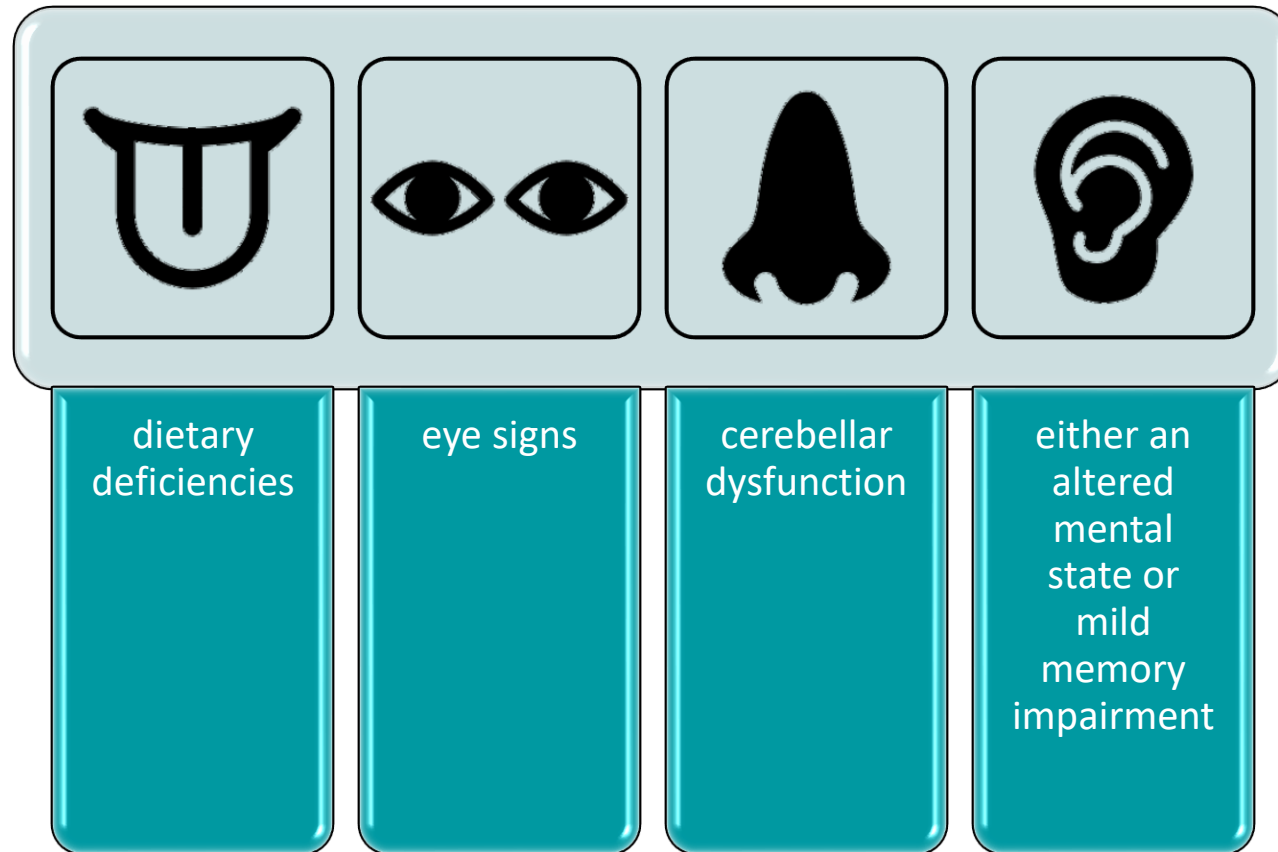
Elevated PEth and EtG confirm recent alcohol consumption, while negative values suggest little or no use in the past several weeks - most helpful when self-report is unreliable or unavailable.

	Positive PEth	Negative PEth	PEth thresholds
Positive EtG	At risk for AWS; further risk stratification needed to guide monitoring and treatment.	Possible recent alcohol use or exposure, with previous low or no alcohol use.	>200 sustained heavy
Negative EtG	Possible recent 3-5 day period of alcohol abstinence, with previous alcohol use.	Likely low risk for AWS; might not require symptom monitoring or treatment.	20-200 moderately heavy
Further study is needed to demonstrate this in clinical populations.			<20 minimal or none

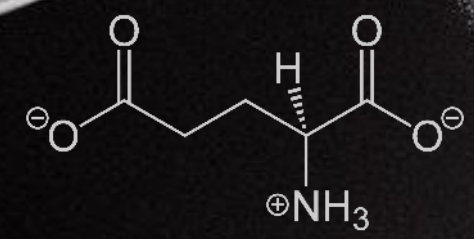
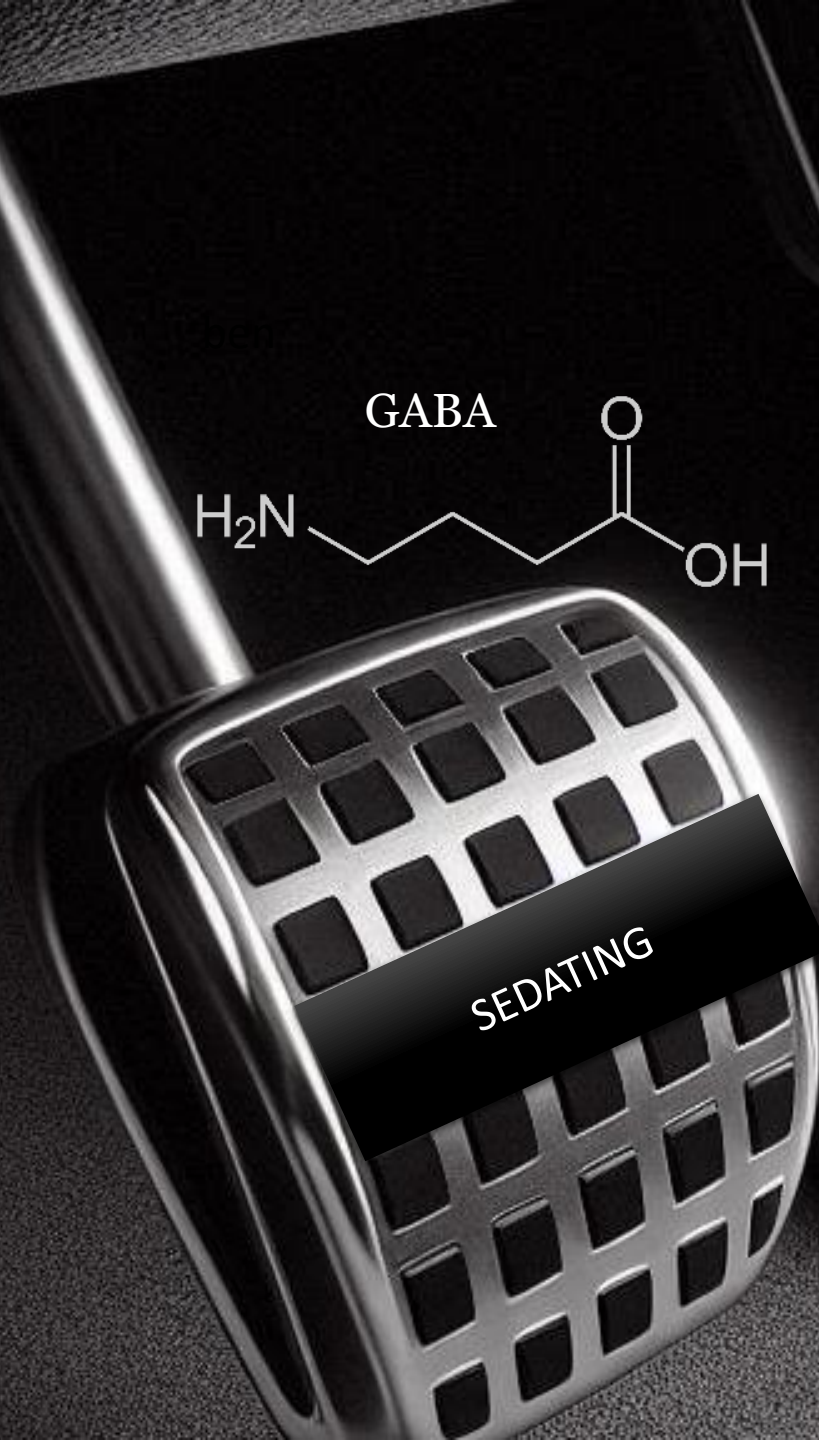
Kast KA, Sidelnik SA, Nejad SH, Suzuki J. Management of alcohol withdrawal syndromes in general hospital settings. *BMJ*. 2025;388:e080461. Published 2025 Jan 8. doi:10.1136/bmj-2024-080461



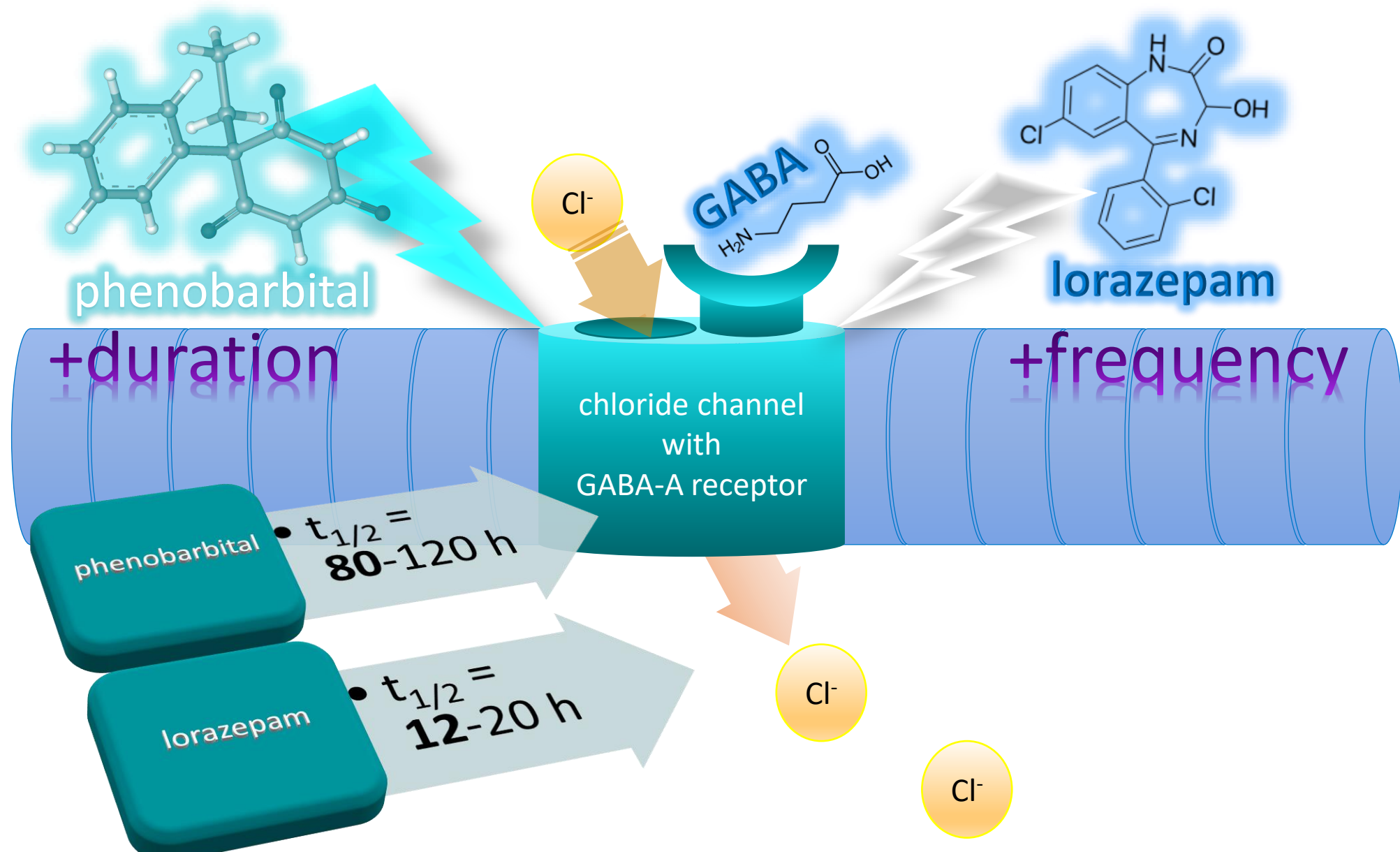
Caine Criteria



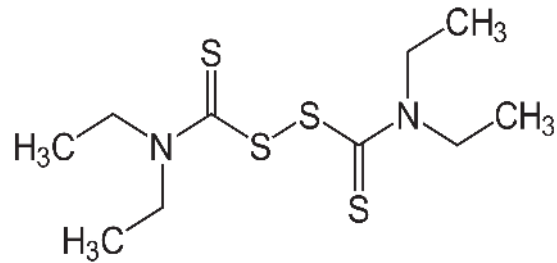
2+ → Caine-Positive



NMDA

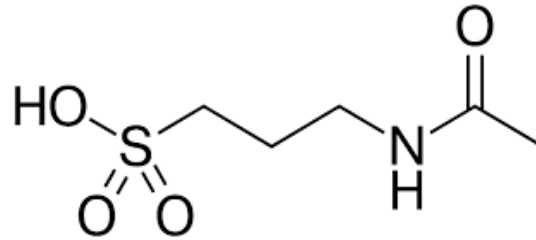


FDA-approved medications for the treatment of alcohol use disorder (mAUD)



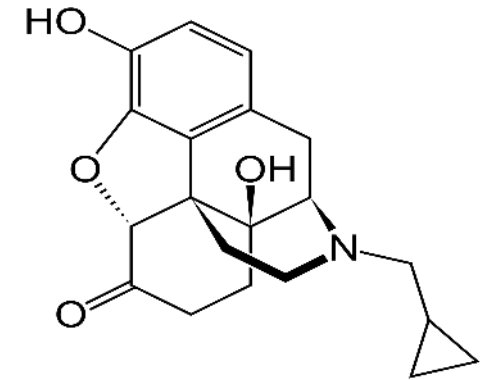
Disulfiram
[Antabuse]

1951



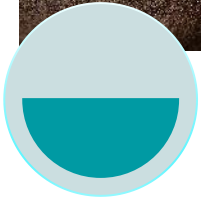
Acamprosate
[Campral]

2004



Naltrexone
[Revia/Vivitrol]

1994/2006

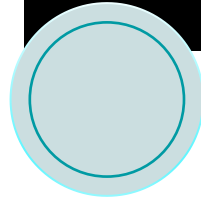


*To Drink **Less**?*

Naltrexone

[Gabapentin?]

[Semaglutide?]



*To Drink **Nothing**?*

Acamprosate

Disulfiram

[GLP-1s?]

What is the
goal of the
treatment?

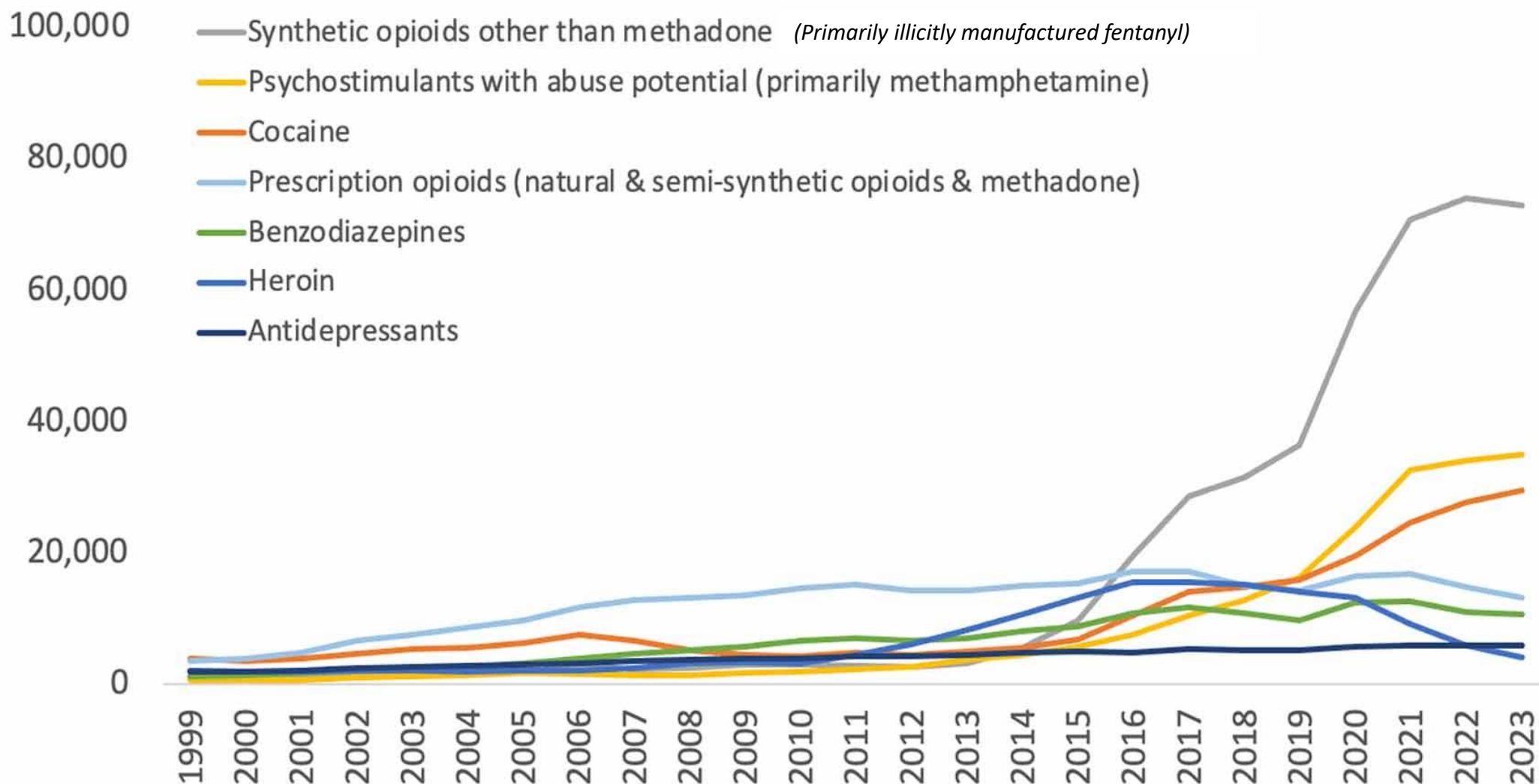
Learning Objective #2

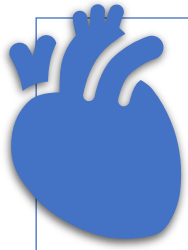
Diagnose opioid use disorder and implement guideline-based **opioid agonist therapy**, and harm reduction strategies.



U.S. Overdose Deaths

Select Drugs or Drug Categories, 1999-2023





Hypertension/anxiety

- **Clonidine** 0.1mg PO TID
- Hold if using methadone
- Hold if hypotensive



Diarrhea

- **Loperamide** 4mg PO with first loose stool
- Then 2mg per loose stool
- Max 24 mg per day



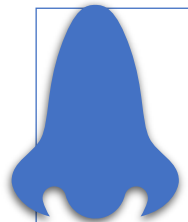
Pain

- **Ibuprofen** 600mg *or*
- Acetaminophen 650 mg PO q4-6h



Abdominal cramping

- **Dicyclomine** 20mg po q4h



Nasal congestion

- **Diphenhydramine** 50mg PO q4h



Muscle cramps

- **Methocarbamol** 750mg PO q6h



Insomnia

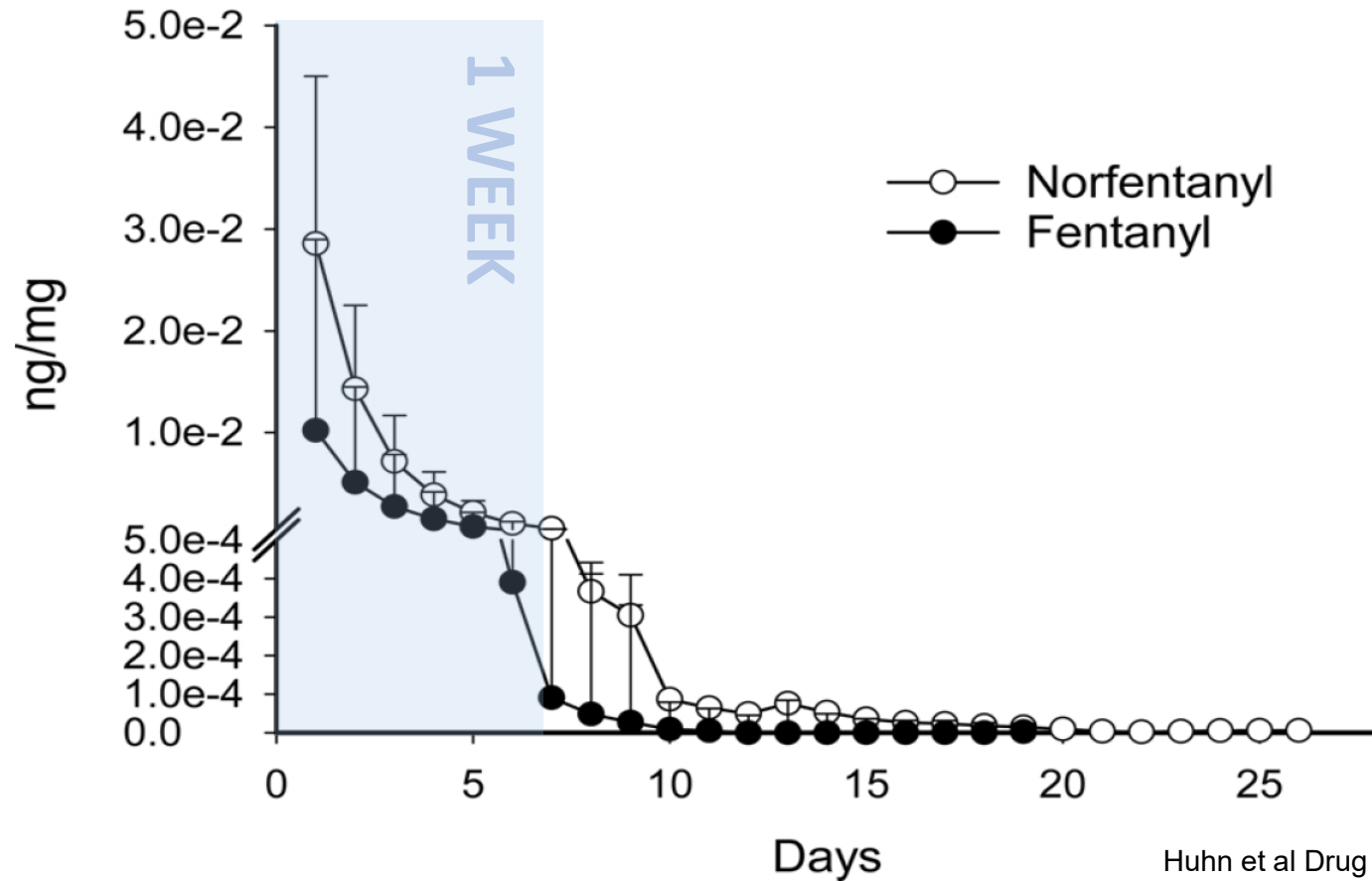
- **Trazodone** 50-100mg PO qHS

What precipitated withdrawal feels like



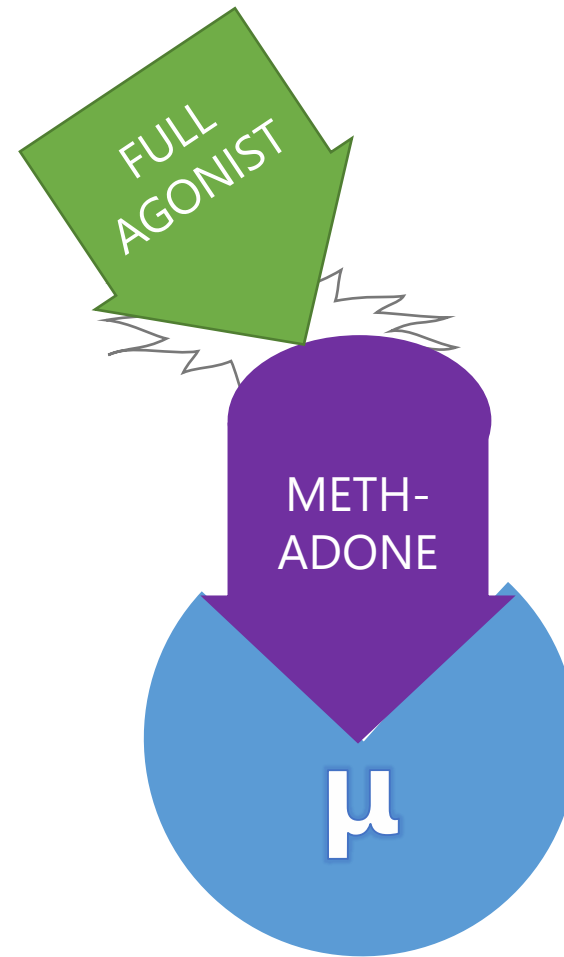
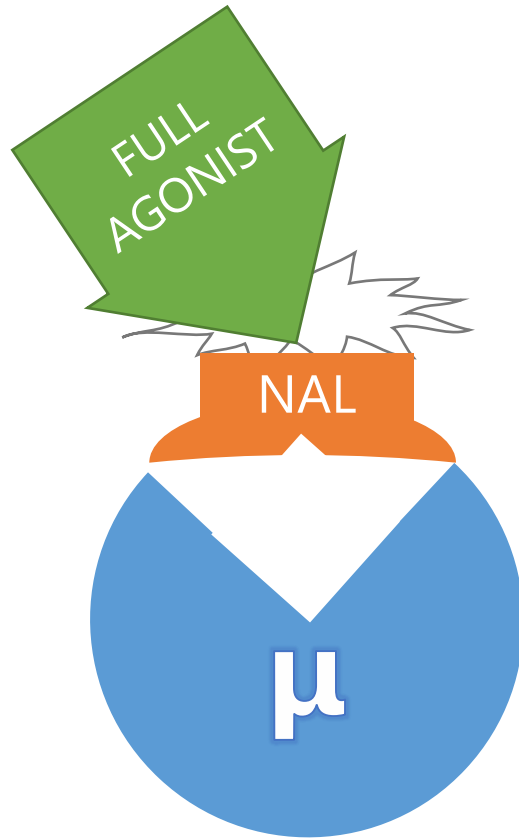
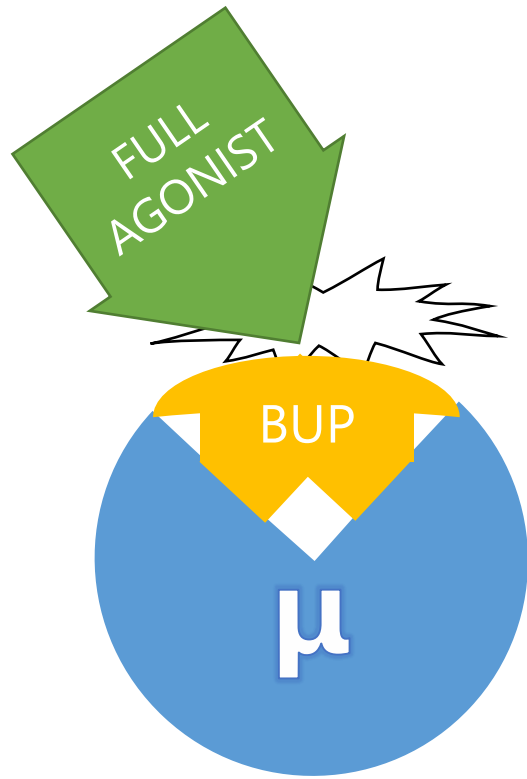
When mu receptor activation drops precipitously (e.g., when you administer naloxone to a patient high on fentanyl)

Fentanyl and Norfentanyl Elimination

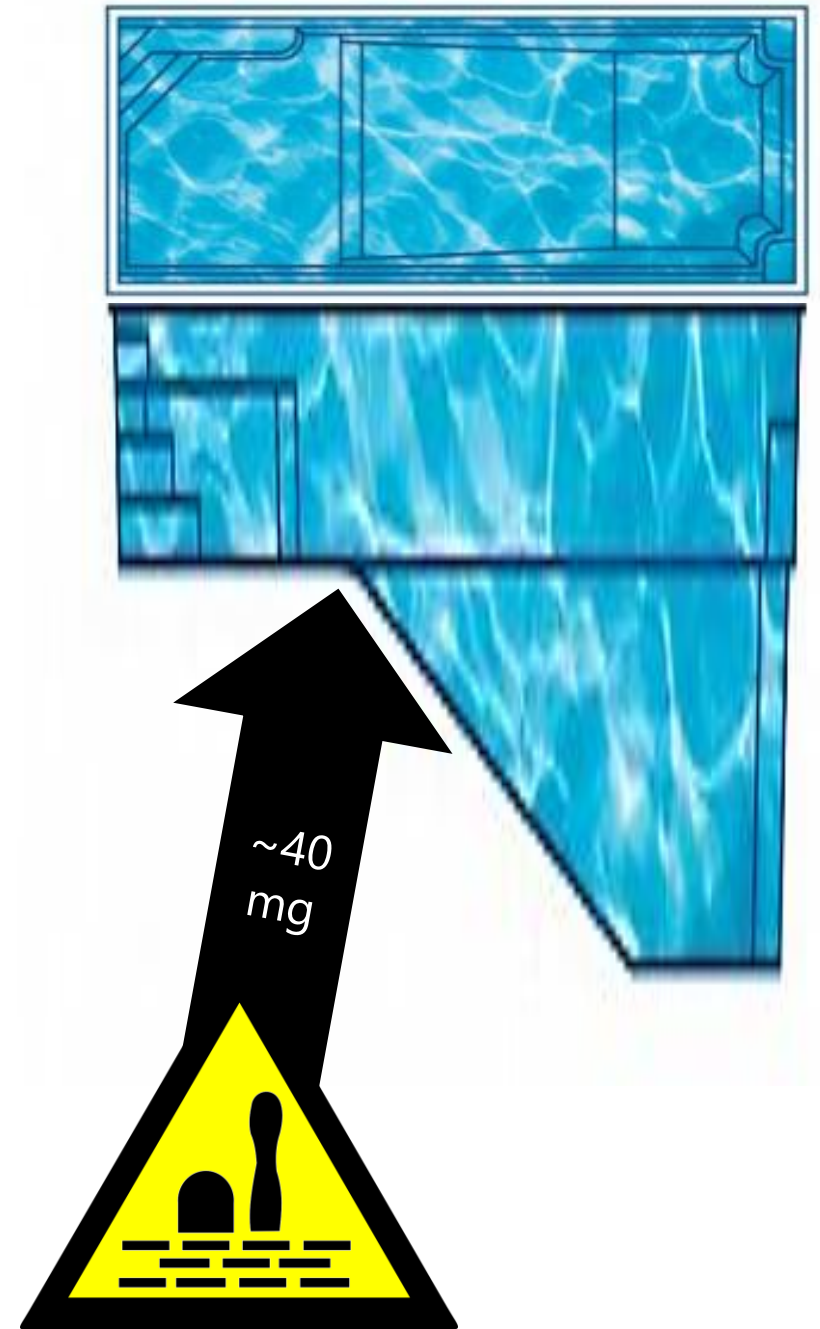


Huhn et al Drug Alc Dep 2020

**Delayed
clearance of
fentanyl and
norfentanyl**



Beware of the deep end:
Methadone dosing is NON-LINEAR



Butrans

Brixadi
Sublocade
Probuphine

*Long-acting
OUD
treatments*

Belbuca
IV

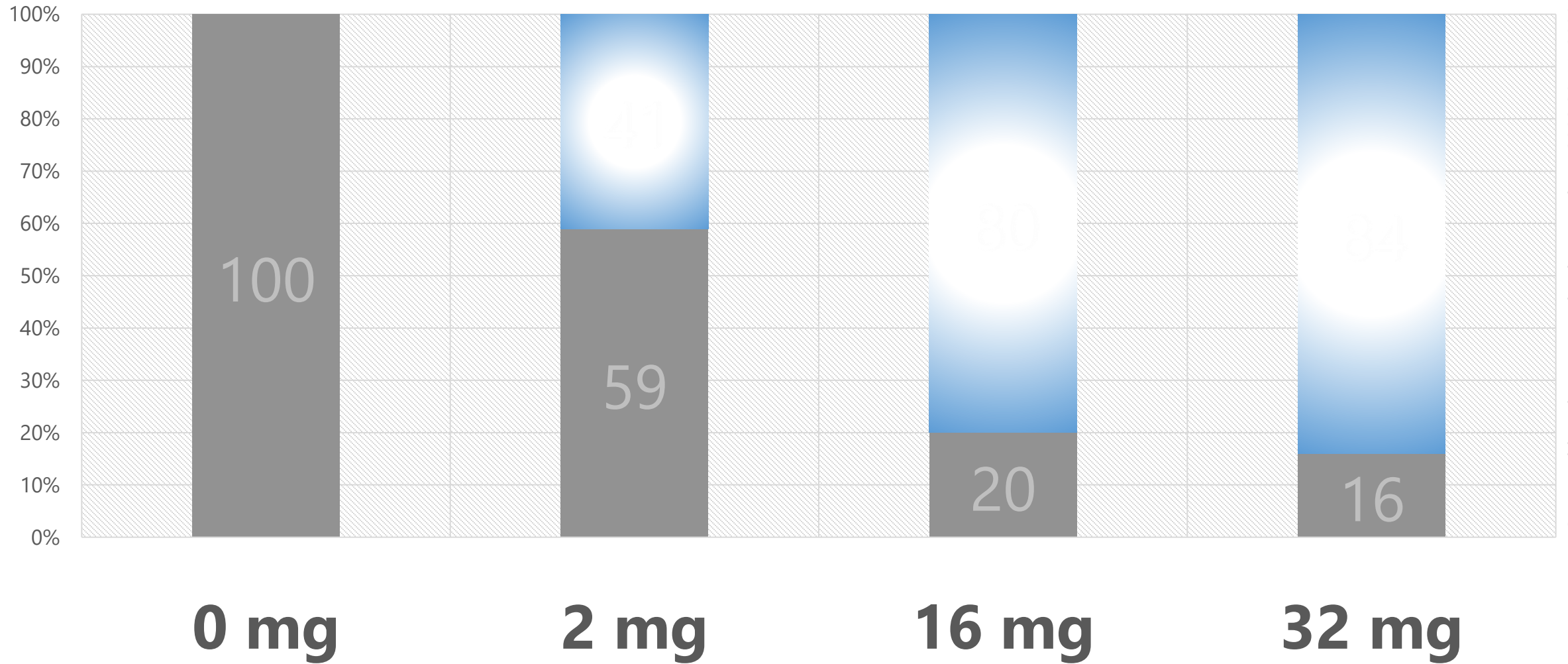
Suboxone
Subutex
Zubsolv

*Short-acting
non-OUD
treatment*

*Short-acting
OUD
treatments*

μ opioid receptor availability at various daily buprenorphine concentrations

■ Available
■ Not available



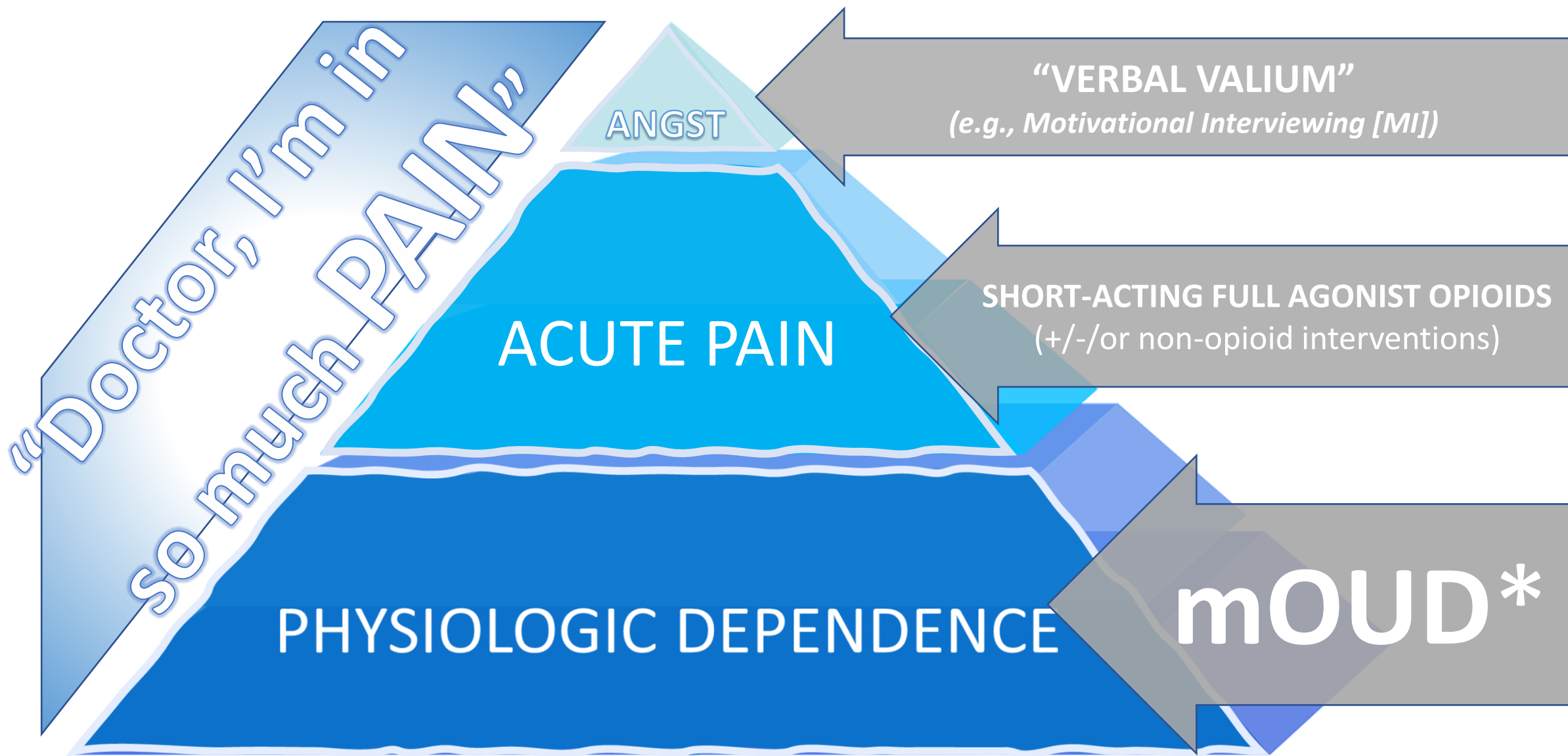
Greenwald et al. Neuropsychopharmacology. 2003;28(11):2000-9.

Table 2. μ -Opioid Receptor Binding Affinities (K_i) for Commonly Used Opioids and Antagonists

Opioid	K_i (nM)
Sufentanil	0.1380 ³
Buprenorphine	0.2157³
Hydromorphone	0.3654 ³
Morphine	1.168 ³
Fentanyl	1.346 ³
Naloxone	1.518 ³
Methadone	3.378 ³
Remifentanil	21.1 ⁴
Oxycodone	25.87 ³
Hydrocodone	41.58 ³
Codeine	734.2 ³
Tramadol	12,486 ³

Buprenorphine
has extremely
high affinity
relative to other
opioids

(Leighton et al 2017)



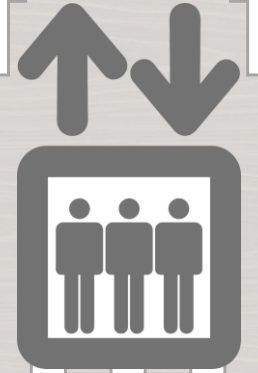
*mOUD = medication to treat opioid use disorder; e.g., methadone or buprenorphine-naloxone

Methadone, Oxycodone, etc. (→100%)

Buprenorphine (~40%)

Naloxone (~0%)

opioid receptor occupancy x drug activity



COWS SCORE ~ acceleration



Opioid Withdrawal Order Set

Manage User Versions

Starting medication treatment

The selection of medication to treat opioid withdrawal (e.g., methadone or buprenorphine) should be based on a shared decision-making process which integrates both the preferences and past experiences of patients and the clinical judgment of providers (see below).

Methadone	Buprenorphine
- Avoid in patients with <i>QT prolongation</i> - May be started immediately to treat opioid withdrawal, regardless of recent exposure to fentanyl or other opioids - Patients who receive a few doses of methadone to treat withdrawal <i>may still initiate buprenorphine later</i> in their hospitalization**	- May restart immediately if patient took their last dose of buprenorphine in the last 72 hours - Otherwise, wait for <u>COWS score</u> of 8 or higher before giving first dose** **Special circumstances which may necessitate low-dose buprenorphine initiation (microdosing) or consult to addiction / psychiatry (if available): - Transitioning from methadone to buprenorphine - Fentanyl exposure† in the last week - History of precipitated withdrawal - Severe pain requiring round-the-clock treatment with high-dose opioid medications

*Buprenorphine here refers to both buprenorphine-naloxone and buprenorphine monoprodukt

†Assume fentanyl exposure (unless proven otherwise by laboratory toxicology results) in any patient who has injected or insufflated non-prescription opioids within the last week

General

Notify Responding Clinician

☐ Notify responding clinician

Routine Until discontinued

Low-Dose Buprenorphine Initiation (“Microdosing”)

low-dose buprenorphine initiation **indicated for patient** (see earlier)

Patient managed with
methadone maintenance treatment (MMT)
(e.g., 40+ mg of methadone for 7+ days)

Consider LONG protocol

Patient **NOT** managed with MMT, but
may have had recent opioid exposures, such as:

- Fentanyl (iatrogenic or illicit)
- Short-acting opioids (e.g., oxycodone)
- Brief course of low dose methadone (e.g., ≤40 mg x 2-3 days)

Consider SHORT protocol

SHORT protocol for low-dose buprenorphine initiation

Day 1

- Consider starting taper of full-agonist opioids if patient’s clinical condition allows (e.g., adequate pain control)*
- Apply buprenorphine patch (20 mcg, or equivalent) at 8:00 AM (ideally)

Day 2

- Administer the first 2 mg dose of a buprenorphine-containing product[§] around 10:00 AM**
- As tolerated / if requested by patient, consider administering additional doses of buprenorphine in 2 - 4 mg increments every 2 to 4 hours,** up to a maximum total dose of 8 mg of buprenorphine on day 2†
- Remove buprenorphine patch at 8:00 pm (approximately 36 hours after administration)

Day 3

- Administer the AM dose of a buprenorphine-containing product equal to the cumulative dose administered on Day 2**
- As tolerated / if requested by patient, consider administering additional doses of buprenorphine in 2-4 mg increments every 2 to 4 hours,** up to a maximum total dose of 12 mg of buprenorphine on day 3†

LONG protocol for low-dose buprenorphine initiation

Day 1

- Continue methadone

Day 2

- Administer the first 2 mg dose

Days 3 - 7

- Continue methadone or

Day 8

- Stop methadone



Buprenorphine Long-acting Injectables (LAIs)

Sublocade

Monthly - every 4 weeks

- 100 mg or 300 mg every 4 weeks
- Requires a 4 mg transmucosal dose first
- Not before withdrawal has begun
- 2nd dose can come as early as 1 week
- Refrigerated; warm 15 min before use

Brixadi

Weekly or monthly

- 8-32 mg weekly; 64-128 mg monthly
- Weekly can start at COWS 4+, no SL lead-in
- Typical start 24 mg; observe 2 hours
- Weekly form preferred in pregnancy
- Stored at room temperature

Steady-state average plasma concentration (C_{avg}, ng/mL)



Manufacturer prescribing information; blockade range approximate.

Both require DSM-5 opioid use disorder plus documented inability to continue transmucosal buprenorphine (diversion, treatment failure, or adherence).

Subcutaneous only - abdomen, thigh, or buttock; Sublocade may also use the upper arm, Brixadi only after four consecutive doses elsewhere.



High dose, low dose, & standard buprenorphine initiation



	Fastest → slowest	High-dose (HDB) Fastest	Standard Intermediate	Low-dose + opioid continuation Slowest
Opioid withdrawal required first?		Yes	Yes	No
Initial SL buprenorphine dose		8-16+ mg	2-8 mg	0.25-1 mg
Time to stabilization		≤2 hours	1-3 days	3-10 days
Continue a full agonist?		No	No	Yes - e.g. methadone or hydromorphone
Best suited for		Rapid stabilization; bridges access barriers	Most common, best-described approach	Avoids withdrawal; abstinence not required first

Weimer MB, Herring AA, Kawasaki SS, Meyer M, Kleykamp BA, Ramsey KS. ASAM Clinical Considerations: Buprenorphine Treatment of Opioid Use Disorder for Individuals Using High-potency Synthetic Opioids. *J Addict Med.* 2023;17(6):632-639. doi:10.1097/ADM.0000000000001202

Conclusion: SUD is treatable in medical settings



- Hospitalization is a clinical opportunity to identify and initiate treatment for alcohol and opioid use disorders.
- FDA-approved medications for alcohol use disorder (naltrexone, acamprosate, disulfiram) support recovery.
- Opioid use disorder treatment includes opioid agonist therapy (methadone, buprenorphine) and harm reduction strategies.

Selected References

Kast KA, Sidelnik SA, Nejad SH, Suzuki J. Management of alcohol withdrawal syndromes in general hospital settings. *BMJ*. 2025;388:e080461. Published 2025 Jan 8. doi:10.1136/bmj-2024-080461

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Winder GS, Clifton EG, Denysenko L, et al. "But I didn't drink!": What to do with discordant phosphatidylethanol results. *Liver Transpl*. 2024;30(2):213-222. doi:10.1097/LVT.0000000000000223





Mass General Brigham