

# Alcohol Use Disorder: Outpatient Therapy

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# Disclosures

- Educational purposes
- No relevant financial relationship(s) with ineligible companies to disclose
- The content of this presentation should not be considered as legal advice.

# Educational Objective

- Explain how to establish a diagnosis for Alcohol Use Disorder (AUD)
- Assess the rationale for using pharmacotherapy for AUD
- Describe dosing and mechanism of action for the following medications:
  - FDA approved (naltrexone, acamprosate, disulfiram)
  - Off-label (topiramate, gabapentin)
  - Apply appropriate pharmacological and non-pharmacological treatments (eg, Alcoholics Anonymous or 12-Step programs) for individuals with alcohol use disorder.
- Identify AUD pharmacotherapy options through a case vignette

# AUD, Medications utilized

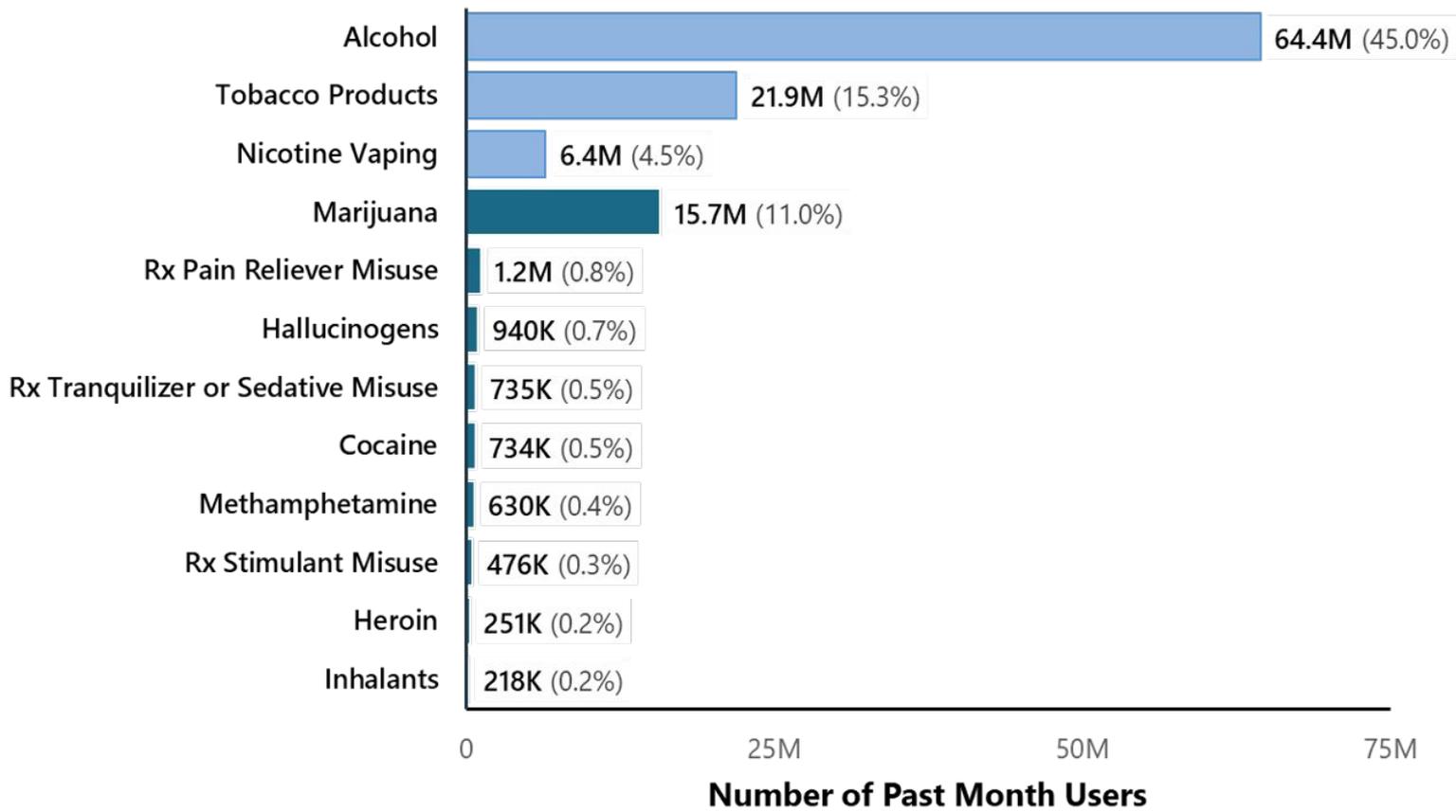
Alcohol use disorder (AUD) is one of only 3 substance use disorders with FDA approved medications

- tobacco, opioids, alcohol

- Yet very little use of AUD medications.
- According to the 2021 National Survey on Drug Use and Health (NSDUH), **29.5 million people ages 12 and older (10.6% in this age group) had AUD in the past year.**

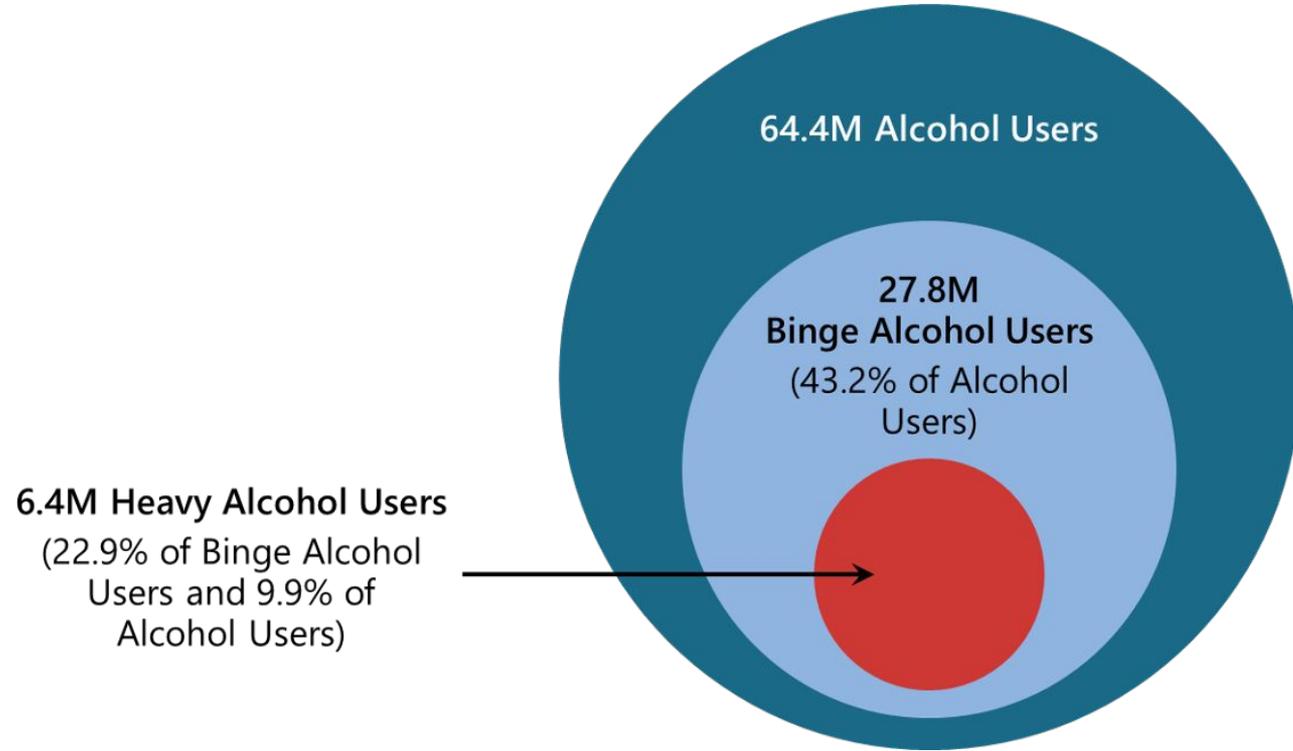
About 7% of individuals with AUD receive a formal treatment including medications.





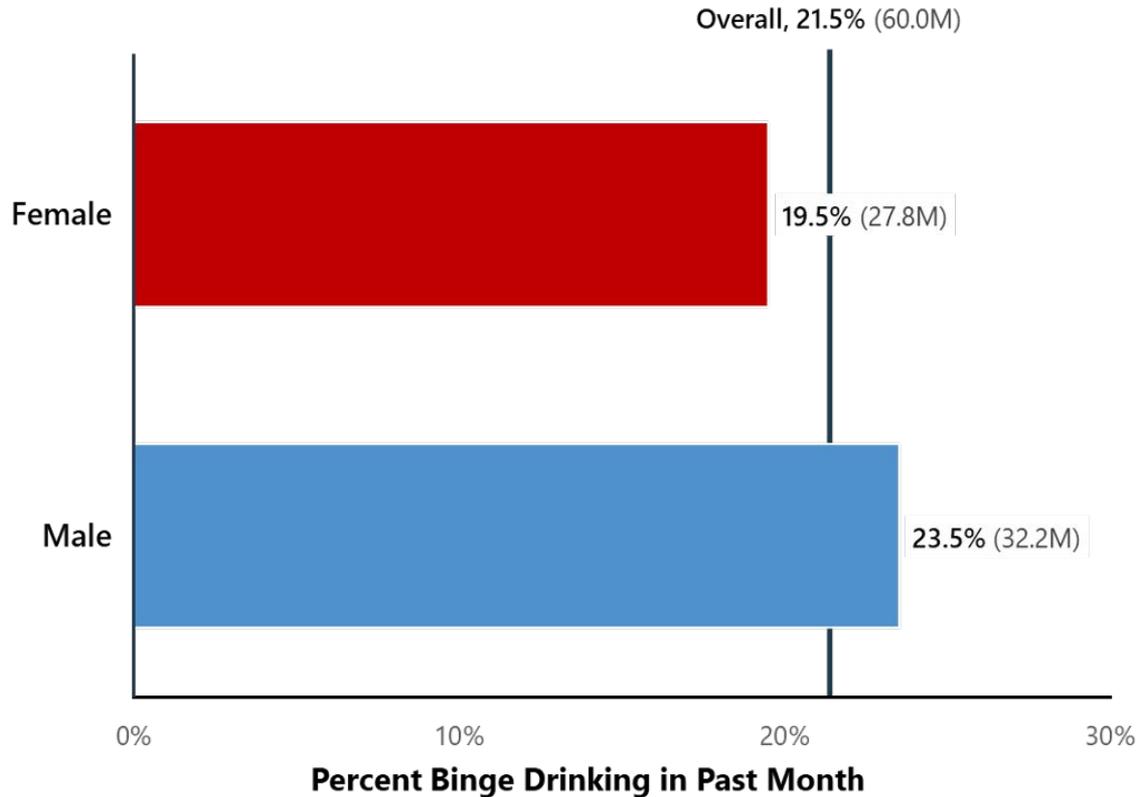
Rx = prescription.

Note: The estimated numbers of current users of different substances are not mutually exclusive because people could have used more than one type of substance in the past month.



- More than **40%** of past month alcohol users were binge drinkers

# Epidemiology



- **Females** were less likely to binge drink in the past month than Males

# Context for the Use of Pharmacology

- Addiction is a chronic, relapsing brain disease characterized by compulsive use despite harmful consequences
- Medications may be used as a tool within a comprehensive treatment plan:
  - Medications (Bio)
  - Behavioral interventions (Psycho)
  - Social support, lifestyle changes (Social)

I only drink one glass per day, Doc.



**12 fl oz of  
regular beer**

=

**8–9 fl oz of  
malt liquor**  
(shown in a  
12 oz glass)

=

**5 fl oz of  
table wine**

=

**1.5 fl oz shot of  
80-proof spirits**  
(whiskey, gin, rum,  
vodka, tequila, etc.)



about 5%  
alcohol



about 7%  
alcohol



about 12%  
alcohol



about 40%  
alcohol

The percent of "pure" alcohol, expressed here as alcohol by volume (alc/vol), varies by beverage.

**American Psychiatric Association *recommends* (1C) that the initial psychiatric evaluation of a patient with suspected alcohol use disorder include a quantitative behavioral measure to detect the presence of alcohol misuse and assess its severity.**

•Rationale:

- Establish baseline information on alcohol misuse and its severity
- Help in tracking treatment effects
- Improve consistency of information obtained

•Implementation:

- Consider choosing a scale based on patient age, clinical setting, time available for administration, and therapeutic objective
- Example measures: **CRAFT, AUDIT, AUDIT-C, CAGE?**

–AUDIT-C Questionnaire

1.How often do you have a drink containing alcohol?

- [0] Never
- [1] Monthly or less
- [2] 2-4 times a month
- [3] 2-3 times a week
- [4] 4 or more times a week

2.How many standard drinks containing alcohol do you have on a typical day?

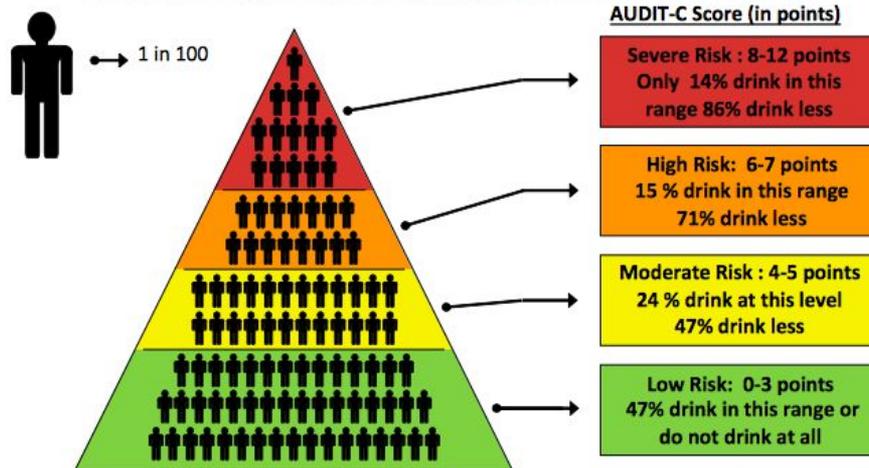
- [0] 1 or 2
- [1] 3 or 4
- [2] 5 or 6
- [3] 7 to 9
- [4] 10 or more

3.How often do you have six or more drinks on one occasion?

- [0] Never
- [1] Less than monthly
- [2] Monthly
- [3] Weekly
- [4] Daily or almost daily

Men, age 29 and younger

## How many others drink as much as you?



The **AUDIT-C** is a questionnaire given to thousands of VA patients. This triangle shows how your drinking compares to **Male Veterans, age 29 and younger**.

Men who score 4 or higher drink above recommended limits and are at increased risks for harm.

Source: Survey of Healthcare Experiences of Patients, 2008, VA Office of Quality and Performance

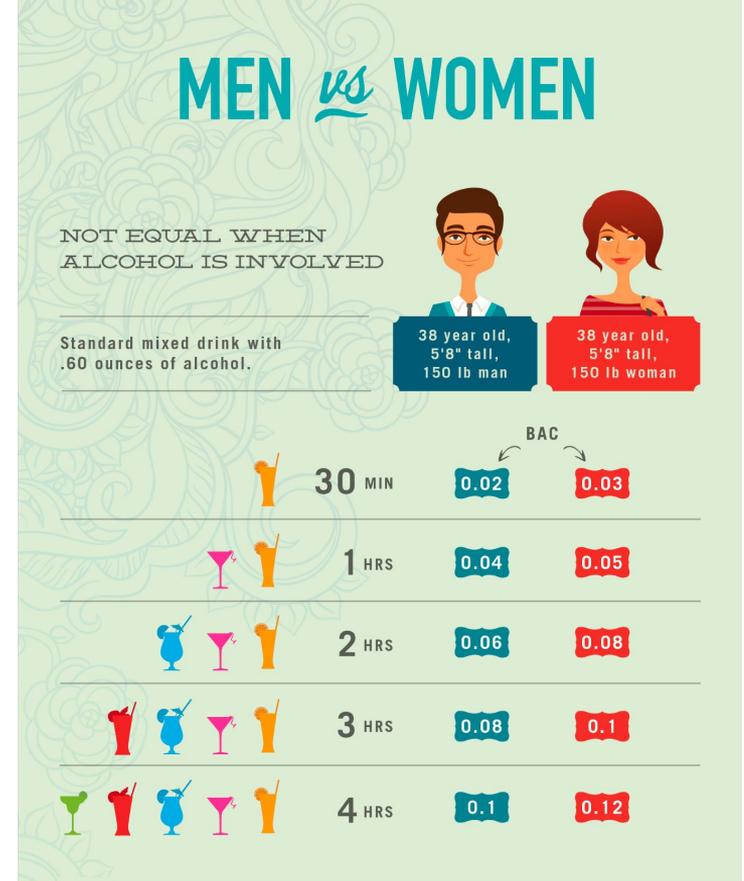
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# 2020-2025 US Dietary Guidelines

## Moderate drinking cutoffs:

- Men: No more than **2** drinks/day
- Women: No more than **1** drink/day

Higher risk of alcohol-related consequences in women



FOUNDATION FOR  
ADVANCING ALCOHOL  
RESPONSIBILITY

[Responsibility.org/virtualbar](https://responsibility.org/virtualbar)

This illustration is not intended to be used as a scientific BAC measurement, and should not take the place of your own responsible decisions about drinking alcohol, or about whether and when it will be safe for you to drive.

# NIAAA: Heavy Drinking and Binge Drinking

## NIAAA heavy (“at risk”) drinking:

cutoffs:

- **Men:** >4 drinks/day or >14 drinks/week
- **Women:** >3 drinks/day or >7 drinks/week
  - 1 in 4 who exceed these limits has an AUD; remainder are at greater risk of development of AUD, injuries, and other health problems
- **NIAAA binge drinking:**
  - Men: 5 or more drinks in approximately 2 hrs
  - Women: 4 or more drinks in approximately 2 hrs
- Levels bring blood alcohol concentration (BAC) to 0.08 g/dL

**BLOOD ALCOHOL CONTENT (BAC)**  
**Table for Male (M) / Female (F)**

Number of Drinks		Body Weight in Pounds								Driving Condition
		100	120	140	160	180	200	220	240	
0	M	.00	.00	.00	.00	.00	.00	.00	.00	Only Safe Driving Limit
	F	.00	.00	.00	.00	.00	.00	.00	.00	
1	M	.06	.05	.04	.04	.03	.03	.03	.02	Driving Skills Impaired
	F	.07	.06	.05	.04	.04	.03	.03	.03	
2	M	.12	.10	.09	.07	.07	.06	.05	.05	
	F	.13	.11	.09	.08	.07	.07	.06	.06	
3	M	.18	.15	.13	.11	.10	.09	.08	.07	
	F	.20	.17	.14	.12	.11	.10	.09	.08	
4	M	.24	.20	.17	.15	.13	.12	.11	.10	Legally Intoxicated
	F	.26	.22	.19	.17	.15	.13	.12	.11	
5	M	.30	.25	.21	.19	.17	.15	.14	.12	
	F	.33	.28	.24	.21	.18	.17	.15	.14	

Subtract .01% for each 40 minutes of drinking.  
 1 drink = 1.5 oz. 80 proof liquor, 12 oz. 5% beer, or 5 oz. 12% wine.  
**Fewer than 5 persons out of 100 will exceed these values.**

# DSM-5

- Use in larger amounts/longer periods than intended
- Persistent desire or unsuccessful attempts to cut down
- Excess time spent obtaining or recovering from use
- Craving or strong desire to use
- Failure to fulfill major role obligations
- Important social or recreational activities given up
- Recurrent use in physically hazardous situations
- Continued use despite knowledge of medical or psychological consequence(s)
- Continued use despite recurrent social or interpersonal problems
- Tolerance
- Withdrawal

**Mild: 2-3 Criteria; Moderate: 4-5 criteria; Severe: 6 or more**

# Labs

**Physiological biomarkers be used to identify persistently elevated levels of alcohol consumption as part of the initial evaluation of patients with alcohol use disorder or in the treatment of individuals who have an indication for ongoing monitoring of their alcohol use.**

•Rationale:

- Help in determining the initial symptom severity and identifying relapses
- Detect physiological damage with some of the indirect biomarkers (e.g., AST, ALT, GGT, CDT, MCV)
- Help to emphasize the medical nature of AUD and potentially reduce stigma

- **PETH** measures a different alcohol metabolite, known as **phosphatidylethanol** (PEth), in whole blood. This new biomarker gives a window of detection of approximately two to four weeks in blood. The window can be longer in individuals who chronically or excessively consume alcohol

LEVEL DETECTED	POSSIBLE DRINKING LEVELS *
10 ng/mL	Equals 2-3 units a day for 30 days or perhaps 2 binge sessions depending on body
20ng/mL (Positive)	7 units in 2 hours for a single day, with collection the next morning for a small to medium sized person
95 ng/mL	2 binge sessions per day

Range	
<b>PEth: &lt; 10 µg/L</b>	Abstinence/Highly unlikely that alcohol has been consumed.
<b>PEth: 10 -35 µg/L</b>	Low (very occasional) alcohol consumption
<b>PEth: 35 -210 µg/L</b>	Social drinking
<b>PEth: &gt; 210 µg/L</b>	Excessive drinker



## How Long Does ALCOHOL Stay in Your System?

### FACTORS THAT INFLUENCE TIME IN BODY



**NOTE:** All times are estimates; multiple factors determine how long a drug stays in a person's system. Age, weight, history, and more are all factors

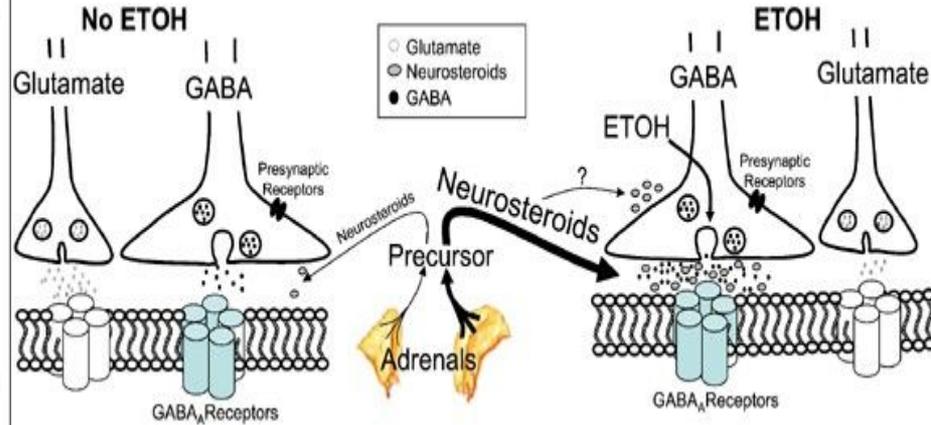
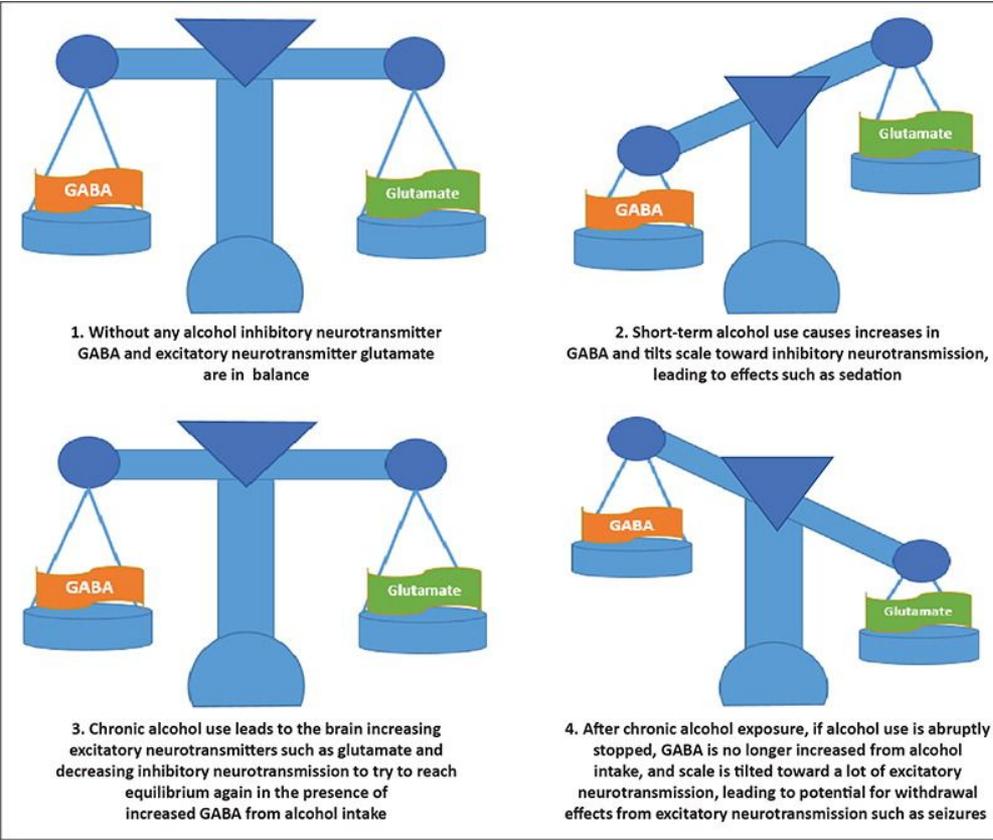
## How Long Can Alcohol Be Detected in Urine?



Biomarker	Specimen Type	Direct or Indirect	Time to elevation	Time to normalization after abstinence	Miscellaneous
<b>Ethyl sulfate</b>	Urine (also whole blood or plasma)	Direct	1-3 hours after alcohol ingestion	24-48 hours	Decreased elimination rates with renal disease False Pos: Alcohol containing products False Neg: UTI
<b>Phosphatidyl-ethanol (PEth)</b>	Whole blood	Direct	50 grams of alcohol daily for several weeks	2-3 weeks	Nearly 100% sensitivity for heavy alcohol consumption

<b>Biomarker</b>	<b>Specimen Type</b>	<b>Direct or Indirect</b>	<b>Time to elevation</b>	<b>Time to normalization after abstinence</b>	<b>Miscellaneous</b>
<b>Ethanol level</b>	Serum	Direct	Minutes to Hours	Depends on amount consumed; usually within hours	
<b>Ethyl glucuronide</b>	Serum/ urine/ hair	Direct	1-3 hours after alcohol ingestion	Urine/hair:2-3 days (urine/hair) 24-48 hours (blood)	Better sensitivity and specificity for active heavy drinking False Pos: Alcohol containing products False Neg: UTI

# Glutamate and GABA



# Alcohol Neuronal Activity in a Nutshell

1. Alcohol is consumed.
2. Endogenous opioids are released into the pleasure centers of the brain.
3. In response to this increased endogenous opioid activity, dopamine is released.
4. Dopamine causes feelings of pleasure. This reinforces the behavior and increases the likelihood that it will recur.

# Case

- 48 y.o. Male construction worker with long history of heavy drinking, reports daily consumption of 15 cans of 12 oz beer, denies other substance use and endorses symptoms of depression and insomnia, patient is endorsing cravings for alcohol at the time of the interview. He meets criteria for alcohol use disorder (AUD), moderate severity

Liver function enzymes are elevated 2 Xs upper limit of normal; macrocytosis is only other lab abnormality, he denies symptoms of alcohol withdrawal or history of complicated withdrawal pt has never received treatment for AUD or psychiatric disorder, he has a history of chronic lower back pain for which he takes, low-dose oxycodone 1-2 X/s month during flare-ups.

# Question

Which medication would you consider for treatment of alcohol use disorder in this patient?

1. Acamprosate
2. Disulfiram
3. Naltrexone (PO or IM)
4. Gabapentin
5. Topiramate

# Treatment of Alcohol Withdrawal Symptoms

- 1<sup>st</sup> step in evaluation process:
  - Would patient benefit from medical withdrawal management (i.e. “detox”)?
- Medications for Symptomatic Treatment
  - Benzodiazepines:
    - Symptom-triggered vs. standing taper
  - Supportive meds
    - Thiamine, folate, and multivitamin

# Alcohol Withdrawal Symptoms

- Minor withdrawal (within 36 hrs)
  - Tremor, diaphoresis, anxiety, insomnia, nausea/vomit
- Seizures (within 1-2 d after reducing/stopping EtOH)
  - Usually singular, generalized tonic clonic
  - Treat with benzos
- Hallucinoses (within 1-2 d after reducing/stopping EtOH)
  - Normal mental status, vitals
  - Usually visual (but may be auditory, tactile)
- Delirium Tremens (DTs) (1-4 d after withdrawal onset)
  - Disorientation, agitation, hallucinations
  - Autonomic instability, 5% mortality risk

Nausea and Vomiting

- 0 – No nausea or vomiting
- 1
- 2
- 3
- 4 – Intermittent nausea with dry heaves
- 5
- 6
- 7 – Constant nausea, frequent dry heaves and vomiting

Paroxysmal Sweats

- 0 – No sweat visible
- 1 – Barely perceptible sweating, palms moist
- 2
- 3
- 4 – Beads of sweat obvious on forehead
- 5
- 6
- 7 – Drenching sweats

Agitation

- 0 – Normal activity
- 1 – Somewhat more than normal activity
- 2
- 3
- 4 – Moderate fidgety and restless
- 5
- 6
- 7 – Paces back and forth during most of the interview or constantly thrashes about

Visual Disturbances

- 0 – Not present
- 1 – Very mild photosensitivity
- 2 – Mild photosensitivity
- 3 – Moderate photosensitivity
- 4 – Moderately severe visual hallucinations
- 5 – Severe visual hallucinations
- 6 – Extreme severe visual hallucinations
- 7 – Continuous visual hallucinations

Tremor

- 0 – No tremor
- 1 – Not visible, but can be felt at finger tips
- 2
- 3
- 4 – Moderate when patient's hands extended
- 5
- 6
- 7 – Severe, even with arms not extended

Tactile Disturbances

- 0 – None
- 1 – Very mild paraesthesias
- 2 – Mild paraesthesias
- 3 – Moderate paraesthesias
- 4 – Moderately severe hallucinations
- 5 – Severe hallucinations
- 6 – Extremely severe hallucinations
- 7 – Continuous hallucinations

Headache

- 0 – Not present
- 1 – Very mild
- 2 – Mild
- 3 – Moderate
- 4 – Moderately severe
- 5 – Severe
- 6 – Very severe
- 7 – Extremely severe

Auditory Disturbances

- 0 – Not present
- 1 – Very mild harshness or ability to frighten
- 2 – Mild harshness or ability to frighten
- 3 – Moderate harshness or ability to frighten
- 4 – Moderately severe hallucinations
- 5 – Severe hallucinations
- 6 – Extremely severe hallucinations
- 7 – Continuous hallucinations

Orientation and Clou ding of the Sensorium

- 0 – Oriented and can do serial additions
- 1 – Cannot do serial additions
- 2 – Disoriented for date but not more than 2 calendar days
- 3 – Disoriented for date by more than 2 calendar days
- 4 – Disoriented for place/person

Cumulative scoring

Cumulative score	Approach
0 – 8	No medication needed
9 – 14	Medication is optional
15 – 20	Definitely needs medication
>20	Increased risk of complications

Brief Alcohol Withdrawal Scale

	0	1	2	3
	None	Mild	Moderate	Severe
<b>Tremor</b>	No tremor	Not visible, but can be felt	Moderate, with arms extended	At rest, without arms extended
<b>Diaphoresis/ Sweats</b>	No sweats	Mild, barely visible	Beads of sweat	Drenching sweats
<b>Agitation</b> <small>Richmond Agitation-Sedation Scale</small>	RASS = 0	RASS = +1	RASS = +2	RASS = +3 or +4
	Alert and calm	Restless, anxious, apprehensive, movements not aggressive	Agitated, frequent non-purposeful movement	Very agitated or combative, violent
<b>Confusion/ Orientation</b>	Orientation to person, place, time	Disoriented to time (e.g., by more than 2 days or wrong month or wrong year) or to place (e.g., name of building, city, state), but not both	Disorientation to time and place	Disorientation to person
<b>Hallucinations (visual, auditory, tactile)</b>	None	Mild (vague report, reality testing intact)	Moderate (more defined hallucinations)	Severe (obviously responding to internal stimuli, poor reality testing)



# Non Pharmacological interventions

- There are several evidence-based options for non-pharmacological treatment that have minimal harms:

- **Motivational Enhancement Therapy (MET)**: manualized psychotherapy based on the principles of motivational interviewing; shown to have a small to medium effect size on achieving abstinence

- **Cognitive Behavioral Therapy (CBT)**: focusing on the relationships between thoughts, feelings, and behaviors; help manage urges and triggers

- **Medical Management (MM)**: manualized treatment that provides education and strategies to support abstinence and promote medication adherence

- **Community based peer support groups such as Alcoholics Anonymous (AA) and other 12-step programs SMART Recovery**: helpful in achieving long-term remission but not for replacing formal medical treatment

	<b>Philosophy: Spiritual/Non- Spiritual</b>	<b>Mutual Problems And Shared Goals: Abstinence Based</b>	<b>Political Stance</b>	<b>Facilitator- Led: Trained/Un- Trained</b>
<b>Alcoholics Anonymous</b>	Yes, Strong	Yes, Strong	None	Untrained
<b>Women For Sobriety</b>	Yes, Moderate	Yes, Strong	Moderate	Trained
<b>Smart Recovery</b>	Yes, Moderate	Yes, Moderate	None	Trained
<b>Moderation Management</b>	None	No	None	Trained
<b>Free Life</b>	None	Yes, Strong	Strong	Untrained

# Pharmacotherapy.

- Rationale:

- Naltrexone and acamprosate have the best available evidence as pharmacotherapy for patients with AUD

- These medications showed small benefits overall on alcohol-related outcomes (moderate strength of evidence)

- Harms for both medications are minimal, particularly compared with the harms of continued alcohol use, when non-pharmacological approaches have not been effective or when patients wish to use one of the medications

	<b>Naltrexone</b>	<b>Acamprosate</b>
<b>Mechanism of Action</b>	Mu-opioid receptor antagonist	Glutamate receptor modulator
<b>Indication</b>	Alcohol use disorder Opioid use disorder	Alcohol use disorder
<b>Clinical Evidence</b>	Reduced likelihood of return to any and heavy drinking; Fewer drinking days overall; Reduced subjective experience of “craving”	Decreased likelihood of returning to drinking after achieving abstinence; Fewer drinking days
<b>Pre-treatment Workup</b>	Check hepatic function	Measure serum creatinine
<b>Dosing</b>	Oral tablet: 50 mg PO daily for most; up to 100mg daily for some 25 mg PO daily then 50 mg PO daily for women due to potential GI side effects Intramuscular injection: 380 mg IM every four weeks	666 mg PO TID

	Naltrexone	Acamprosate
<b>Potential Side Effects</b>	Abdominal pain (11%); Diarrhea (13%); Nausea (29%); Dizziness (13%)	Diarrhea (17%)
<b>Contraindications</b>	None	Contraindication if CrCl <30ml/min Dose reduction if 30 < CrCl >50ml/min
<b>Special Considerations</b>	<p>Be cautious when using in patients with acute hepatitis or liver failure</p> <p>Be abstinent from all opioids for 7-14 days prior to taking naltrexone to avoid precipitated opioid withdrawal</p> <p>May be preferable to acamprosate in patients with comorbid alcohol and opioid use disorder</p>	<p>Start treatment as soon as possible after the patient archives <b>abstinence</b> and continue treatment even if the patient relapses, specially after detox.</p>

# Research on Acamprosate

- In studies leading to FDA approval, participants treated with acamprosate were able to maintain **complete abstinence** more frequently and had prolonged time to first drink than those treated with placebo.
- Participants treated with acamprosate had a greater reduction in the number of drinking days during the entire study than those treated with placebo.
- In all three studies, participants treated with acamprosate were able to regain complete abstinence after one relapse more frequently than those treated with placebo.



## Pharmacotherapy for Adults With Alcohol-Use Disorders in Outpatient Settings

Acamprosate and oral naltrexone have the best evidence for improving alcohol consumption outcomes for patients with alcohol-use disorders. **Head-to-head trials have not consistently established the superiority of one medication.** Thus, other factors may guide medication choices, such as frequency of administration, potential adverse events, coexisting symptoms, and availability of treatments.

*Comparative Effectiveness Reviews, No. 134*

Investigators: Daniel E Jonas, MD, MPH, Halle R Amick, MSPH, Cynthia Feltner, MD, MPH, Georgiy Bobashev, PhD, Kathleen Thomas, PhD, Roberta Wines, MPH, Mimi M Kim, PhD, Ellen Shanahan, MA, C Elizabeth Gass, MPH, Cassandra J Rowe, BA, and James C Garbutt, MD.

# Research on Naltrexone

In some studies, participants treated with naltrexone were not able to maintain complete abstinence more frequently than those treated with placebo.

- More consistently, participants treated with naltrexone had a **greater reduction in return to drinking** during the study than those treated with placebo and had reduced cravings.
- Participants treated with naltrexone had **fewer heavy drinking days than those treated with placebo**

# Extended Release Naltrexone

Dosing: 380mg injection in deep gluteal muscle every 4 weeks; alternate sides each month.

- Blocks opioid receptors for one entire month compared to approximately 28 doses of oral naltrexone.
- Adverse effects: injection site reactions, nausea/vomiting, precipitated opioid withdrawal, depression, elevated LFTs

Note: Large doses of opioids may be required to override the blockade in a medically monitored setting.

# Vivitrol<sup>®</sup>

(naltrexone for extended release injectable suspension)  
380 mg/vial

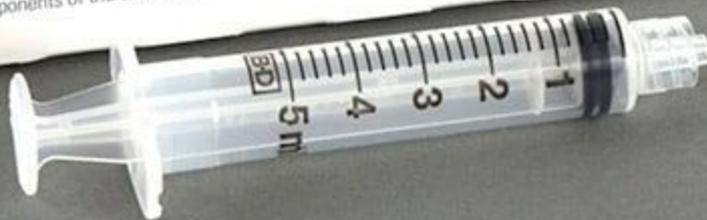
Please see accompanying full prescribing information.  
Dispense the enclosed Medication Guide to each patient.  
For further information call 1-800-848-4876 or visit [www.vivitrol.com](http://www.vivitrol.com).  
Aikermes, Inc., Waltham, MA 02451.

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(naltrexone for extended release injectable suspension)  
380 mg/vial

For gluteal intramuscular injection only. Single use vial. Discard unused portion.  
Must reconstitute VIVITROL Microspheres with the enclosed diluent prior  
to administration. See back panel for contents of carton. Do not substitute  
any components of the carton. Store refrigerated at 2-8 °C (36-46 °F)



# Research on ER Naltrexone

Participants treated with extended-release naltrexone had a greater reduction in the number of heavy drinking days than those receiving placebo.

- Effects on heavy drinking were greatest in those who had at least four days of abstinence from alcohol prior to treatment initiation.
- In the subset abstinent for at least 4 days prior to treatment initiation, extended-release naltrexone also improved continuous abstinence rates.

## Disulfiram

### Mechanism of Action

Inhibitor of aldehyde dehydrogenase, FDA approved in 1951  
When the patient consumes alcohol while taking disulfiram, the accumulation of acetaldehyde causes a physical response such as tachycardia, flushing, headache, nausea, and vomiting

### Indication

Alcohol use disorder

### Clinical Evidence

Increased likelihood of achieving abstinence in patients for whom this is their goal

### Pre-treatment Workup

ECG, physical exam, hepatic function

### Dosing

First dose 12 hours after the last drink;  
500mg PO each morning for 1-2 weeks, then 250 mg PO each morning

## Disulfiram

### Potential Side Effects

Elevations in hepatic enzymes (common and happens fast)  
Potentially fatal acute hepatotoxicity (rare)  
Neuropathy and increased blood pressure

### Contraindications

Recent myocardial infarction or coronary artery disease  
History of a seizure disorder

### Special Considerations

Only for those seeking abstinence from alcohol  
Instruct not to consume alcohol within 12-24 hours of taking disulfiram  
Recommend involving a family or roommate as an observer of daily medication adherence  
Physical reaction can be precipitated by alcohol containing products (e.g., cold medicine, mouthwashes) and certain medications (e.g., sertraline oral concentrate, metronidazole, ritonavir)

# Disulfiram take home points.

- The disulfiram-alcohol reaction usually lasts for 30 to 60 minutes, but can continue for several hours depending on the amount of alcohol consumed.
- Should never be administered to a patient who has consumed alcohol recently or is currently intoxicated from alcohol.
- Should never be administered to a patient that has consumed alcohol-containing preparations such as cough syrup, tonics, etc.

# Off-label medications

Topiramate or gabapentin be offered to patients with moderate to severe alcohol use disorder who:

- have a goal of reducing alcohol consumption or achieving abstinence,
- prefer topiramate or gabapentin or are intolerant to or have not responded to naltrexone and acamprosate, and
- have no contraindications to the use of these medications.

# Topiramate and Gabapentin

- Rationale:

- There is less available evidence on benefits and harms of topiramate and gabapentin compared to naltrexone and acamprosate
- Topiramate and gabapentin showed moderate benefits on alcohol related outcomes (moderate and low strength of research evidence, respectively)

- Implementation:

- These medications are typically used after trying naltrexone and acamprosate but may be used earlier based on patient preference

# Gabapentin for AUD

Off-label but emerging evidence for use in tx of AUD

- Proposed mechanism: reduction of post-acute withdrawal (WD) symptoms (anxiety, insomnia, etc.)
- Study results: Improved rates of abstinence and heavy drinking, particularly at 1800 mg/day total dose (titrate from lower dose, e.g. 300 mg PO TID)
- Improved symptoms of insomnia, dysphoria, and craving • Improved drinking outcomes in 1st 6 weeks when added to naltrexone post-drinking cessation
- Improved drinking outcomes in individuals with pre-study high alcohol WD sx's (1200 mg/day)
- Heavy drinking days and total abstinence
- Adverse effects: dizziness, fatigue, GI sx's, headache, impaired coordination, misuse potential

# Topiramate for AUD

- Approved as anticonvulsant and for migraine prophylaxis
- Off-label for AUD, good evidence from clinical trials in reduction of heavy drinking days, other drinking outcomes
- Mechanism of action: facilitates GABA neurotransmission, inhibits AMPA-kainate glutamate transmission (helps restoring the balance)
  - May reduce post-withdrawal dysphoria, cravings, impulsivity
- Studies have titrated dose slowly up to 300 mg/day
- Adverse effects: cognitive, paresthesias, dizziness, altered taste, weight loss; (rare: kidney stones, metabolic acidosis, narrow-angle glaucoma).

	<b>Topiramate</b>	<b>Gabapentin</b>
<b>Clinical Evidence</b>	Reduction in drinks per drinking day; Reduction in percentage of heavy or any drinking days; Reduction in the subjective experience of “craving”	Increased likelihood of abstinence from drinking and abstinence from heavy drinking
<b>Dosing</b>	Between 200-300mg daily	900-1800mg daily
<b>Potential Side Effects</b>	Short-term memory (3-12%); Dizziness (4-25%); Paresthesias and GI; Less commonly, metabolic acidosis and nephrolithiasis	Dose-dependent sedation (21%)
<b>Contraindications</b>	Renal impairment	Severe renal impairment

<b>Week</b>	<b>AM dose</b>	<b>PM dose</b>	<b>Total daily dose (mg)</b>
1	None	One 25 mg tablet	25
2	None	Two 25 mg tablets	50
3	One 25 mg tablet	Two 25 mg tablets	75
4	Two 25 mg tablets	Two 25 mg tablets	100
5	Two 25 mg tablets	One 100 mg tablet	150
6	One 100 mg tablet	One 100 mg tablet	200
7	One 100 mg tablet	One 100 mg tablet and two 25 mg tablets	250
8	One 100 mg tablet and two 25 mg tablets	One 100 mg tablet and two 25 mg tablets	300

## **Topiramate dose-escalation schedule**

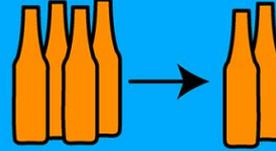
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# Treatment Goals and Recommendations

## FDA-Approved

Disulfiram  
Oral Naltrexone  
Acamprosate  
Extended-Release Naltrexone

## Reduce Heavy Drinking



Oral Naltrexone  
50-100 mg/day

## Unapproved, with Multiple Placebo- Controlled Studies

Baclofen  
Topiramate  
Gabapentin  
Oral Nalmefene\*

## Abstinence

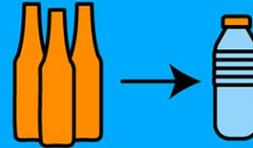


Acamprosate  
1998 mg/day

## Unapproved, with Few Placebo- Controlled Studies

Ondansetron  
Aripiprazole  
Varenicline  
LSD/Psilocybin

## Reduce Drinking Frequency



Topiramate  
Up to 300 mg/day

\*Approved in the European Union

# What about anti depressants?

**APA suggest that antidepressant medications not be used for treatment of alcohol use disorder unless there is evidence of a co-occurring disorder for which an antidepressant is an indicated treatment.**

- Rationale:

- Evidence reported minimal efficacy with antidepressants for individuals with AUD and no co-occurring conditions; outcomes worsened in some studies.

- Implementation:

- Carefully consider differential diagnoses during evaluation; mood or anxiety symptoms can be associated with alcohol use or withdrawal and need not indicate the presence of a mood or anxiety disorder

- Can be combined with other AUD medications if an antidepressant is indicated for a co-occurring disorder

# What about pregnancy ?

**APA recommends (1C) that for pregnant or breastfeeding women with alcohol use disorder, pharmacological treatments not be used unless treating acute alcohol withdrawal with benzodiazepines or unless a co-occurring disorder exists that warrants pharmacological treatment.**

- Rationale:

- There is limited data regarding the use of AUD medications and risks to a fetus or infant, but the use of topiramate was associated with an increased risk of malformation in pregnant women

- Studies with pregnant animals reported a moderate risk for naltrexone use, a high risk for acamprosate use, and possible risks for gabapentin and topiramate use

- Limited data showed potential for toxicity with disulfiram, naltrexone, and topiramate during breastfeeding

- Implementation:

- For women who become pregnant while taking a medication to treat AUD, an individualized decision should be made based on the risk of continuing or stopping the medication after discussion with the patient, her obstetrician, and, if applicable, her partner .

# Case

- 48 y.o. Male construction worker with long history of heavy drinking, reports daily consumption of 15 cans of 12 oz beer, denies other substance use and endorses symptoms of depression and insomnia, meets criteria for alcohol use disorder (AUD), moderate severity, and endorses cravings for alcohol.

Liver function enzymes are elevated 2 Xs upper limit of normal; macrocytosis is only other lab abnormality, he denies symptoms of alcohol withdrawal or history of complicated withdrawal pt has never received treatment for AUD or psychiatric disorder, he has a history of chronic lower back pain for which he takes, low-dose oxycodone 1-2 X/s month during flare-ups.

# Questions.

1. Is naltrexone contraindicated in this patient?
2. Under what circumstance would you consider disulfiram?
3. Under what circumstance would you consider combining medications?
4. What should you recommend in addition to medications?

Thank you

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