Beyond the Bottle:
Pharmacotherapy Updates for Alcohol Use Disorder

Jeremy Daniel, PharmD, BCPS, BCPP, FAAPP
Pharmacy Supervisor, Avera Behavioral Health Hospital
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Learning Objectives

- Identify a patient with alcohol use disorder using validated screening tools
- Compare first-line and emerging therapies for AUD
- Apply current evidence to initiate and monitor MAUD in clinical practice

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DSM-5-TR AUD Diagnosis

- Used in larger amounts than intended
- Persistent desire with unsuccessful attempts to cut down
- Lots of time spent obtaining alcohol
- Cravings
- Failure to fulfill major life obligations
- Continued use despite interpersonal problems
- Giving up activities to consume alcohol
- Use despite physical hazards
- Continued use despite knowledge of harm
- Tolerance
- Withdrawal

- Mild – 2-3 sx
- Moderate – 4-5 sx
- Severe – 6+ sx

APA. DSM-5-TR

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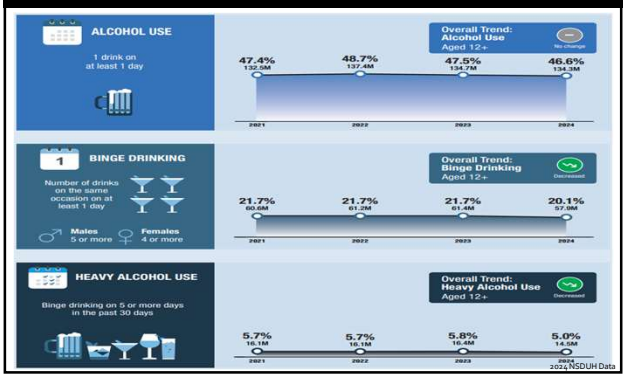
Alcohol Use in Past Month



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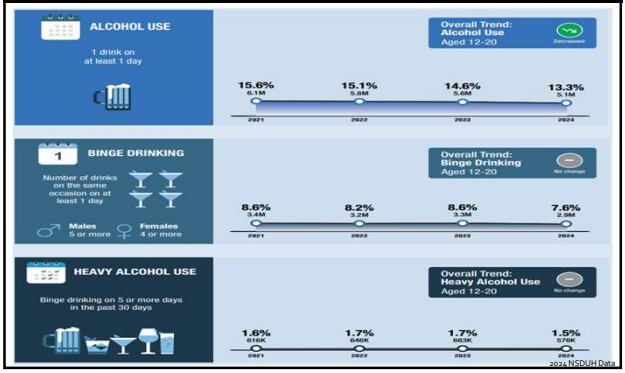
Underage Alcohol Use (Past Month)



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South Dakota Data

- Alcohol Use in Past Month (12+) = 49.84%
  - Underage (12-20) = 13.16%
- Binge Drinking in Past Month (12+) = 23.3%
  - Underage (12-20) = 8.15%
- We are worse in all categories
  - Screening is important

2024 NSDUH Data

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Screening Tools for AUD

- Alcohol Use Disorders Identification Test (AUDIT)
- Consumption (AUDIT-C)
- NIAAA Single Alcohol Screening Question (SASQ)
- CAGE Assessment
- CRAFFT Assessment

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CAGE and CRAFFT

- CAGE no longer recommended
  - **C**ut down drinking, **A**nnoyed by criticism, **G**uilty feelings, **E**ye-opener needed
  - 2+ thought to be positive screen
  - Only detects problem drinking, not milder AUD
- CRAFFT specific for adolescents
  - **C**ar, **R**elax, **A**lone, **F**orget, **F**riends, **T**rouble
  - 2+ positive screen
  - Sensitivity/specificity good for this population
    - Does not hold up in adults

NIH. Screen and Assess
US Preventative Services Task Force. JAMA. 2018

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AUDIT(-C)

- Full AUDIT is 10 questions
  - Each question scored 0-4
  - AUDIT-C is first three questions only
- See handout
- For AUDIT, score of 8+ is positive for 6.5x likelihood of AUD diagnosis
  - Sometimes used with cutoff of 4+ in primary care to identify unhealthy drinking behaviors
- On AUDIT-C, score of 4+ in men, 3+ in women is positive
- No significant difference in accuracy between the two
  - Use AUDIT-C

NIH. Screen and Assess
US Preventative Services Task Force. JAMA. 2018
Johnson JA et al. Alcohol Clin Exp Res. 2023
Kranzler HR et al. JAMA. 2018

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SASQ

- "How many times in the past year have you had ___ or more drinks in a day?"
  - 5 for men
  - 4 for women
- Performed similarly to AUDIT and AUDIT-C
  - The AUDITs provide more information that is typically helpful

Krist AH et al. N Engl J Med. 2025

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Treatment Guidelines

- Numerous guidelines exist
  - American Psychiatric Association (APA) 2018
  - VA/DoD 2021
  - Canadian guidelines 2023
- Consistent first-line options
  - Naltrexone
  - Acamprosate
- Mixed evidence on disulfiram and other medications (e.g. gabapentin)
- 2023 systematic review of 118 articles confirmed outcomes
  - Naltrexone – moderate evidence
    - Return to any drinking (NNT 18)
    - Return to heavy drinking (NNT 11)
    - Percentage of drinking days
  - Acamprosate
    - Return to any drinking (NNT 11)
    - Percentage of drinking days

Reus VI et al. AM J Psychiatry. 2018
Perry C et al. Ann Intern Med. 2022
Wood E et al. CMAJ. 2023
McPheeters M et al. JAMA. 2023

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Naltrexone

- Available as
  - 50 mg tablet
  - 380 mg injection (given IM)
- MOA
  - Opioid antagonist
    - Blocks endorphin binding to mu receptor, no dopamine release
- ADEs
  - GI upset is common when starting (think opioid receptors in gut)
  - Can cause hepatotoxicity
- Important considerations
  - Must be opioid free for 7-10 days prior to starting
  - Vivitrol has REMS program
  - Avoid in pregnancy

Naltrexone Package Insert
Vivitrol Package Insert

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Acamprosate

- Available as
  - 333 mg tablet
- MOA
  - NMDA antagonist and positive modulator of GABA
    - Attempts to correct imbalance/stabilize glutamate? Maybe…
- ADEs
  - Dose-related diarrhea/GI upset
  - Can cause depression/anxiety
- Important considerations
  - Contraindicated in active SI and CrCl < 30 mL/min
    - Can dose adjust for 30-50 mL/min
  - TID dosing is challenging for adherence

Acamprosate Package Insert

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Comparing the Two

Factor	Favors Naltrexone	Favors Acamprosate
Treatment Goal	Reduced heavy drinking	Maintain abstinence
Drinking Phenotype	Reward drinking	Relief drinking
Liver Disease	Contraindicated	Safe
Concurrent Opioid	Contraindicated	Safe
Renal Impairment	Safe	Dose adjustment/ contraindication
Dosing	Daily	Thrice daily
Can Start While Drinking?	Yes	Better evidence with abstinence first

Krist AH et al. N Engl J Med. 2025

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Emerging Treatments?

- GLP-1 receptor agonists
- Topiramate
- Baclofen
- Ketamine
- **NOTE:** none of these agents are FDA-approved for AUD

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GLP-1 RAs

- GLP-1 receptors are present in brain areas associated with reward
  - Nucleus accumbens, ventral tegmental area, amygdala, hippocampus, and nucleus tractus solitarius
- GLP-1 activation reduces alcohol-dopamine interaction
  - Read: dopamine is constant, not increased by alcohol use
- Interestingly, DPP-4 inhibitors (keep GLP around longer) don't have same effect

Rehm J et al. Lancet. 2025
Farokhnia M et al. J Clin Invest. 2025

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GLP-1 RAs

- 2025 Hendershot Study
  - 48 patient prospective study
  - Titration to semaglutide 1 mg/week vs placebo
  - Self-administered alcohol in a lab
  - No reduction in number of drinks per day
  - Reduced drinks per drinking day and weekly alcohol cravings (moderate impact)
  - Also found reduction in cigarette use as well
- 2025 Lahteenvuo Study
  - 227,866 patient observational cohort study
  - Use of semaglutide or liraglutide
  - GLP-1 RAs associated with lower hospitalization rate (semaglutide HR 0.64, liraglutide HR 0.72)
  - Authors commented risk is lower than currently approved medications

Hendershot CS et al. JAMA Psychiatry. 2025
Lahteenvuo M et al. JAMA Psychiatry. 2025

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The Future?

- It's possible, but…
- Considerations
  - Access issues
  - Cost
  - Impact on other medications
  - Still hypothetical MOA
    - Well…more than others…

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Key Take-Aways

- Multiple screening techniques
  - SD is worse than rest of nation
  - The shorter the screen, the better (as long as it works)
- Naltrexone and acamprosate are our first-line options
  - Vary in MOA, ADEs, and benefit
  - Factoring in patient choice is important!
- GLP-1's might be coming
  - Evidence is certainly there
  - Many considerations that preclude use

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Question 1

- You are screening a 24-year-old female in your ambulatory care clinic for AUD. Which screening tool is best?
  - AUDIT
  - AUDIT-C
  - CAGE
  - CRAFFT

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Question 2

- A 35-year-old male with a 20-year history of alcohol use is admitted to your hospital. His longest period of sobriety is 4 months when he was 19. He consumes at least one 750 mL bottle of rum daily to keep from withdrawal and has occasional marijuana use. After 5 days of hospitalization, labs have returned to normal limits. The patient would like to attend treatment and start MAUD. Which is most appropriate to initiate?
  - Gabapentin
  - Acamprosate
  - Naltrexone
  - Semaglutide

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Question 3

- What lab(s) are necessary to monitor when starting naltrexone?
  - (Free response)

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Questions?

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