

RECOVERY



Alcohol Use Disorder Leading the Charge in the Treatment of Alcohol Use Disorder (AUD)

VA



U.S. Department of Veterans Affairs

Veterans Health Administration
PBM Academic Detailing Service

Alcohol Use Disorder

Leading the Charge in the Treatment of Alcohol Use Disorder (AUD)

A VA Clinician's Guide

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Real Provider Resources

Real Patient Results

Your Partner in Enhancing Veteran Health Outcomes

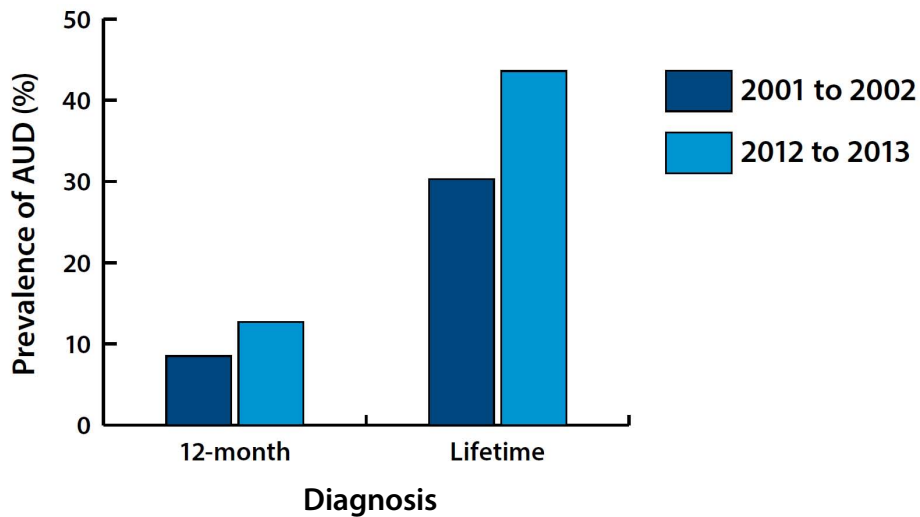
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In the U.S., alcohol use is among the top 5 leading contributors to disease burden.¹

Figure 1. Greater Than 40% Increased Prevalence of AUD in the U.S. Between 2001–2002 and 2012–2013²



Data displayed is adults ≥ 18 years old who met diagnostic criteria for AUD.



In the U.S., excessive drinking accounted for 1 in 10 deaths among working-age adults (2006–2009), shortening the lives of those who died by an average of 30 years.^{3,4}

- ✓ Rate of AUD in U.S. Veterans: 40% Veterans screen positive at one point in their lives.⁵
- ✓ Compared to Veterans without AUD, those with AUD are at higher risk for death by all causes.⁶

Despite the risks associated with excessive alcohol use, AUD continues to be undertreated.⁷ Only 7.7% of those diagnosed with AUD within 12 months received treatment.²

Alcohol Risks

- Drinking above the recommended limits (table 1) is considered unhealthy and accounts for most of the morbidity and mortality attributed to AUD⁸
- This has immediate and long-term effects that increase the risk of many harmful health conditions⁴

Figure 2. Heavy Drinking and AUD Consequences^{4,9-15,16-18}

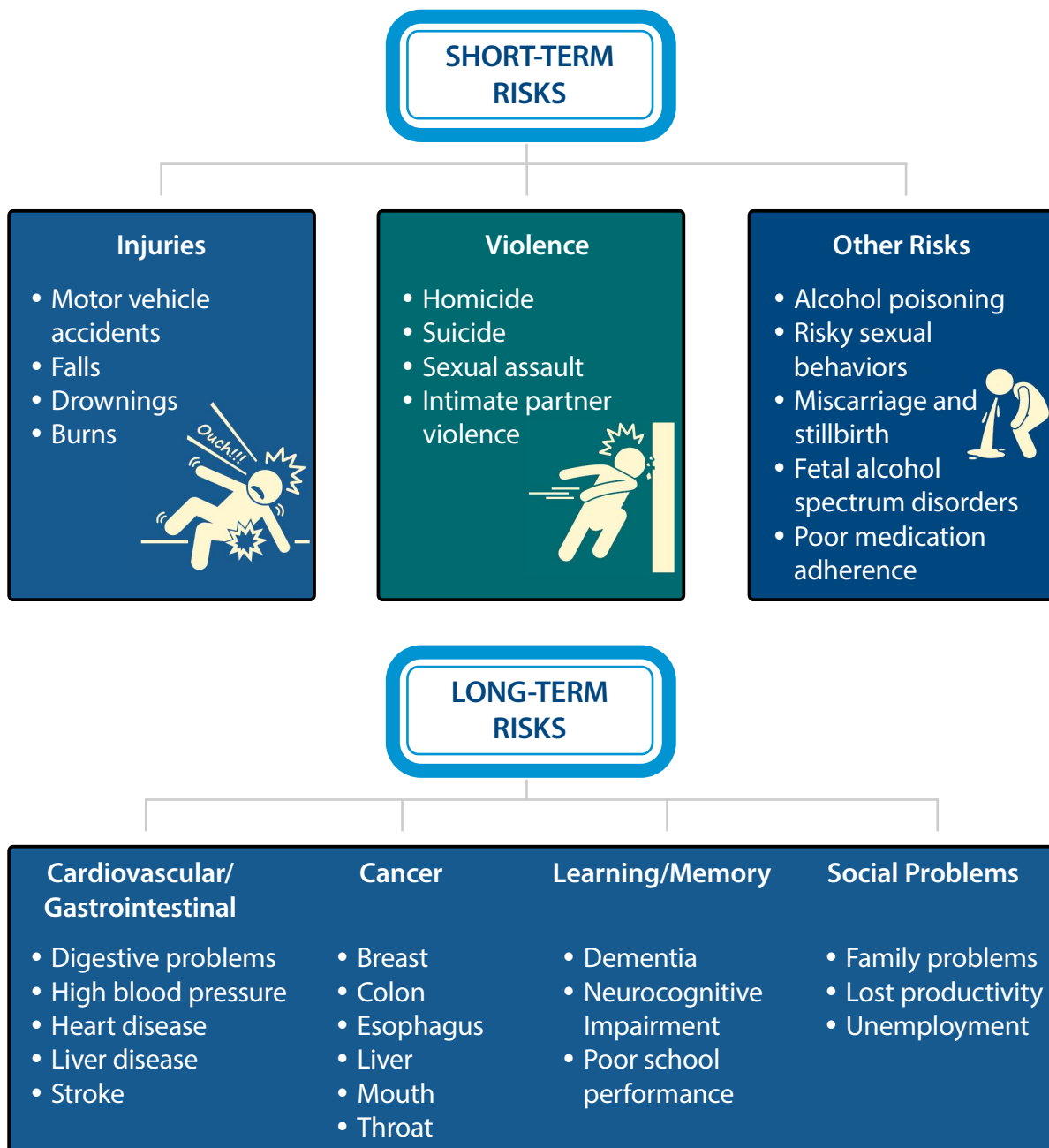


Table 1. Recommended Drinking Limits

| Gender | Single-day Limit | Weekly Limit |
|----------------------------|-------------------------|---------------------------|
| Men | ≤4 standard-size drinks | ≤14 standard-sized drinks |
| Women or Age >65 | ≤3 standard-size drinks | ≤7 standard-sized drinks |

Please see [Clinical Pearls for Treatment of Alcohol Use Disorder](#) for additional information on standard drink sizes.

Patients with AUD Need Treatment NOT Stigma

- Substance use disorders are stigmatized more than any other health condition and are often treated as a moral and criminal issue, rather than a health concern¹⁹
- Many individuals, who are untreated for AUD, identify stigma as a major barrier^{7,20}

As health care providers, we can counter stigma by using accurate, nonjudgmental language to describe AUD, those it affects, and its treatment.^{19,21}

Table 2. Changing the Conversation²¹

| | Instead of Saying... | Consider Saying... |
|--------------------------------------|---|--|
| Avoid Labeling Patients | Mr. X is a drunk and/or alcoholic. | Mr. X has an alcohol use disorder. |
| | That Veteran is a problem drinker. | That Veteran is drinking alcohol above recommended limits. |
| Avoid Judgemental Terminology | You have to stop your alcohol habit. | I would like to help you get treatment for your challenges with alcohol. |
| Be Supportive | There is no cure for your disease. | Recovery is achievable. |
| | I can't help you if you choose to keep using alcohol. | We understand that no one chooses to develop alcohol use disorder. We consider this a medical disorder that can be managed with treatment. |

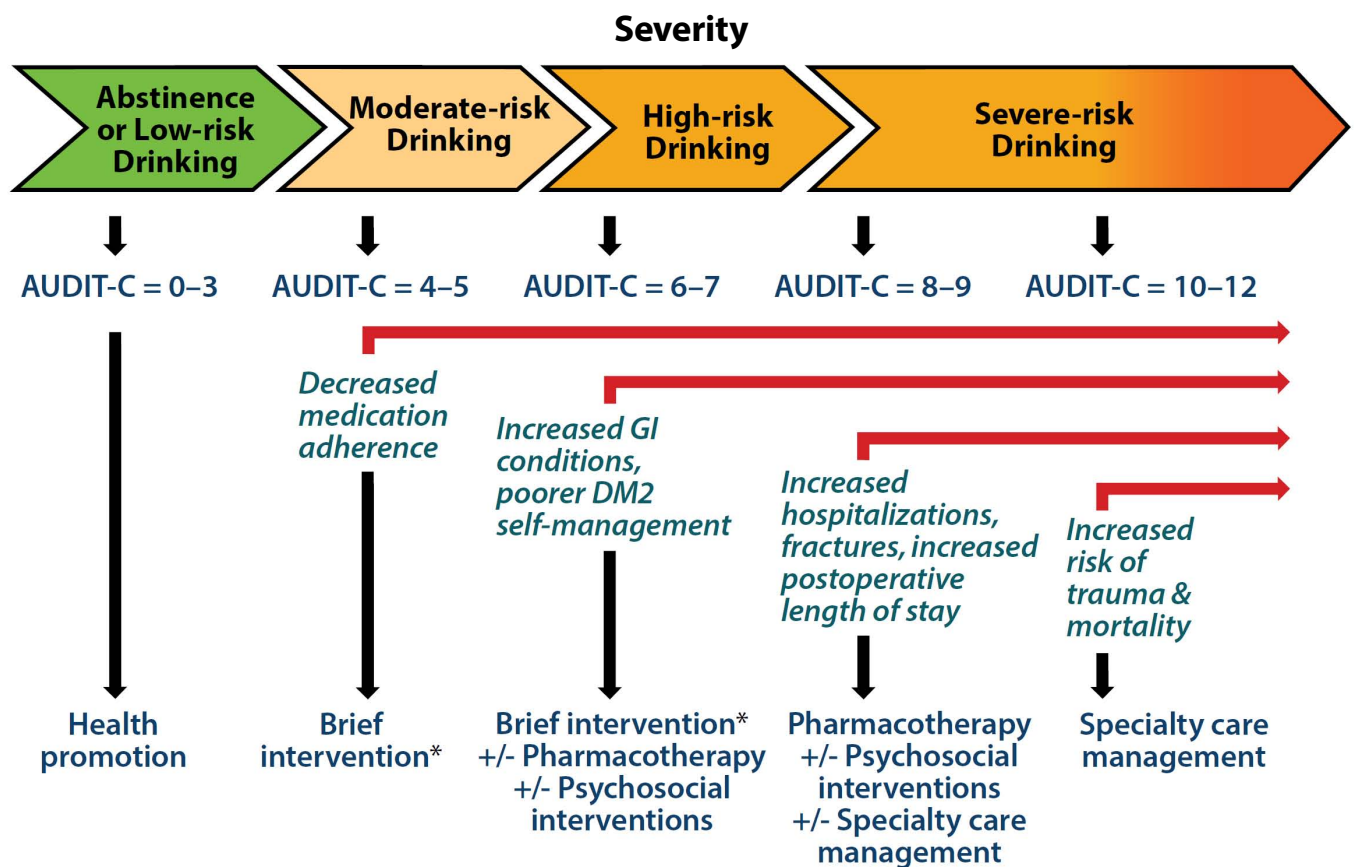
Identifying AUD

Every clinician has the opportunity to identify patients at risk for problems related to drinking alcohol.

The Alcohol Use Disorders Identification Test Consumption (AUDIT-C) questions aim to identify patients along the entire spectrum of unhealthy alcohol use from lower risk drinking to severe AUD.^{7,22} AUDIT-C scores have been correlated with rates of morbidity and mortality and can be used as a tool to guide treatment.²³⁻³³

Use the AUDIT-C to identify unhealthy alcohol use in our Veterans.

Figure 3. Spectrum of Unhealthy Alcohol Use with AUDIT-C Score and Recommended Treatment²⁵⁻³⁵



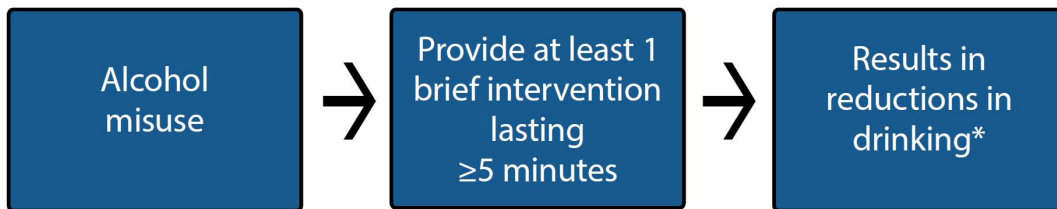
*For VA, documentation of a brief alcohol counseling is required with an AUDIT-C ≥ 5 , for both men and women. DM2 = diabetes mellitus type II; GI = gastrointestinal.

AUD Treatment Options

Brief Alcohol Interventions

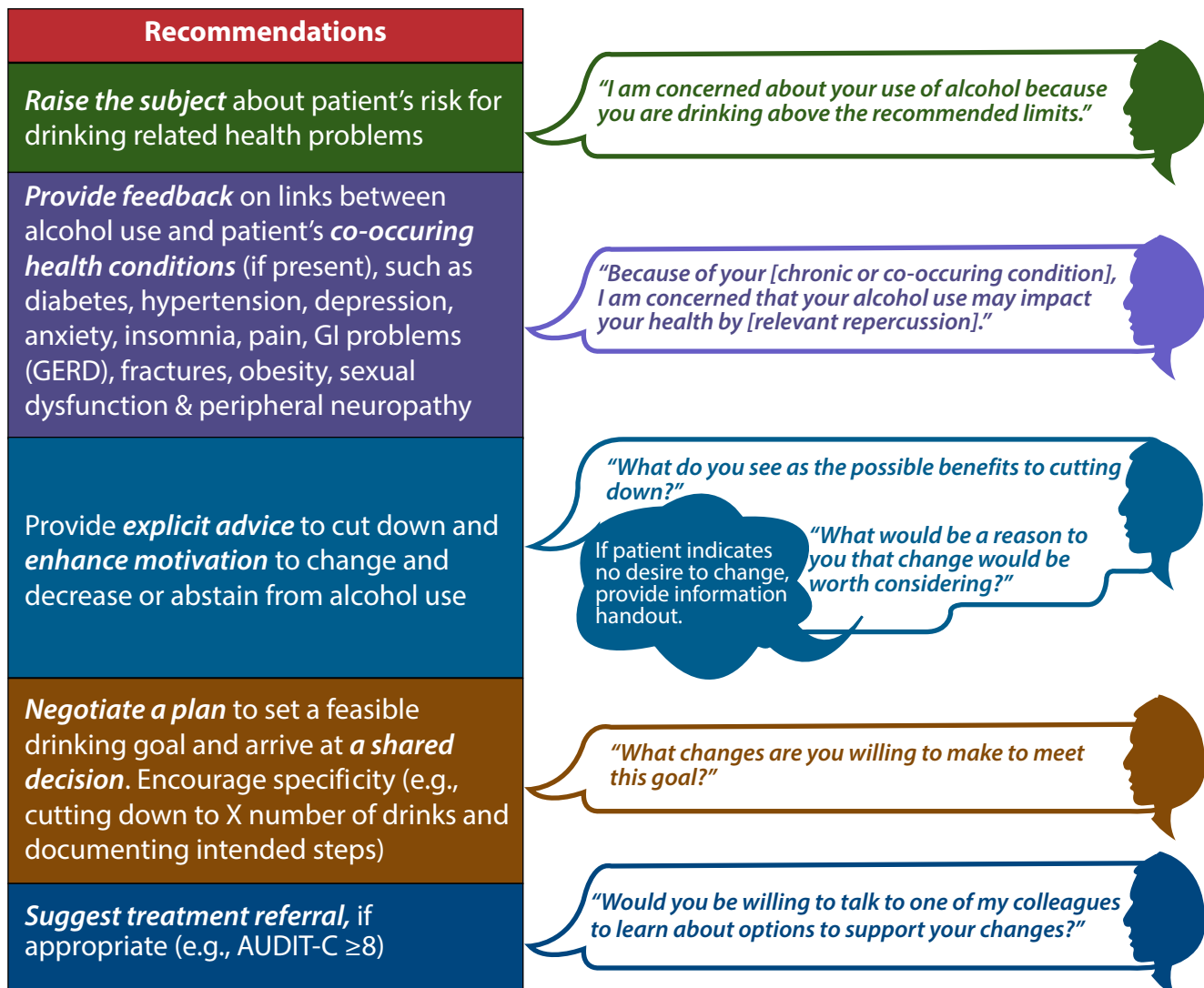
Screening for unhealthy alcohol use, followed by advice and education regarding alcohol-related risks, is effective at reducing drinking.^{7,34}

Figure 4. Brief Intervention⁷



*Outcomes best for those with unhealthy alcohol use (AUDIT-C 4–7).

Figure 5. Brief Intervention Recommendations and Example^{7,34}



Provide at least one 5-minute brief intervention to all Veterans with moderate unhealthy drinking (AUDIT-C 4–7).

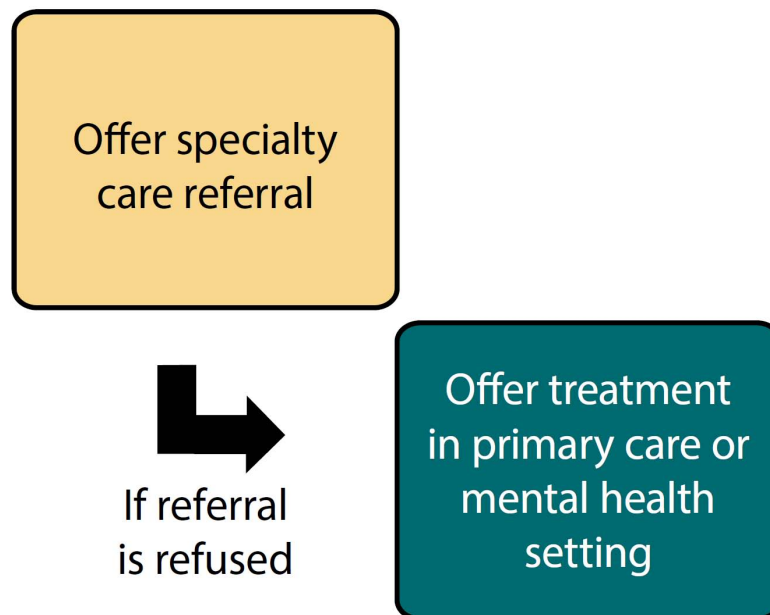
Individuals may agree to reduce drinking rather than trying for complete abstinence — consider a harm reduction approach for patients with fewer alcohol-related problems.³⁵

Patients with more severe unhealthy drinking or alcohol-related problems should be offered other treatment options, including psychosocial interventions, specialty treatment, referral, and pharmacotherapy.

Determining Treatment Setting

- Many will not accept referrals to a specialty clinic for reasons including:^{2,7,36}
 - Lack of perceived need and/or readiness for treatment
 - Fear of stigma
 - Time restrictions
 - Travel demands
- Discussion of need for referral to specialty care may help the patient recognize that there is significant concern⁷

Figure 6. Determining Treatment Setting⁷



The good news is that AUD can be successfully treated in primary care or general mental health settings.³⁷⁻³⁹

Figure 7. Why Management of AUD is Effective in Primary Care or General Mental Health Settings^{39,40}

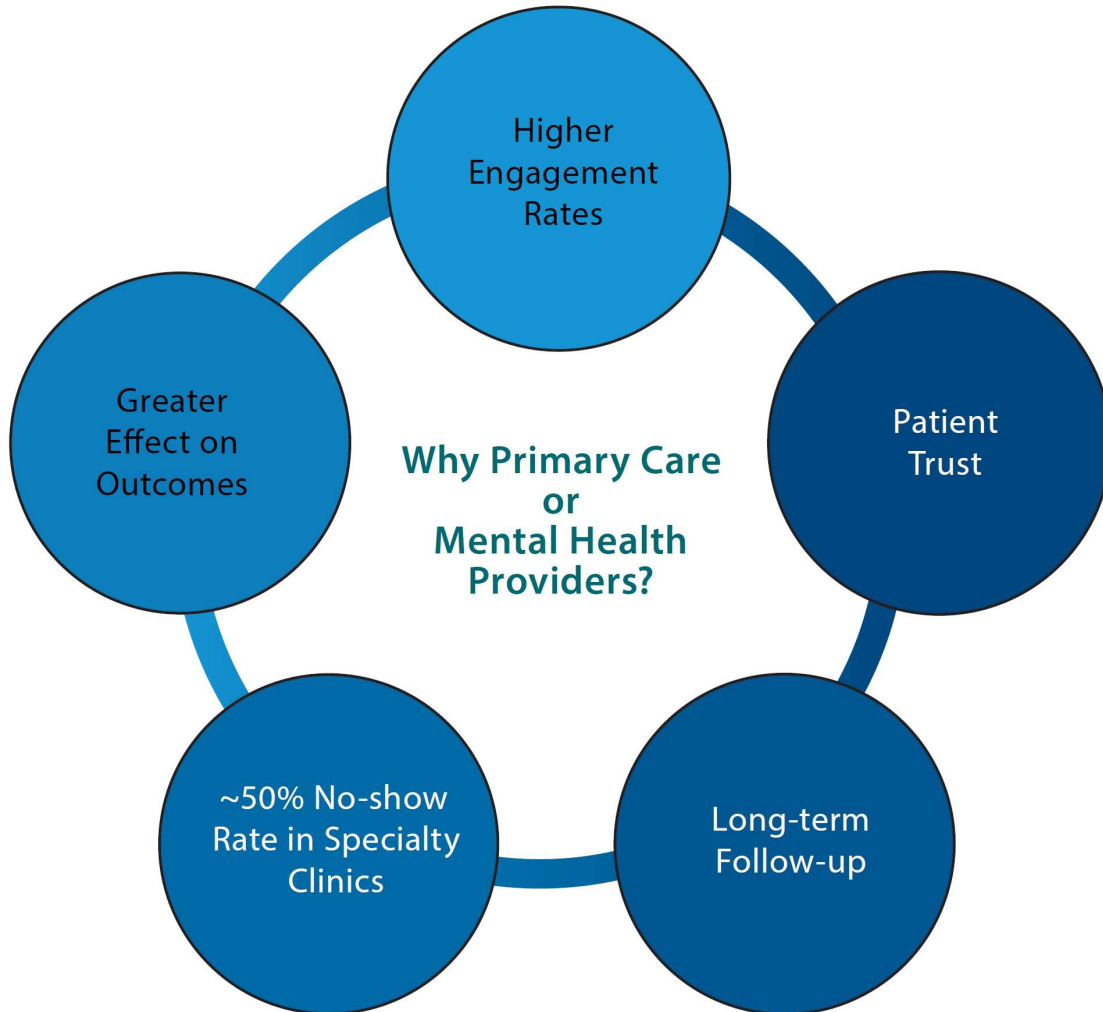
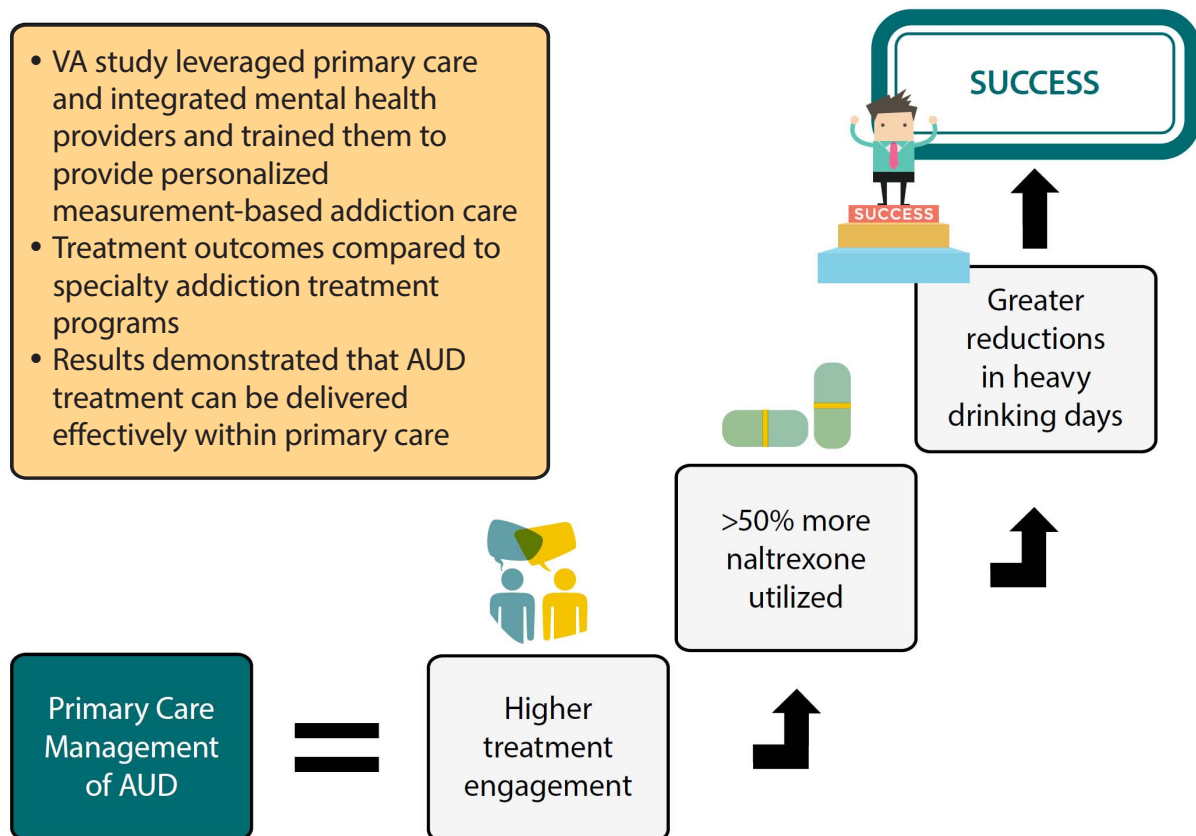


Figure 8. AUD Treatment in Primary Care Leads to Greater Rates of Treatment Engagement and Reductions in Heavy Drinking³⁸

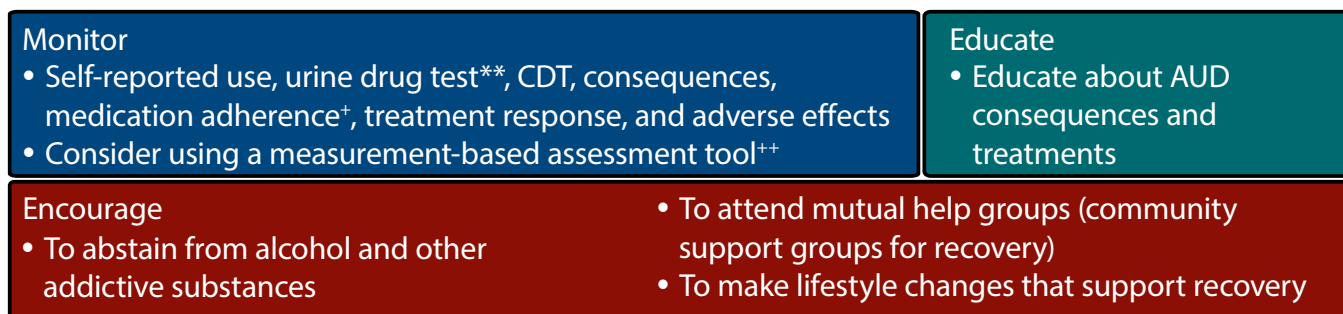


This management should include both pharmacotherapy and addiction-focused medical management.

Addiction-focused Medical Management

Structured psychosocial intervention is designed to be delivered by a medical professional (e.g., physician, nurse, physician assistant, clinical pharmacy specialist) in a primary care or general mental health setting.^{7,37}

Figure 9. Components of Addiction-focused Medical Management*



*Session structure varies according to the patient’s substance use status and treatment compliance; **Ethyl glucuronide, ethyl sulfate (alcohol analytes) can be detected in the urine for 72 hours; ⁺When adherence is inadequate develop a mutually agreed upon adherence plan; ⁺⁺Example: Brief Addiction Monitor (BAM); CDT = carbohydrate-deficient transferrin.

Pharmacotherapy

Despite their efficacy and recommendations for their use, medications for AUD are underutilized. **Among the Veterans diagnosed with AUD in FY13, only 5.8% received evidenced-based pharmacotherapy.**^{40,41}

Figure 10. AUD Pharmacotherapy Options^{7,37,42-50}


VA/DoD SUD Guideline: Recommended AUD Pharmacotherapy

First-line:

- Acamprosate*
- Disulfiram*
- Naltrexone* (oral or extended release injection)
- Topiramate

Second-line:

- Gabapentin



*FDA approved for the treatment of AUD

Consider Diagnostic Evaluation and/or Pharmacotherapy

- AUDIT-C ≥ 8 OR
- AUDIT-C ≥ 6 and current alcohol use when contraindicated (e.g. previously diagnosed with AUD, knowledge of medical contraindications)

Length of Pharmacotherapy Treatment

- ≥ 3 months; continuing pharmacotherapy up to and beyond one year may be necessary to prevent relapse
- Relapse risk is greatest during the first 90 days

Combining Different Pharmacotherapies

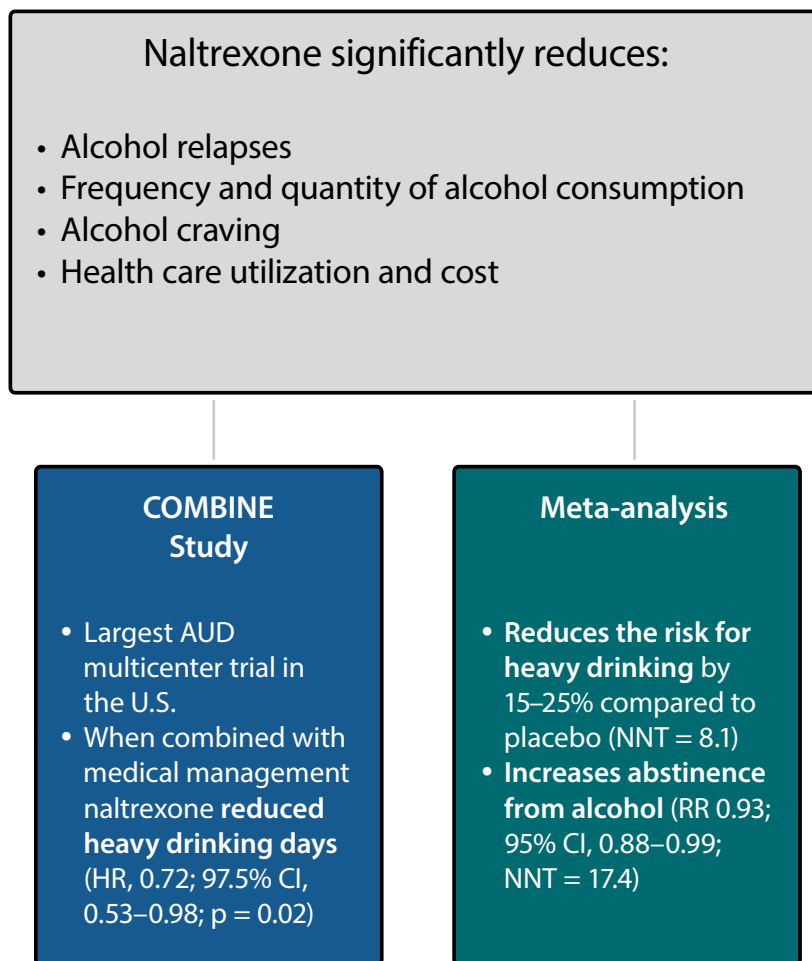
- Little evidence to support combination pharmacotherapy
- Short-term combinations may be used if patients experience a poor response to adequate trials of monotherapy combined with psychosocial interventions

Offer pharmacotherapy along with addiction-focused medical management to your Veterans with AUD

Naltrexone

The largest body of evidence supports the use of the opioid-antagonist naltrexone.^{37,45,51–54}

Figure 11. Naltrexone Reduces Heavy Drinking and Improves Abstinence^{37,45,51–55}



Naltrexone extended-release Injection should be considered when adherence is a concern.⁷

Naltrexone is an effective first-line medication for AUD. It reduces alcohol consumption and to a lesser extent promotes abstinence.

Acamprosate

This medication is an effective option for maintaining abstinence.^{7,45,56–60}

- Improved abstinence rates when used in combination with psychotherapy (NNT = 9)^{60,61}
- The risk of individuals returning to any drinking at 6 months is significantly lower than placebo (RR = 0.83, 95% CI = 0.78–0.89)⁵⁷

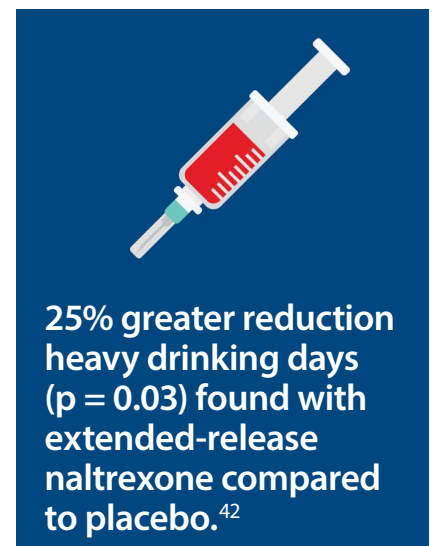
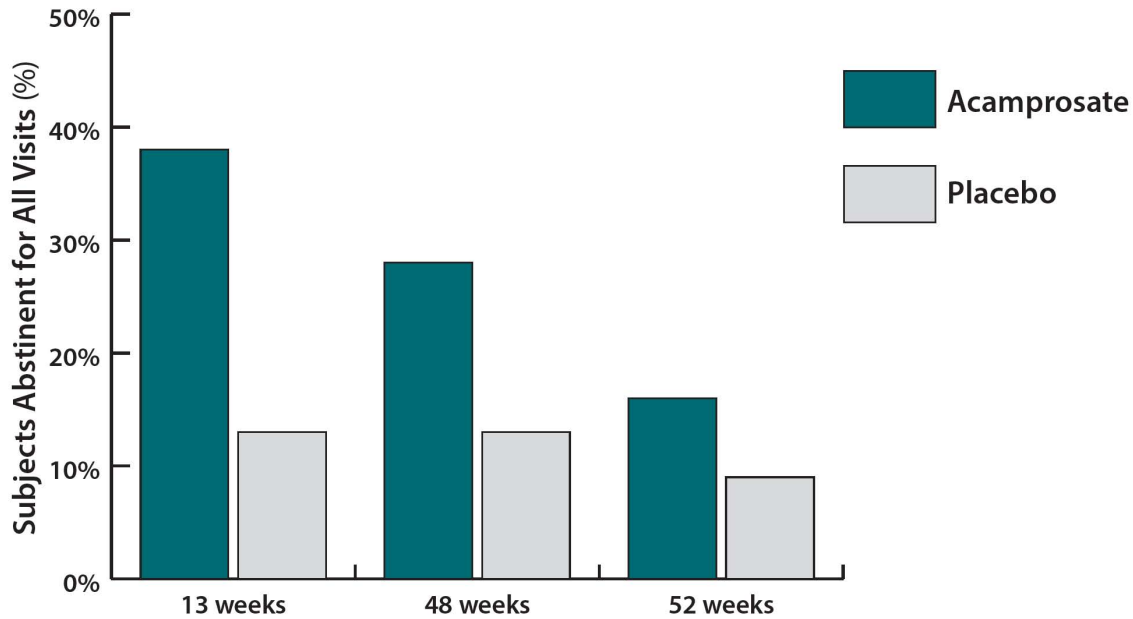


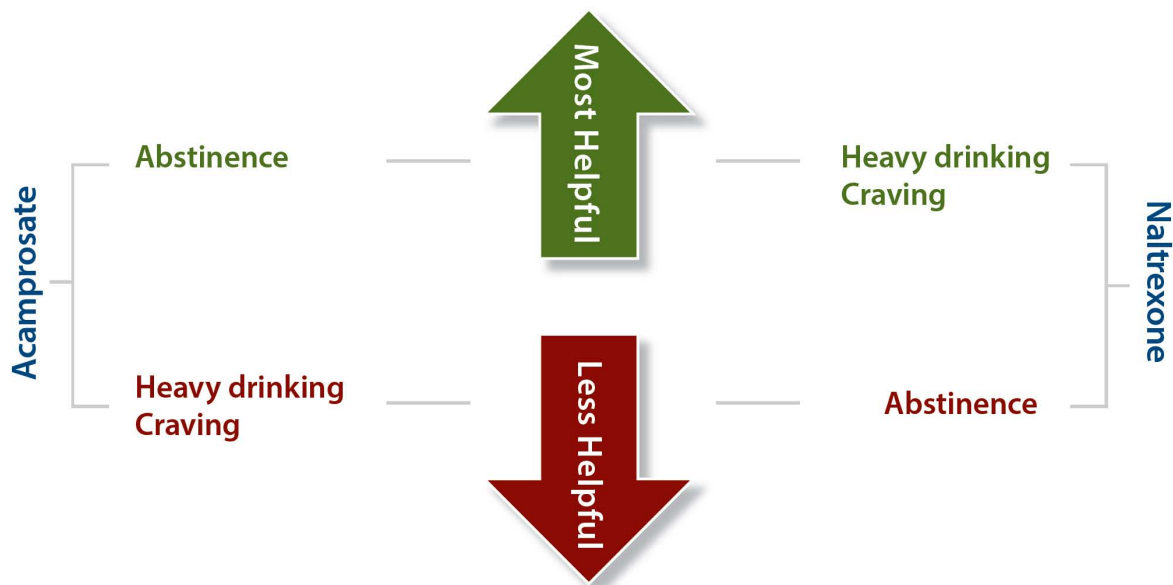
Figure 12. Complete Abstinence Two Times More Likely in Patients Taking Acamprosate at 52 Weeks Compared to Placebo⁵⁶



Efficacy data presented for three pivotal trials (n = 998). Rate of complete abstinence, time to first drink, and % days abstinence was significantly higher with acamprosate than placebo.

Naltrexone vs. Acamprosate

Figure 13. When are These Medications Most Helpful?⁴⁵



Naltrexone has a significant effect on the prevention of heavy drinking and to a lesser extent the maintenance of abstinence. Acamprosate supports abstinence; it does not influence alcohol consumption after the first drink.

Disulfiram

Disulfiram supports abstinence by creating an adverse physical reaction in which alcohol consumption is quickly followed by adverse effects (e.g. nausea, vomiting, headache, flushing). Disulfiram has been found to be most effective with monitored administration.^{63–66}

Disulfiram should only be used if:⁶⁷

- The patient is committed to a goal of complete abstinence from alcohol and is highly motivated and cognitively intact
- Veteran must be abstinent at least 24 to 48 hours before disulfiram is started

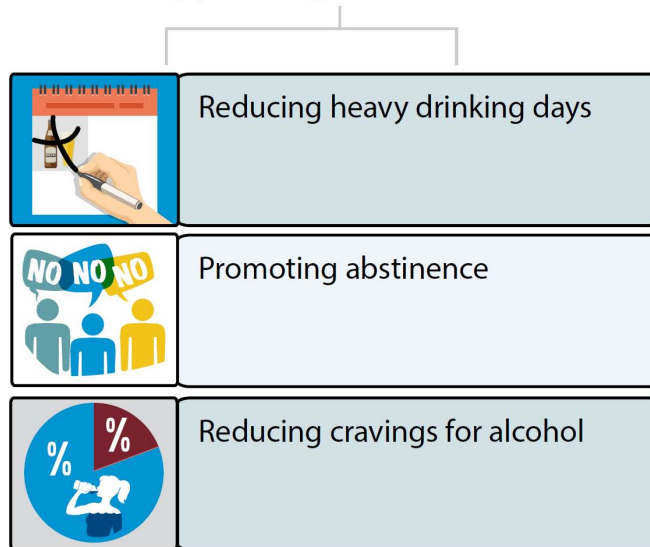
For motivated and informed patients, disulfiram can be an effective part of their recovery program, especially if there is monitored administration.^{7,63,68}

Topiramate

Topiramate is not FDA approved for AUD but is well-supported by evidence. Recent guidelines recommend it as a first line treatment option.⁷

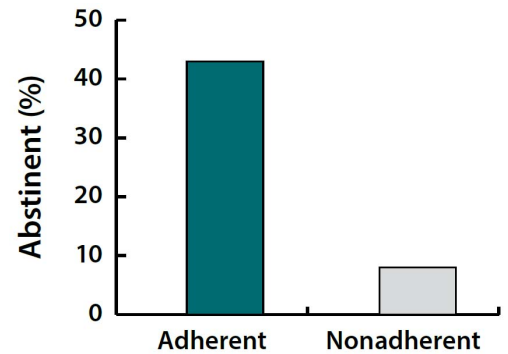
Figure 15. Topiramate^{7,69,72–74}

Evidences Supports Topiramate Effectiveness at:



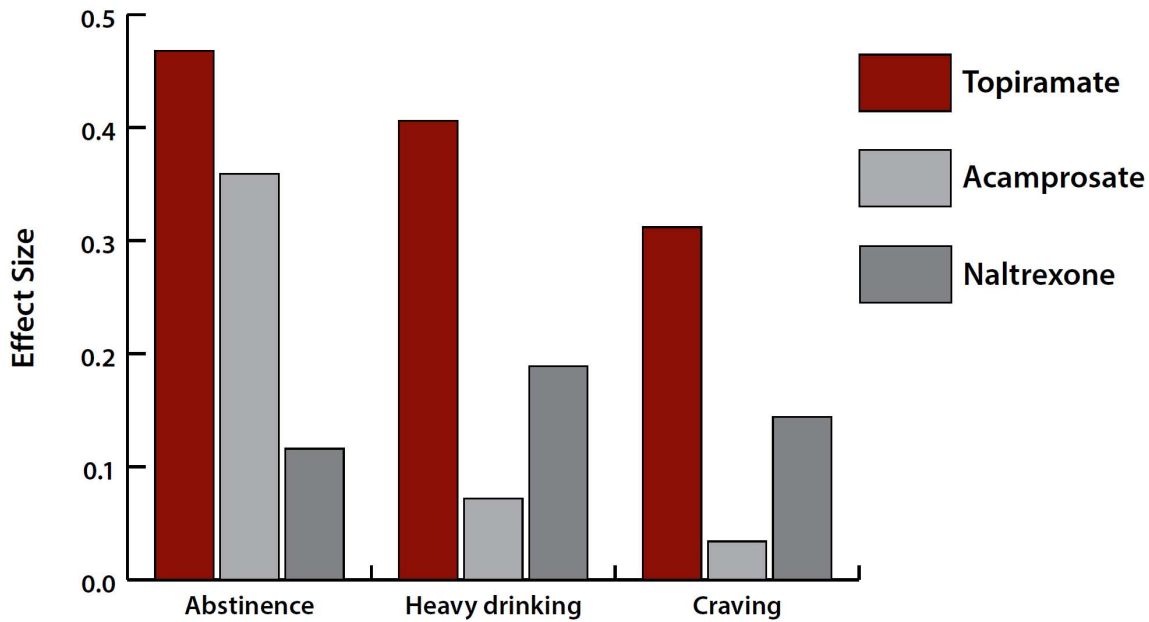
Topiramate is at least as effective as naltrexone and acamprosate, and evidence suggests that it may have a greater magnitude of effect.^{69–71}

Figure 14. Disulfiram Improves Abstinence Rates in Treatment Adherent Veterans^{7,62}



A 12-month, controlled, blinded, multicenter VA study in 605 subjects. Adherence improves with monitored administration.

Figure 16. Topiramate Meta-Analysis Finds Comparable Outcomes to a Meta-Analysis of Naltrexone and Acamprosate^{45,69}



Data summarized from two meta-analyses. Although sample difference should be taken into consideration, for each of the 3 outcome domains that were in both analysis, the overall effects of topiramate was larger than naltrexone and acamprosate.

Co-occurring Posttraumatic Stress Disorder (PTSD) and AUD

Small pilot trial found that topiramate:⁷⁵

- Reduced alcohol consumption, alcohol craving
- Reduced PTSD symptom severity—particularly hyperarousal symptoms

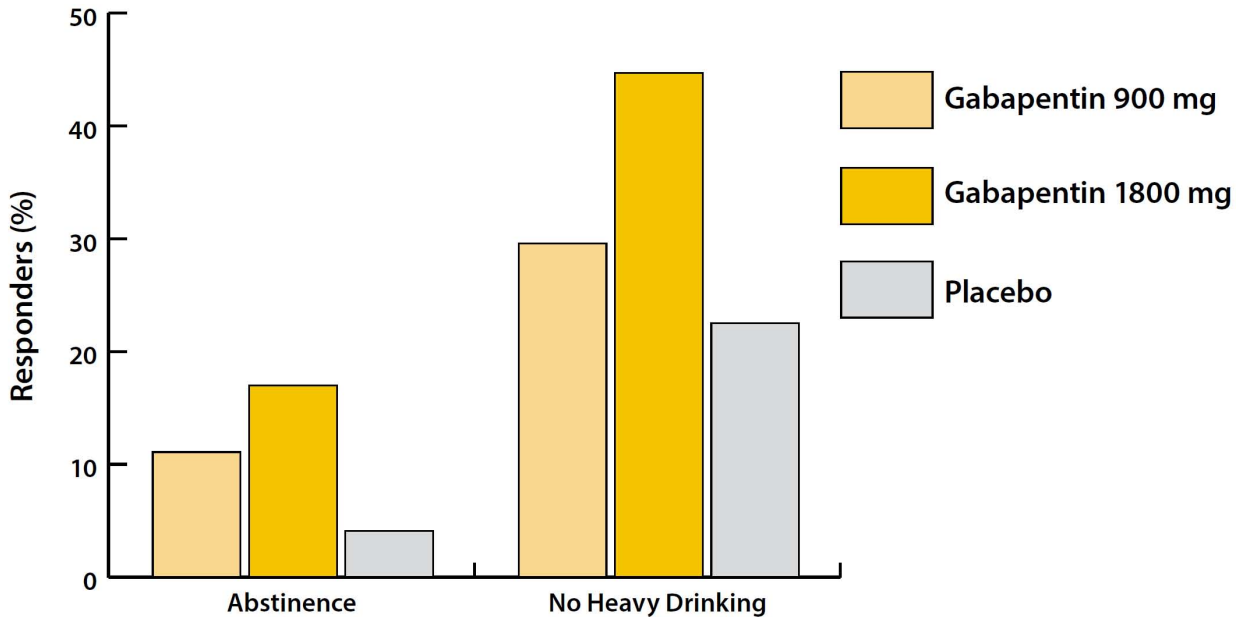
Topiramate is an effective first line treatment option for maintaining abstinence and reducing heavy drinking.

Evidence does not support one first-line medication over another; therefore selection of medications for AUD should be individualized based on the patient's needs and preferences.⁷

Gabapentin

Gabapentin is a second-line treatment option for patients with AUD for whom first-line pharmacotherapy is contraindicated or ineffective.⁷

Figure 17. Gabapentin in a linear Dose Effect Improved Abstinence and Reduced Drinking⁷⁶



In this 12 week, double-blind trial (n = 150) significant linear dose effects were reported with abstinence rate, no heavy drinking, cravings, mood, and sleep. These effects were more pronounced in the gabapentin 1800 mg group (abstinence: NNT = 8; no heavy drinking: NNT = 5).

- Gabapentin:⁷⁶⁻⁷⁹
 - Reduces heavy drinking
 - Increases abstinence
 - Improves sleep
 - Reduces acute or protracted alcohol withdrawal symptoms
- Gabapentin added to oral naltrexone may improve outcomes over naltrexone alone⁸⁰

Consider utilizing gabapentin in patients for whom first-line medications are contraindicated or not tolerated.

Table 3. AUD Pharmacotherapy Pearls and Clinical Precautions

| Medication | Good Agent For... | Not Ideal Agent For... |
|-----------------------------------|--|--|
| 1st Line Treatment Options | | |
| Acamprosate | <ul style="list-style-type: none"> • Maintaining abstinence <ul style="list-style-type: none"> • Not proven to help induce abstinence • Abstinence ≥4 days prior to initiation may improve results • Hepatic impairment • Naltrexone contraindicated secondary to opioid use | <ul style="list-style-type: none"> • Severe renal impairment (CrCl <30 mL/min) • Concerns with adherence (3x/day) • Primary goal is reducing heavy drinking |
| Disulfiram | <ul style="list-style-type: none"> • When goal of therapy is complete abstinence • May be useful under monitored administration | <ul style="list-style-type: none"> • Active alcohol use • Unsupervised administration • Cognitive deficits • Rare toxicity concerns <ul style="list-style-type: none"> • Serious liver injury • Peripheral neuropathy • Toxic psychosis • Medications that contain alcohol may precipitate reaction (e.g. ritonavir, lopinavir/ritonavir, timpranavir, fosamprenavir) |
| Naltrexone | <ul style="list-style-type: none"> • Reducing heavy drinking, cravings • Once daily dosing • Ok to initiate if patient is still drinking • Long acting injection can help with adherence • Abstinence ≥4 days prior to initiation may improve results | <ul style="list-style-type: none"> • Severe hepatic impairment • Acute hepatitis • Opioid use within the last 7 days (e.g. positive UDS) |

See [Clinical Pearls for Treatment of Alcohol Use Disorder](#) for specific monitoring recommendations.

Table 3. AUD Pharmacotherapy Pearls and Clinical Precautions (Cont.)

| Medication | Good Agent For... | Not Ideal Agent For... |
|-------------------|--|---|
| Topiramate | <ul style="list-style-type: none"> • Potential benefit in Veterans with AUD with co-occurring PTSD • Co-morbid disease states (e.g. migraine headaches) • Reducing heavy drinking • Promoting abstinence | <ul style="list-style-type: none"> • Patients who may have cognitive dysfunction or impairment • Gradual titration necessary • History of renal stones • Anorexia |

2nd Line Treatment Options

| | | |
|-------------------|---|--|
| Gabapentin | <ul style="list-style-type: none"> • Co-occurring neuropathic pain • Patients with hepatic disease who do not respond or cannot take acamprosate • Patients with anxiety or insomnia • Augmenting efficacy of naltrexone during early abstinence period | <ul style="list-style-type: none"> • Severe renal impairment • Abuse potential |
|-------------------|---|--|

See [Clinical Pearls for Treatment of Alcohol Use Disorder](#) for specific monitoring recommendations.

Other Pharmacotherapy Options Still Under Investigation

Several trials have looked at other pharmacotherapy modalities for the treatment of AUD including: baclofen, ondansetron, and varenicline. The level of evidence and risks and benefits must be carefully considered before starting any of these medications to treat AUD.

Consideration of use for baclofen, ondansetron and varenicline should only occur in patients for whom first-line and second line pharmacotherapy is contraindicated or ineffective. These medications could be useful as adjunct agents in patients with comorbid AUD and disease states for which these agents are FDA-approved.

Figure 18. Baclofen^{7,81-90}

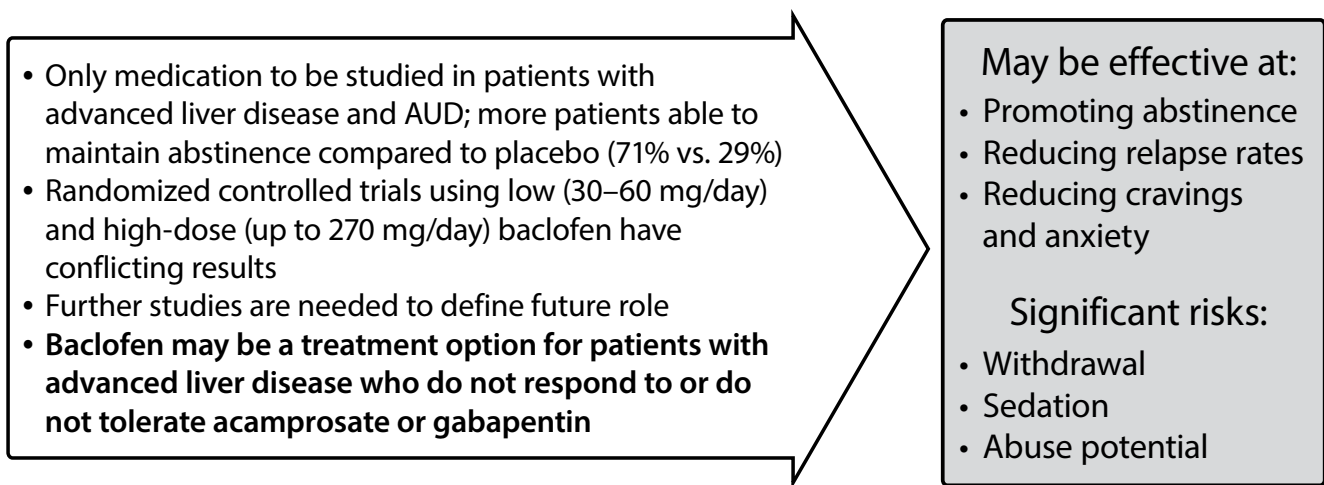
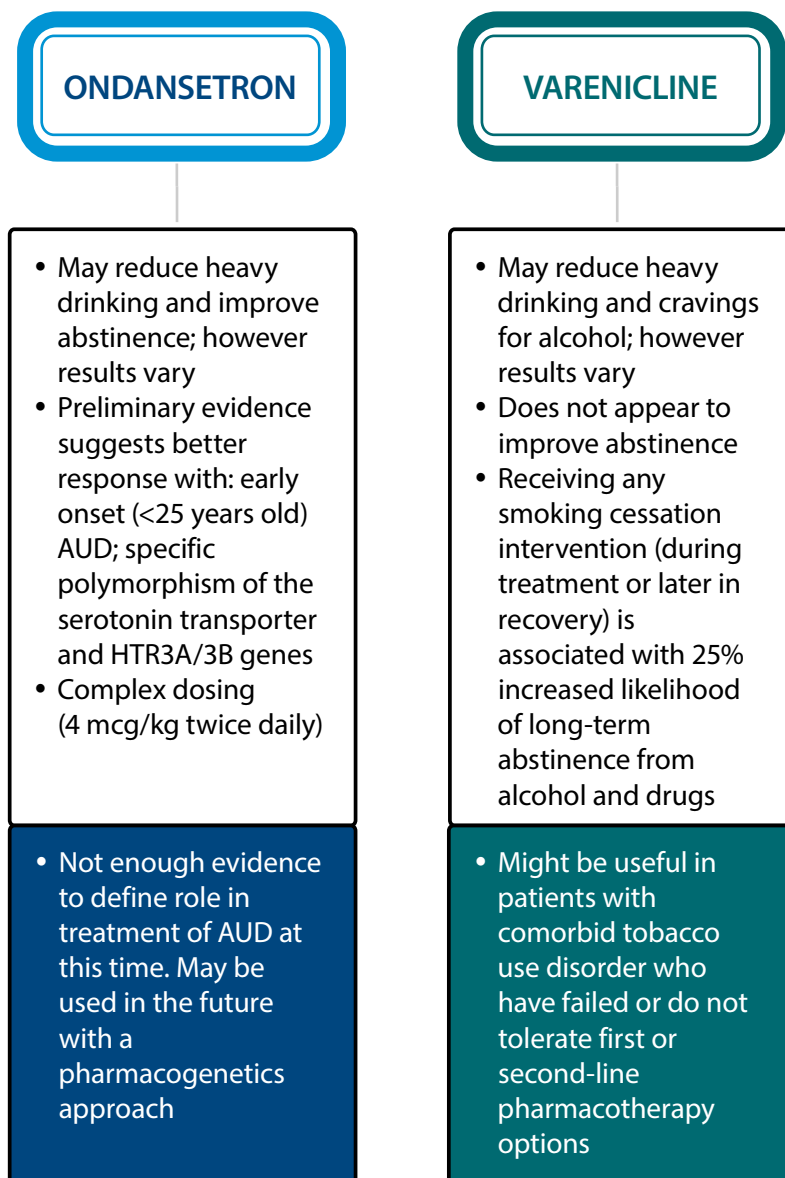


Figure 19. Additional Medications Studied^{82,90-97}



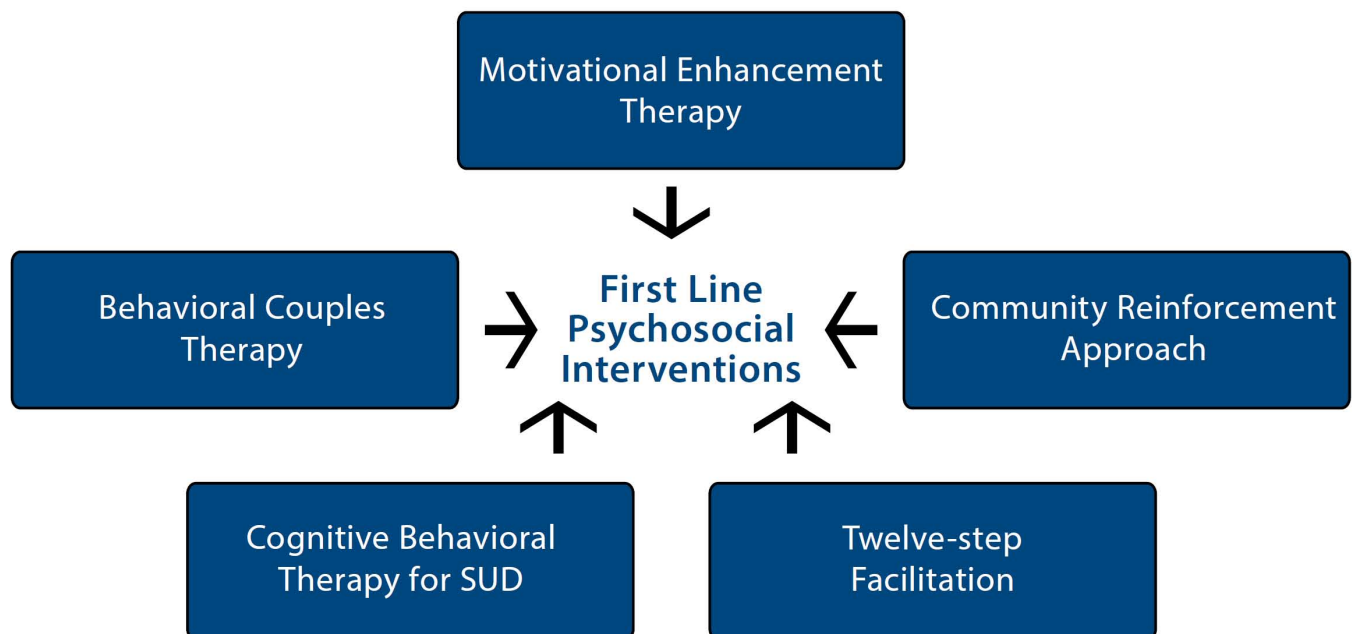
Psychosocial and Behavioral Interventions

For Veterans with alcohol use disorder it can be useful to offer, when available, one or more time limited psychosocial or behavioral interventions.⁷ In addition, encourage active involvement in group mutual help programs like Alcoholics Anonymous and SMART recovery.

Regular contact with the Veteran can positively influence treatment adherence and outcomes.

Encourage Veterans with AUD to engage in available, psychosocial counseling, behavioral interventions, and mutual help programs.

Figure 20. Effective Psychosocial Interventions⁷



Assessing Treatment Effectiveness

It is recommended to provide periodic monitoring of the Veteran's response to treatment using standardized and valid measurement instruments (e.g. Brief Addiction Monitor) and alcohol biomarkers (e.g. Carbohydrate-deficient Transferrin), whenever possible.⁷

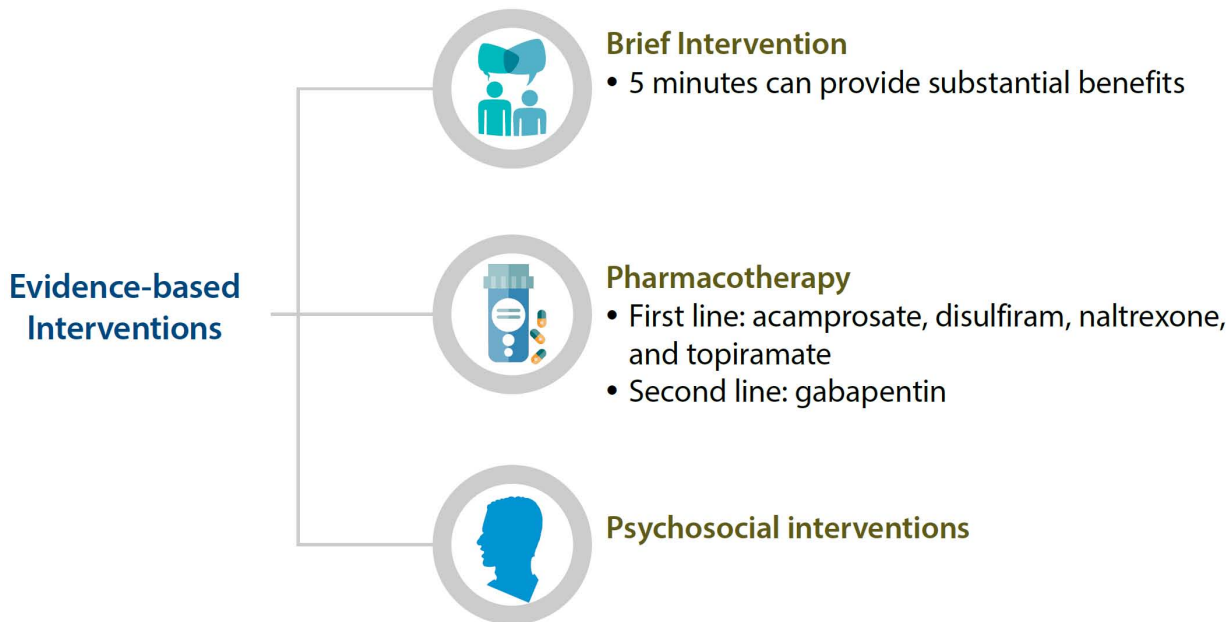
Monitor alcohol use and recovery goals to optimize treatment outcomes at periodic predetermined intervals.

Indicators of treatment response⁷:

- Current alcohol use
- Cravings
- Medication side effects
- Emerging symptoms

Summary

There are a variety of effective evidence-based pharmacotherapy and psychosocial interventions available to treat AUD.



All VA clinicians have the opportunity to be advocates for our Veterans' recovery from unhealthy alcohol use. Identifying alcohol-related risk and encouraging Veterans to obtain treatment for AUD is the right investment of VA resources.

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