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# Consider these medications to help patients stay sober

## Naltrexone can help prevent relapse in recently detoxified patients with alcohol use disorder. The evidence for acamprosate is not quite as strong.

**PRACTICE CHANGER**

Consider prescribing oral naltrexone (50 mg/d) for patients with alcohol use disorder who wish to maintain abstinence after a brief period of detoxification.[1]

**STRENGTH OF RECOMMENDATION**

**A:** Based on a meta-analysis of 95 randomized controlled trials.

Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. *JAMA*. 2014;311:1889-1900.

**ILLUSTRATIVE CASE**

Your patient, a 42-year-old man with alcohol use disorder (AUD), detoxifies from alcohol during a recent hospitalization. He doesn't want to resume drinking, but reports frequent cravings. Are there any medications you can prescribe to help prevent relapse?

Excessive alcohol consumption is responsible for 1 of every 10 deaths among US adults ages 20 to 64 years.[2] Twenty percent to 36% of patients seen in a primary care office have AUD.[3] Up to 70% of people who quit with psychosocial support alone will relapse.[3]

The US Preventive Services Task Force gives a grade B recommendation to screening all adults for AUD, indicating that physicians should provide this service.[4] For patients with AUD who wish to abstain but struggle with cravings and relapse, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) recommends considering medication as an adjunct to brief behavioral counseling.[5]

**STUDY SUMMARY**

### Evidence shows naltrexone can prevent a return to drinking

In a meta-analysis, Jonas et al[1] reviewed 123 studies (N=22,803) of pharmacotherapy for AUD. After excluding 28 studies (7 were the only study of a given drug, one was a prospective cohort, and 20 had insufficient data), 95 randomized control trials were included in the analysis. Twenty-two were placebo-controlled for acamprosate (1000-3000 mg/d), 44 for naltrexone (50 mg/d oral, 100 mg/d oral, or injectable) and 4 compared the 2 drugs. Additional studies evaluated disulfiram as well as 23 other off-label medications such as valproic acid and topiramate.

Two investigators independently reviewed the studies, checking for completeness and accuracy. Studies were also analyzed for bias using predefined criteria; those with high or unclear risk of bias were excluded from the main analysis but included in the sensitivity analysis. Funnel plots showed no evidence of publication bias.

Participants were primarily recruited as inpatients and in most studies the mean age was in the 40s. Most patients were diagnosed with alcohol dependence based on criteria in the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision* (*DSM-IV-TR*); this diagnosis translates to

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likely moderate to severe AUD in *DSM-5*. Prior to starting medications, participants underwent detoxification or achieved at least 3 days of sobriety. Most studies included psychosocial intervention in addition to medication, but the types of interventions varied. The duration of the trials ranged from 12 to 52 weeks.

Researchers analyzed 5 drinking outcomes—return to any drinking, return to heavy drinking (defined as ≥4 drinks/d for women and ≥5 drinks/d for men), number of drinking days, number of heavy drinking days, and drinks per drinking day. They also evaluated health outcomes (accidents, injuries, quality of life, function, and mortality) and adverse effects.

Acamprosate and oral naltrexone (50 mg/d) significantly decreased return to any drinking, with a number needed to treat (NNT) of 12 (95% confidence interval [CI], 8-26) for acamprosate and 20 (95% CI, 11-500) for naltrexone. Oral naltrexone (50 mg/d) also decreased return to heavy drinking (NNT=12; 95% CI, 8-26), while acamprosate did not. Neither medication showed a decrease in heavy drinking days. In a post hoc subgroup analysis of acamprosate for return to any drinking, the drug appeared to be more effective in studies with a higher risk of bias and less effective in studies with a lower risk of bias; the 2 studies with the lowest risk of bias found no significant effect.

Disulfiram had no effect on any of the drinking outcomes analyzed.

Of the off-label medications, topiramate showed a decrease in drinking days (weighted mean difference [WMD]=-6.5%; 95% CI, -12.0% to -1.0%), heavy drinking days (WMD=-9.0%; 95% CI, -15.3% to -2.7%), and drinks per drinking day (WMD=-1.0; 95% CI, -1.6 to -0.48).

There were no significant differences in health outcomes for any of the medications. Adverse events were greater in treatment groups than placebo groups. Acamprosate was associated with increased risk of diarrhea (number needed to harm [NNH]=11; 95% CI, 6-34), vomiting (NNH=42; 95% CI, 24-143), and anxiety (NNH=7; 95% CI, 5-11). Naltrexone was associated with increased risk of nausea (NNH=9; 95% CI, 7-14), vomiting (NNH=24; 95% CI, 17-44), and dizziness (NNH 16; 95% CI, 12-28).

## WHAT'S NEW

### Consider prescribing naltrexone to prevent relapse

While previous studies suggested that pharmacotherapy could help patients with AUD remain abstinent, this methodologically rigorous meta-analysis compared the efficacy of several commonly used medications and found clear evidence favoring oral naltrexone. Prescribe oral naltrexone 50 mg/d to help patients with moderate to severe AUD avoid returning to any drinking or heavy drinking after alcohol detoxification. Acamprosate may also decrease return to drinking, although the evidence is not as strong (the studies with low bias showed no effect).

**Oral naltrexone 50 mg/d significantly decreased the number of patients who resumed drinking after detoxification.**

## CAVEATS

### Medication should be used with psychosocial treatments

Pharmacotherapy for AUD should be reserved for patients who want to quit drinking and used in conjunction with psychosocial intervention.[3] Only one of the studies analyzed by Jonas et al[1] was conducted in primary care. That said, many of the psychosocial interventions—such as regular follow-up visits to encourage adherence and monitor for adverse effects, in conjunction with attendance at Alcoholics Anonymous meetings—could be done in primary care settings.

Comorbidities may limit therapy options. Naltrexone is contraindicated in acute hepatitis and liver failure, and in combination with opioids.[5] Acamprosate is contraindicated in renal disease.[5]

## CHALLENGES TO IMPLEMENTATION

### Cost, adherence may be factors for some patients

Perhaps the greatest hurdle in pharmacotherapy for AUD in primary care is a lack of familiarity with these medications. For physicians who are comfortable with prescribing these medications, implementation may be

## INSTANT POLL

**Approximately what percentage of your patients have alcohol use disorder?**

- ☐ <10%
- ☐ 10%-25%
- ☐ 26%-50%
- ☐ 51%-75%
- ☐ >75%

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hindered by a lack of available psychosocial resources for successful abstinence.

Additionally, the medications are expensive. The branded version of naltrexone 50 mg costs approximately $118 for a 30-day supply,[6] and the branded version of acamprosate costs approximately $284 for a 30-day supply.[7]

As is the case with any chronic medical condition, medication adherence is a challenge. Naltrexone is taken once daily, while acamprosate is taken 3 times a day. The risk of relapse is high until 6 to 12 months of sobriety and then wanes over several years.[5] The NIAAA recommends treatment for a minimum of 3 months.[5] JFP

**Medications for alcohol use disorder should be reserved for patients who want to quit drinking, and should be combined with psychosocial interventions.**

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