

# 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.

Sydney Hendry, MD, Anne Mounsey, MD

## 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.<sup>1</sup>

## STRENGTH OF RECOMMENDATION

**A:** Based on a meta-analysis of 95 randomized controlled trials.<sup>1</sup>

## 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?

**E**xcessive alcohol consumption is responsible for one of every 10 deaths among US adults ages 20 to 64.<sup>2</sup> About 20% to 36% of patients seen in a primary care office have AUD.<sup>3</sup> Up to 70% of people who quit with psychosocial support alone will relapse.<sup>3</sup>

The US Preventive Services Task Force gives a grade B recommendation to screening all adults for AUD, indicating that clinicians should provide this service.<sup>4</sup> For patients with AUD who wish to abstain but struggle with cravings

Sydney Hendry and Anne Mounsey are in the Department of Family Medicine at the University of North Carolina at Chapel Hill.

and relapse, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) recommends considering medication as an adjunct to brief behavioral counseling.<sup>5</sup>

## STUDY SUMMARY

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

In a meta-analysis, Jonas et al<sup>1</sup> reviewed 123 studies (N = 22,803) of pharmacotherapy for AUD. After excluding 28 studies (seven were the only study of a given drug, one was a prospective cohort, and 20 had insufficient data), 95 randomized controlled trials were included in the analysis. Twenty-two were placebo-controlled for acamprosate (1,000 to 3,000 mg/d), 44 for naltrexone (50 mg/d oral, 100 mg/d oral, or injectable) and four compared the two 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 for 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 likely moderate to severe AUD in *DSM-5*. Prior to starting medications, participants underwent detoxification or achieved at least three days of sobriety. Most studies included psychosocial intervention in addition to medication, but the types of intervention varied. The duration of the trials ranged from 12 to 52 weeks.

Researchers analyzed five drinking outcomes—return to any drinking, return to heavy drinking (defined as  $\geq 4$  drinks/d for women and  $\geq 5$  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 for acamprosate and 20 for naltrexone. Oral naltrexone (50 mg/d) also decreased return to heavy drinking (NNT, 12), while acamprosate did not. Neither medication showed a de-

crease 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 for bias and less effective in studies with a lower risk for bias. The two studies with the lowest risk for bias found no significant effect.

Disulfiram had no effect on any of the outcomes analyzed.

Of the off-label medications, topiramate showed a decrease in drinking days (weighted mean difference [WMD], -6.5%), heavy drinking days (WMD, -9.0%), and drinks per drinking day (WMD, -1.0).

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 for diarrhea (number needed to harm [NNH], 11), vomiting (NNH, 42), and anxiety (NNH, 7). Naltrexone was associated with increased risk for nausea (NNH, 9), vomiting (NNH, 24), and dizziness (NNH, 16).

## 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).

## CAVEATS

### Medication should be used with psychosocial treatments

Pharmacotherapy for AUD should be reserved for patients who want to quit drinking and should be used in conjunction with psychosocial intervention.<sup>3</sup> Only one of the studies analyzed by Jonas et al<sup>1</sup> 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.<sup>5</sup> Acamprosate is contraindicated in renal disease.<sup>5</sup>

## 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 clinicians who are comfortable with prescribing these medications, implementation may be 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,<sup>6</sup> and the branded version of acamprosate costs approximately \$284 for a 30-day supply.<sup>7</sup>

As is the case with any chronic medical condition, medication

adherence is a challenge. Naltrexone is taken once daily, while acamprosate is taken three times a day. The risk for relapse is high until six to 12 months of sobriety is achieved and then wanes over several years.<sup>5</sup> The NIAAA recommends treatment for a minimum of three months.<sup>5</sup> **CR**

## REFERENCES

1. 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.
2. CDC. Fact sheets - Alcohol use and your health. [www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm](http://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm). Accessed April 13, 2015.
3. Johnson BA. Pharmacotherapy for alcohol use disorder. UpToDate. [www.uptodate.com/contents/pharmacotherapy-for-alcohol-use-disorder](http://www.uptodate.com/contents/pharmacotherapy-for-alcohol-use-disorder). Accessed April 13, 2015.
4. US Preventive Services Task Force. Final recommendation statement: Alcohol misuse: Screening and behavioral counseling interventions in primary care. [www.uspreventiveserVICEStaskforce.org/Page/Document/RecommendationStatementFinal/alcohol-misuse-screening-and-behavioral-counseling-interventions-in-primary-care](http://www.uspreventiveserVICEStaskforce.org/Page/Document/RecommendationStatementFinal/alcohol-misuse-screening-and-behavioral-counseling-interventions-in-primary-care). Accessed April 13, 2015.
5. US Department of Health and Human Services; National Institutes of Health; National Institute on Alcohol Abuse and Alcoholism. Excerpt from *Helping Patients Who Drink Too Much: A Clinician's Guide*. [http://pubs.niaaa.nih.gov/publications/Practitioner/Clinicians\\_Guide2005/PrescribingMeds.pdf](http://pubs.niaaa.nih.gov/publications/Practitioner/Clinicians_Guide2005/PrescribingMeds.pdf). Accessed April 13, 2015.
6. Drugs.com. Revia prices, coupons and patient assistance programs. [www.drugs.com/price-guide/revia](http://www.drugs.com/price-guide/revia). Accessed April 13, 2015.
7. Drugs.com. Campral prices, coupons and patient assistance programs. [www.drugs.com/price-guide/campral](http://www.drugs.com/price-guide/campral). Accessed April 13, 2015.

## ACKNOWLEDGEMENT

The PURLs Surveillance System was supported in part by Grant Number UL1RR024999 from the National Center For Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources or the National Institutes of Health.

Copyright © 2015. The Family Physicians Inquiries Network. All rights reserved.

Reprinted with permission from the Family Physicians Inquiries Network and *The Journal of Family Practice*. 2015;64(4):238-240.