

Implementing AHRQ Effective Health Care Reviews

Helping Clinicians Make Better Treatment Choices

Pharmacotherapy for Adults with Alcohol Use Disorder

Practice Pointers by ELIZABETH SALISBURY-AFSHAR, MD, MPH, *Heartland Health Outreach, Chicago, Illinois*

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to produce evidence to improve health care and to make sure the evidence is understood and used. A key clinical question based on the AHRQ Effective Health Care Program systematic review of the literature is presented, followed by an evidence-based answer based upon the review. AHRQ's summary is accompanied by an interpretation by an *AFP* author that will help guide clinicians in making treatment decisions. For the full review, clinician summary, and consumer summary, go to <https://www.effectivehealthcare.ahrq.gov/ehc/index.cfm/search-for-guides-reviews-and-reports/?pageAction=displayProduct&productId=2161>.

This series is coordinated by Kenny Lin, MD, MPH, Associate Deputy Editor for *AFP* Online.

A collection of Implementing AHRQ Effective Health Care Reviews published in *AFP* is available at <http://www.aafp.org/afp/ahrq>.

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 90.

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Key Clinical Issue

What are the potential benefits and adverse effects of medications used to treat alcohol use disorder (AUD) in adult outpatients?

Evidence-Based Answer

The oral medications acamprosate, naltrexone, and disulfiram, and the long-acting injectable formulation of naltrexone have been approved by the U.S. Food and Drug Administration for AUD. Acamprosate and oral naltrexone improve alcohol consumption outcomes for patients with AUD. (Strength of recommendation [SOR]: C, based on disease-oriented evidence.) However, studies directly comparing these medications have not consistently established the superiority of one medication over another. Evidence related to injectable naltrexone is currently limited. Evidence from well-controlled trials of disulfiram suggests that treatment with disulfiram does not result in an overall reduction in alcohol consumption. (SOR: C, based on disease-oriented evidence.)

Evidence is insufficient to permit conclusions about the effect of acamprosate or naltrexone on health outcomes (e.g., mortality, quality of life, function, accidents).

Practice Pointers

Primary care physicians commonly encounter adults with AUD. In 2013, the prevalence of AUD among adults in the United States was 7%,¹ and alcohol misuse is the third leading cause of preventable death in the United States, after tobacco use and obesity.² The U.S. Preventive Services Task Force recommends that physicians routinely screen adults for alcohol misuse and provide brief behavioral counseling interventions to reduce

alcohol misuse.³ Alcohol use was previously subcategorized as harmful use, alcohol abuse, and alcohol dependence; however, the *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., outlines criteria for a single diagnosis of AUD that is measured from mild to severe depending on symptoms.⁴

Of the medications approved by the U.S. Food and Drug Administration for AUD, there is moderate evidence that acamprosate and oral naltrexone reduce alcohol consumption outcomes. A meta-analysis comparing acamprosate and oral naltrexone did not find a statistically significant difference between the two drugs with regard to return to any drinking⁵⁻⁸ or return to heavy drinking.⁵⁻⁷ Most studies included a psychosocial intervention in addition to the medication.

Important factors to consider when deciding between acamprosate and oral naltrexone for AUD include dosing regimen, contraindications, and potential adverse effects. Acamprosate dosing is two 333-mg tablets three times per day, compared with 50 to 100 mg once per day for oral naltrexone. Because acamprosate is cleared through the kidneys, it is contraindicated in patients with renal failure, and dosing should be adjusted for patients with moderate renal impairment. Oral naltrexone is metabolized through the liver, and is therefore contraindicated in patients with liver failure and acute hepatitis; caution should be used in the presence of other liver diseases depending on potential risks and benefits. Additionally, naltrexone blocks opioid receptors, so it should not be used in patients who are using, or will need to use, opioids because it inhibits the effects and can precipitate withdrawal symptoms in dependent individuals. Results of a meta-analysis found that patients taking

acamprosate were more likely to report anxiety, diarrhea, and vomiting compared with those taking placebo. Patients taking oral naltrexone had higher rates of dizziness,

nausea, and vomiting compared with those taking placebo. A free guide for clinicians on medications for the treatment of AUD is available from the Substance Abuse and

Clinical Bottom Line: Efficacy and Effectiveness of Medications for Alcohol Use Disorder

Acamprosate (vs. placebo)

Reduced the risk of return to any drinking: RD = -0.09 (95% CI, -0.14 to -0.04), NNT = 12 ●●○

Had similar effect on return to heavy drinking: RD = -0.01 (95% CI, -0.04 to 0.03) ●●○

Reduced the percentage of drinking days: WMD = -8.8 (95% CI, -12.8 to -4.8) ●●○

Disulfiram (vs. placebo) did not have a significant effect on return to any drinking: RD = -0.04 (95% CI, -0.11 to 0.03) ●○○

Naltrexone, 50 mg orally (vs. placebo)

Reduced the risk of return to any drinking: RD = -0.05 (95% CI, -0.10 to -0.00), NNT = 20 ●●○

Reduced the risk of return to heavy drinking: RD = -0.09 (95% CI, -0.13 to 0.04), NNT = 12 ●●○

Reduced the percentage of drinking days: WMD = -5.4 (95% CI, -7.5 to -3.2) ●●○

Reduced the percentage of heavy drinking days: WMD = -4.1 (95% CI, -7.6 to -0.61) ●●○

Naltrexone injection (vs. placebo)

Had similar effect on return to any drinking: RD = -0.04 (95% CI, -0.10 to 0.03) ●○○

Had similar effect on return to heavy drinking: RD = -0.01 (95% CI, -0.14 to 0.13) ●○○

Reduced the percentage of heavy drinking days: WMD = -4.6 (95% CI, -8.5 to -0.56) ●○○

Topiramate* (vs. placebo)

Reduced the percentage of drinking days: WMD = -8.5 (95% CI, -15.9 to -1.1) ●●○

Reduced the percentage of heavy drinking days: WMD = -11.5 (95% CI, -18.3 to -4.8) ●●○

Reduced the number of drinks per drinking day: WMD = -1.1 (95% CI, -1.7 to -0.4) ●●○

Other drugs*

The evidence is insufficient to determine the efficacy of other drugs, including amitriptyline, aripiprazole, atomoxetine, baclofen, buspirone, citalopram, desipramine, fluoxetine, fluvoxamine, gabapentin, imipramine, olanzapine, ondansetron, paroxetine, quetiapine, varenicline, and viloxazine.

Acamprosate vs. naltrexone

No significant difference between the two medications in return to any drinking ●●○

No significant difference between the two medications in return to heavy drinking ●●○

No significant difference between the two medications in the percentage of drinking days ●○○

NOTE: Studies typically included psychosocial interventions, and effect sizes reflect the added benefits of medications beyond those of psychosocial interventions. Alcohol use disorder is defined as meeting criteria in the Diagnostic and Statistical Manual of Mental Disorders, 5th ed.

CI = confidence interval; NNT = number needed to treat; RD = risk difference; WMD = weighted mean difference.

*— Not approved by the U.S. Food and Drug Administration for the treatment of alcohol dependence, alcohol abuse, or alcohol use disorder.

Strength of evidence scale

High: ●●● There are consistent results from good-quality studies. Further research is very unlikely to change the conclusions.

Moderate: ●●○ Findings are supported, but further research could change the conclusions.

Low: ●○○ There are very few studies, or existing studies are flawed.

Insufficient: ○○○ Research is either unavailable or does not permit estimation of a treatment effect.

Adapted from the Agency for Healthcare Research and Quality, Effective Health Care Program. Pharmacotherapy for adults with alcohol use disorder (AUD) in outpatient settings. Clinician research summary. Rockville, Md.: Agency for Healthcare Research and Quality; February 2016. <https://www.effectivehealthcare.ahrq.gov/ehc/products/477/2161/alcohol-misuse-drug-therapy-clinician-160211.pdf>. Accessed March 25, 2016.

Mental Health Services Administration at <http://store.samhsa.gov/shin/content//SMA15-4907/SMA15-4907.pdf>.

EDITOR'S NOTE: *American Family Physician* SOR ratings are different from the AHRQ Strength of Evidence (SOE) ratings.

Address correspondence to Elizabeth Salisbury-Afshar, MD, MPH, at Elizabeth.salisbury@gmail.com. Reprints are not available from the authors.

REFERENCES

1. National Institute on Alcohol Abuse and Alcoholism. Alcohol facts and statistics. <http://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/alcohol-facts-and-statistics>. Accessed March 5, 2016.
2. Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. *JAMA*. 2004;291(10):1238-1245.
3. Moyer VA. Screening and behavioral counseling interventions in primary care to reduce alcohol misuse: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2013;159(3):210-218.
4. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, Va.: American Psychiatric Association; 2013.
5. Anton RF, O'Malley SS, Ciraulo DA, et al.; COMBINE Study Research Group. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. *JAMA*. 2006;295(17):2003-2017.
6. Kiefer F, Jahn H, Tarnaske T, et al. Comparing and combining naltrexone and acamprostate in relapse prevention of alcoholism: a double-blind, placebo-controlled study. *Arch Gen Psychiatry*. 2003;60(1):92-99.
7. Morley KC, Teesson M, Reid SC, et al. Naltrexone versus acamprostate in the treatment of alcohol dependence: a multi-centre, randomized, double-blind, placebo-controlled trial. *Addiction*. 2006;101(10):1451-1462.
8. Mann K, Lemenager T, Hoffmann S, et al.; PRE-DICT Study Team. Results of a double-blind, placebo-controlled pharmacotherapy trial in alcoholism conducted in Germany and comparison with the US COMBINE study. *Addict Biol*. 2013;18(6):937-946. ■

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