Pharmacotherapy for Adults With Alcohol Use Disorder in Outpatient Settings

KEY ISSUE

Medications can be effective in treating alcohol use disorder (AUD) when used in combination with psychosocial interventions. Evidence from epidemiological studies suggests that improving alcohol consumption outcomes (such as reduction in return to drinking or in percentage of drinking days) would likely result in improved health outcomes. However, medications are underutilized in treating AUD, thus providing opportunities for expanding treatment optimization. This is a summary of a systematic review evaluating the efficacy, comparative effectiveness, and adverse effects of medications in adults with AUD. The systematic review included 167 articles published from January 1, 1970, to October 11, 2013. The full report, listing all studies, is available at *www.effectivehealthcare.ahrq.gov/alcohol-disorder*.

BACKGROUND

Alcohol use disorder (AUD) includes harmful use of alcohol, alcohol abuse, and alcohol dependence. In the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), alcohol abuse and alcohol dependence are no longer distinguished and are identified together as AUD. The prevalences of 12-month and lifetime AUD among adults in the United States in 2012 and 2013 were 13.9 percent (32.6 million individuals) and 29.1 percent (64.5 million individuals), respectively.[1] Between 2006 and 2010, there were, on average, nearly 85,000 deaths per year related to alcohol consumption in the United States.

Current guidelines by the Veterans Administration, the National Institute on Alcohol Abuse and Alcoholism, and the Substance Abuse and Mental Health Services Administration all recommend that pharmacotherapy be offered as an adjunct to psychosocial therapies (e.g., cognitive behavioral therapy, 12-step programs). However, estimates indicate that fewer than 1 in 3 patients with AUD receives treatment, and fewer than 1 in 10 patients receives pharmacotherapy as part of their treatment. Medications approved by the U.S. Food and Drug Administration for AUD include acamprosate (Campral®, thrice daily), disulfiram (Antabuse®, once daily), oral naltrexone (ReVia®, once daily), and extended-release injectable naltrexone (Vivitrol®, once monthly). In addition, medications such as topiramate have not been approved to treat AUD but have been used or studied as treatment for AUD.

Health care utilization studies* report reduced medical costs among patients treated with AUD medication when compared with patients treated without it.[2] A meta-analysis of three health care utilization studies on alcohol dependence reported that total medical costs were $3,649 less among patients on AUD medication than those not on the medication.[3]

Summary of Evidence From the Systematic Review

- ✓ Acamprosate and oral naltrexone improve alcohol consumption outcomes for patients with AUD. Head-to-head trials have not consistently established the superiority of one medication over another. (*See Table 1.*)
- ✓ Evidence related to injectable naltrexone is currently limited.
- ✓ Evidence from randomized controlled trials does not support the efficacy of disulfiram.
  - » Disulfiram may be recommended to individuals who have a goal of abstinence but for whom acamprosate and oral naltrexone are not suitable or to individuals who prefer disulfiram and understand its risks.[4]
- ✓ Most studies evaluated medications in combination with a psychosocial cointervention; the potential benefits of using the medications alone are not well established.
- ✓ Evidence from randomized controlled trials was insufficient to determine the effectiveness of AUD medications for improving health outcomes (e.g., mortality, quality of life, and function).
  - » Epidemiological studies consistently related heavy alcohol consumption to an increased risk of serious health problems and suggest that improving alcohol consumption outcomes would likely result in improved health outcomes.

*Considerations for Programs and Policies**

Given the underutilization and the effectiveness of pharmacotherapy for AUD, individuals responsible for AUD programs and policies may consider:

- ✓ Reducing barriers to access by promoting benefit coverage for oral and injectable prescriptions in combination with psychosocial therapy
- ✓ Encouraging patients to use medication adherence programs and educating them about how the medications and psychosocial programs work to treat AUD
- ✓ Educating health care providers (physicians, counselors, therapists, etc.) about the effectiveness of available pharmacotherapies in conjunction with psychosocial therapies as recommended by current clinical guidelines
- ✓ Providing education to employee assistance program providers and occupational medicine providers to enable them to more effectively support employees with AUD during their treatment

* These studies and considerations were not evaluated in the systematic review but are offered to assist policymakers in applying this evidence.

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Table 1: Summary of Findings and Strength of Evidence for the Efficacy and Effectiveness of Medications Used To Treat AUD
(Note: Studies assessed in this review typically included psychosocial cointerventions in addition to medications.)

Medication	Outcome	N Studies[a]	N Subjects	Finding	SOE
Acamprosate vs. placebo	Return to any drinking	16	4,847	Reduced by acamprosate	●●○
	Return to heavy drinking	7	2,496	No difference	●●○
	Percentage of drinking days	13	4,485	Reduced by acamprosate	●●○
Disulfiram vs. placebo	Return to any drinking	2	492	No difference	●○○
Naltrexone 50 mg oral vs. placebo	Return to any drinking	16	2,347	Reduced by naltrexone	●●○
	Return to heavy drinking	19	2,875	Reduced by naltrexone	●●○
	Percentage of drinking days	15	1,992	Reduced by naltrexone	●●○
	Percentage of heavy drinking days	6	521	Reduced by naltrexone	●●○
Naltrexone injection vs. placebo	Return to any drinking	2	939	No difference	●○○
	Return to heavy drinking	2	615	No difference	●○○
	Percentage of heavy drinking days	2	926	Reduced by naltrexone	●○○
Topiramate[b] vs. placebo	Percentage of drinking days	2	521	Reduced by topiramate	●●○
	Percentage of heavy drinking days	2	521	Reduced by topiramate	●●○
	Number of drinks per drinking day	2	521	Reduced by topiramate	●●○
Other drugs[b]	The evidence is insufficient to determine the efficacy of other medications because of inconsistency, imprecision, or lack of sufficient studies in the literature (e.g., amitriptyline, aripiprazole, atomoxetine, baclofen, buspirone, citalopram, desipramine, fluoxetine, fluvoxamine, gabapentin, imipramine, olanzapine, ondansetron, paroxetine, quetiapine, varenicline, viloxazine).				

N = number; SOE = strength of evidence

[a] This column only includes studies rated as having a low or medium risk of bias that were included in the main analysis; these numbers do not include studies rated as having a high or unclear risk of bias that were included in sensitivity analyses.

[b] These medications have not been approved by the U.S. Food and Drug Administration as treatment for alcohol dependence, alcohol abuse, or AUD.

STRENGTH OF EVIDENCE SCALE

●●● **HIGH**–High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.

●●○ **MODERATE**–Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.

●○○ **LOW**–Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.

○○○ **INSUFFICIENT**–Evidence either is unavailable or does not permit a conclusion.

RESOURCES FOR CLINICIANS AND CONSUMERS

The clinician research summary, *Pharmacotherapy for Adults With Alcohol Use Disorder (AUD) in Outpatient Settings,* and the consumer research summary, *Medicines To Treat Alcohol Use Disorder: A Review of the Research for Adults,* are free companions to this policymaker research summary. They are meant to assist clinicians and consumers in informed decisionmaking. Additional resources on AUD for clinicians and consumers are offered by the National Institute on Alcohol Abuse and Alcoholism and are available at *www.niaaa.nih.gov/publications.*

ORDERING INFORMATION

For electronic copies of this policymaker research summary, the clinician research summary, the consumer research summary, and the full systematic review, visit *www.effectivehealthcare.ahrq.gov/alcohol-disorder.*

REFERENCES

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