

Patient abusing alcohol or drugs? Help starts with a single question

Although binge drinking and drug use are rarely discussed during office visits, they're common, costly, and potentially fatal. Help patients stop with these easy-to-use screening tools and effective intervention strategies.

Daniel C. Vinson, MD, MSPH
Family and Community
Medicine, University
of Missouri, Columbia

VinsonD@health.missouri.edu

The author reported no potential conflict of interest relevant to this article.

PRACTICE RECOMMENDATIONS

- › Screen patients for substance use disorders, with a single (validated) question for alcohol and another for drugs. **(A)**
- › Follow a positive screen for alcohol with an assessment to distinguish between hazardous drinking and drinking that is indicative of alcohol dependence. **(C)**
- › Approach a substance use disorder as you would any chronic medical condition, seeking to engage the patient to encourage behavior change. Motivational interviewing is a useful tool. **(C)**
- › Consider pharmacotherapeutic options for patients with alcohol or drug dependence. **(A)**

Strength of recommendation (SOR)

- (A)** Good-quality patient-oriented evidence
- (B)** Inconsistent or limited-quality patient-oriented evidence
- (C)** Consensus, usual practice, opinion, disease-oriented evidence, case series

Episodic heavy drinking, like alcoholism and drug addiction, is increasingly recognized as a medical problem that primary care physicians can, and should, address.¹ But it is rarely the chief reason for an office visit. Nor is it a subject patients are likely to bring up.

However, patients *are* generally willing to talk to a trusted doctor who asks about their use (or misuse) of alcohol or other substances. And primary care physicians can do much to help—with brief interventions, a growing armamentarium of pharmacotherapy, and referrals as needed. In the pages that follow, you'll find easy-to-use screening tools and effective intervention strategies.

Screening needn't be time-consuming

Screening for substance use isn't difficult. In fact, it can usually be accomplished with 2 targeted questions—one for alcohol use and one for drugs.

■ **Alcohol.** Two single-question screens to detect hazardous drinking have been validated, despite having different parameters. Ask either:

Q: When was the last time you had more than ____ drinks (4 for women and 5 for men) in one day?

or

Q: How many times in the past year have you had ____ or more drinks (4 for women and 5 for men) in one day?

For the first question, any answer within the past 3 months is a positive screen for hazardous drinking.² For the second, anything other than zero is positive.^{3,4}

Initial screening can also be done with the AUDIT-C (**TABLE**), a validated short (3-question) version of the Alcohol Use Disorders Identification Test that can be self-administered.^{5,6}

CONTINUED

TABLE

3-question AUDIT-C screen for alcohol dependence^{5,6}

1. How often do you have a drink containing alcohol?	
<u>0</u> Never	<u>3</u> 2 to 3 times a week
<u>1</u> Monthly or less	<u>4</u> 4 or more times a week
<u>2</u> 2 to 4 times a month	
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	
<u>0</u> I don't drink.	<u>2</u> 5 or 6
<u>0</u> 1 or 2	<u>3</u> 7 to 9
<u>1</u> 3 or 4	<u>4</u> 10 or more
3. How often do you have 6 or more drinks on one occasion?	
<u>0</u> Never	<u>3</u> Weekly
<u>1</u> Less than monthly	<u>4</u> Daily or almost daily
<u>2</u> Monthly	

Scoring the AUDIT-C

	Alcohol dependence	
	Men	Women
Threshold score	5	4
Sensitivity (%)	80	76
Specificity (%)	74	78
AROC	0.769	0.767

AROC, area under the receiver operating characteristic curve; AUDIT, Alcohol Use Disorders Identification Test.

■ **Drugs.** Only one single-question screen for drug use has been validated:

Q: How many times in the past year have you used an illegal drug or taken a prescription medication for nonmedical reasons?

Any answer other than never is a positive screen for hazardous drug use.⁷

CASE ► Jason F, a healthy and fit 28-year-old, has been your patient, along with his family, for years. He's in your office because of a knee injury he incurred while running, and you take a moment to ask him, for the first time, how much he drinks and whether he takes drugs. His answer—that he drinks 3 or 4 times a week and often has multiple drinks at parties or nights out with the guys—takes you a bit by surprise.

Now what?

Tell me more about it

It is important to respond to a positive screen by requesting more information. In the conversation that ensues, the patient may provide the details you need to determine whether the drinking or drug use is indicative of a diagnosable substance use disorder, an umbrella term for alcohol or drug abuse and alcohol or drug dependence.

■ **Alcohol or drug abuse vs dependence.** Criteria for alcohol or drug abuse in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, text revision (DSM-IV-TR) include risky behavior, such as drinking and driving; problems with work and/or close relationships; or run-ins with the law, such as an arrest for driving while intoxicated. Criteria for alcohol or drug dependence include the inability to cut down or stop using the substance; evidence of tol-

erance and withdrawal; spending more time ingesting the substance; increasing attention to substance use while interest in other activities diminishes; and continued use despite recurrent problems.⁸

Tools zero in on extent of problem

To learn more about your patient's situation, consider using the following criteria and tools:

■ **DSM criteria.** Ask the following 2 questions, which are among DSM-IV-TR criteria for alcohol dependence:

1. How many times in the last year have you had a lot more to drink than you intended?
2. How many times in the last year have you been drinking in situations where it could have been hazardous, where you could have caused an accident or gotten hurt?

Any answer other than zero to either question is suggestive of a substance use disorder. In exploratory analyses, this approach had positive likelihood ratios of 4.7 to 16 and negative likelihood ratios of 0.05 to 0.30.^{9,10}

Although the above questions refer to alcohol use, they could be revised to learn more about a patient's use of marijuana or other drugs, as well. (There are few tools for the assessment of drug use, because *any* illegal or nonmedical use of controlled substances has clear risks of major harm.)

■ **CAGE.** Another tool that is effective in assessing alcohol use is the 4-question CAGE—an acronym for **C**ut down, **A**nnoyed, **G**uilty, and **E**ye opener:

- Have you ever felt that you should cut down on your drinking?
- Have people annoyed you by criticizing your drinking?
- Have you ever felt bad or guilty about your drinking?
- Have you ever had a drink in the morning to get rid of a hangover?

One meta-analysis found that a positive CAGE test—ie, a positive response to one or more of the questions—had a sensitivity of 0.85 and a specificity of 0.78 in identifying alcohol dependence in a primary care setting (using DSM criteria as the gold standard).¹¹

■ **AUDIT.** This 10-item tool, a longer ver-

sion of the AUDIT-C (available at <http://www.medstudentlearning.com/node/6556>), can also be used to determine the extent of alcohol use. This test provides detailed information about the quantity and frequency of alcohol use; however, it does not clearly distinguish between hazardous drinking and alcohol use disorders.¹²

If the patient is a teen

Assessment methods can be adjusted without difficulty to fit the age of the patient. The National Institute on Alcohol Abuse and Alcoholism has published the *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*, available at <http://www.niaaa.nih.gov/Publications/EducationTrainingMaterials/Pages/YouthGuide.aspx>. The 6-question CRAFFT (for **C**ar, **R**elax, **A**lone, **F**orget, **F**riends, **T**rouble) is a validated tool designed to assess adolescents' use of both alcohol and drugs (<http://www.ceasar-boston.org/clinicians/crafft.php>).^{13,14}

CASE ► You give Mr. F the CAGE test, and he answers No to all 4 questions. You conclude that while his drinking may be hazardous, he does not appear to have alcohol abuse or dependence.

Follow up with a brief intervention

For decades, evidence has shown that brief interventions are often effective in helping hazardous drinkers like Mr. F cut back to safer levels.¹⁵⁻¹⁸ In some cases, the impact has been great enough to reduce health care and societal costs for up to 4 years¹⁹ and to cut the risk of alcohol-related death by about half.²⁰ As a result, the US Preventive Services Task Force has given a **B** rating to counseling to reduce alcohol misuse by primary care providers.²¹ (There is less evidence that brief interventions are effective for drug problems,²² or in settings other than primary care.²³)

Treat drug/alcohol problems

If you determine that your patient is engaging in hazardous alcohol or drug use or has a diagnosable substance use disorder, you do not have to drop everything else or treat it



Cutting down on drug use may be a reasonable step toward change if a patient isn't ready to think about stopping completely.

WATCH THE VIDEO



Patient misusing alcohol or drugs? See how to elicit change

Courtesy of:
Project ADEPT/MOSBIRT

@ jfonline.com



as an acute event. What matters is long-term success, which is best achieved by partnering with the patient.

Start by approaching drug and alcohol problems as you would a case of newly elevated blood pressure. Bring up the problem, seeking to engage the patient in addressing it.

If he or she does not agree to quit or cut back on drinking the first time you broach the subject, don't be surprised or discouraged. Keep in mind that patients do not always respond positively to advice about handling chronic medical conditions either, particularly at first, and that you'll be working together over time. What's important, in the jargon of the Stages of Change model,²⁴ is to help the patient move from precontemplation to contemplation, and perhaps beyond that to planning or action.

Use motivational interviewing to partner with patients

Motivational interviewing is useful in helping patients change health-related behaviors. The technique, which is not hard to learn or apply, is based on the recognition that a simple shift in style toward a guiding (rather than directive) approach can often reap benefits that are immediately apparent.²⁵⁻²⁸

Motivational Interviewing: Helping People Change (3rd ed, by William R. Miller and Stephen Rollnick; Guilford Press, 2013) is an excellent resource for clinicians who wish to master this technique. An online tutorial in screening and brief intervention for alcohol or drug misuse is available free at <https://adept.missouri.edu>. Video demonstrations of motivational interviewing to address these issues are also available here; to access them, click on "Training," then on "Go to SBIRT videos").

CASE ► Before Mr. F's visit is concluded, you initiate a conversation about alcohol use, stating: "As your doctor, I'm concerned that the amount of alcohol you're drinking could be hazardous to your health. I recommend that you cut down to no more than 4 drinks in any one day and to no more than 14 drinks a week." You make it clear that change is up to him, and ask what he thinks about what you've said.

You also schedule a return visit in one month, at which time you will continue the conversation.

Pharmacotherapy is a useful tool

Increasingly, alcohol and drug dependence—like other chronic conditions—can be effectively addressed with medication.

Drugs to treat alcohol dependence

■ **Naltrexone.** A daily dose of naltrexone, starting at 25 mg daily for a few days and going as high as 100 mg/d, can help patients with alcohol dependence limit their drinking to safe levels (number needed to treat [NNT]=9).²⁹ This will reduce the risk of alcohol-related harm while the patient considers quitting.

The most common adverse effect is nausea, but a low starting dose may alleviate it. Naltrexone, also available as a 380-mg intramuscular (IM) depot injection once every 4 weeks, is an opioid antagonist and should not be given to any patient who's taking opioids.

A 2010 Cochrane review found only 4 trials of naltrexone IM, and failed to show significant reductions in drinking.²⁹ But post hoc analyses of trials of both oral and IM naltrexone found that those in which compliance was assured (either by direct observation or IM administration) had better outcomes than those in which it was not.³⁰ Another post hoc analysis found that patients whose alcohol dependence was more severe derived greater benefits from the drug than those who were less severely affected.³¹

■ **Acamprosate.** Two 333-mg pills tid can help newly abstinent drinkers remain alcohol-free (NNT=9).^{32,33} The most common adverse effect is diarrhea, which may subside with continued use.

Combining acamprosate and naltrexone does not appear to be more effective than either drug alone. In a recently published meta-analysis comparing the 2 drugs, those taking acamprosate had slightly better rates of abstinence from alcohol, while naltrexone was slightly better in reducing heavy drinking.³⁴

■ **Disulfiram** Unlike naltrexone and acamprosate, which work by altering the brain's reward circuits, disulfiram blocks metabolism of ethanol, leading to the accumu-

lation of a toxic metabolite and its punishing syndrome. The major problem with the drug is noncompliance, which can be addressed by enlisting the help of a caregiver or partner to ensure that it is taken daily.³⁵⁻³⁷

■ **Other medications** that have been tested (though not approved by the US Food and Drug Administration [FDA]) as a treatment for alcohol dependence include:

- topiramate, which has been found to have modest efficacy in increasing the number of abstinent days and decreasing heavy-drinking days;³⁸
- baclofen, which has shown efficacy in small clinical trials;³⁹ and
- ondansetron, which has been shown to effectively treat early-onset alcohol dependence.^{40,41}

For patients with depression and alcohol dependence, the combination of naltrexone and sertraline has been found to be superior to either drug by itself—and to have fewer adverse effects.⁴² Gabapentin and lorazepam have been compared in treating alcohol withdrawal, with gabapentin resulting in greater efficacy and fewer adverse effects than lorazepam.^{43,44}

Pharmacotherapy for drug abuse, dependence

■ **For methamphetamine abuse and dependence.** Two randomized clinical trials have studied medications for methamphetamine abuse and dependence. In one small study, topiramate did not increase the proportion of patients who achieved abstinence, but in a post hoc subgroup analysis, it did appear to help newly abstinent patients avoid relapse.⁴⁵

In another study, mirtazapine significantly decreased the proportion of patients whose weekly urine tests were positive for methamphetamine (from 73% to 44%); no significant change was found among those on placebo.⁴⁶

Both drugs were well tolerated, but compliance was low in both trials despite weekly counseling. Each has only one clinical trial to support its use, and neither has FDA approval for addiction treatment.

■ **For marijuana dependence.** In a study of 50 people seeking treatment for marijuana dependence, gabapentin 400 mg 3 times a

day significantly improved the proportion reporting no cannabis use and whose urine tested negative for the drug.⁴⁷

Another recent trial randomized adolescents dependent on cannabis to placebo or N-acetylcysteine 1200 mg twice a day. Those on the active drug were 2.4 times more likely than those on placebo to have negative urine tests with a number needed to treat of 7.⁴⁸ Both trials ran for about 3 months. Neither drug is FDA approved to treat marijuana dependence.

■ **For opioid dependence.** As maintenance medication for patients dependent on opioids, both methadone and buprenorphine have been shown to reduce the use of illicit opioids, lower mortality, and improve retention compared with treatment without medication.⁴⁹ Methadone would be a better choice than buprenorphine, which is a partial agonist with a ceiling on both its good (eg, stopping craving) and bad (eg, overdose risk) effects. In an open-label observational study of patients' preferences, those who chose methadone maintenance over buprenorphine were twice as likely to remain in treatment.⁵⁰ Both drugs are FDA-approved for treating opioid dependence.

Methadone is a full agonist that can be given for opioid dependence only in a federally licensed methadone maintenance clinic. It has been shown to reduce the use of other opioids, reduce criminal behaviors,⁵¹ improve function in many areas,⁵² and reduce mortality.⁵³ In a cohort study of Massachusetts Medicaid data, methadone reduced mortality, which was 75% higher among those receiving abstinence-based treatment.^{52,54}

Buprenorphine (alone and in combination with naloxone), effectively reduces the use of illicit opioids and improves functional status.⁵⁵⁻⁵⁷

■ **Naltrexone**, an opioid antagonist, may be effective in the treatment of opioid dependence. As with disulfiram for alcohol dependence, a major limitation of naltrexone for opioid dependence is noncompliance. But once a patient has been on oral naltrexone, he or she can be switched to naltrexone IM, which can be administered every 4 weeks. A Cochrane review published in 2011 found no evidence that naltrexone was superior to pla-



As maintenance medication for patients dependent on opioids, both methadone and buprenorphine have been shown to reduce the use of illicit drugs and lower mortality.

>
When a referral to an addiction specialist or treatment program is indicated, consider getting the specialist on the phone while the patient is in your office so they can “meet.”

cebo,⁵⁸ but since then another randomized clinical trial has been published that found naltrexone 380 mg IM every 4 weeks was superior to IM placebo. Patients on naltrexone were more likely to remain in treatment and have opioid-free urine tests, and reported less craving for opioids.⁵⁹ Both oral and depot injection naltrexone are FDA approved for treatment of opioid dependence. No comparisons of naltrexone vs either methadone or buprenorphine have been published.

To learn more about pharmacotherapy for opioid dependence, see “Diagnosing and treating opioid dependence” (*J Fam Pract.* 2012;61:588-596).

Dealing with the challenges

As noted earlier, some patients with substance use disorders, like some patients with depression or hypertension, respond well to care and counseling, and some do not. Just as with other conditions, consultation with a specialist often helps.

A major difference in arranging consultations for patients with substance use disorders, however, is that clinicians who specialize in substance abuse and dependence often work in health care systems that are largely, or entirely, separate from those in which primary care physicians typically work. This, plus the stigma that surrounds problems with substance use, presents barriers to patients, who may shy away from going

across town or to another city to see a provider they don't know for a problem they're either resistant to “owning” or ashamed of.

Yet it is possible to reach across this divide and make it easier for patients. One way to do that might be to partner with a local alcohol- and drug-treatment program so that your patients are referred, not to a faceless agency, but rather to a specific clinician; you might even call the provider while the patient is in your office so they can “meet.” Another approach, taken by some multispecialty practices, is to add psychotherapists to the staff so that patients can simply walk down the hall to obtain the mental health care they need.

Reaching across this divide is also a useful strategy for primary care physicians, who may welcome opportunities to meet with someone from a local treatment agency, not just for referrals but to learn more about treating patients with substance use problems. The Patient Protection and Affordable Care Act, which cites substance use disorders as one of 6 chronic health conditions that primary care medical homes are expected to address, may lead to better integration of health care systems that address physical health, as well as mental health and substance use disorders. **JFP**

CORRESPONDENCE

Daniel C. Vinson, MD, MSPH, MA306E Health Sciences, Family and Community Medicine, University of Missouri, Columbia, MO 652312; vinsond@health.missouri.edu

References

1. Friedman PD. Alcohol use in adults. *N Engl J Med.* 2013;368:365-373.
2. Williams RH, Vinson DC. Validation of a single question screen for problem drinking. *J Fam Pract.* 2001;50:307-312.
3. Smith PC, Schmidt SM, Allensworth-Davies D, et al. Primary care validation of a single-question alcohol screening test. *J Gen Intern Med.* 2009;74:783-788.
4. Dawson DA, Pulay AJ, Grant BF. A comparison of two single-item screeners for hazardous drinking and alcohol use disorder. *Alcohol Clin Exp Res.* 2010;34:364-374.
5. Bush K, Kivlahan DR, McDonnell MB, et al. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. *Arch Intern Med.* 1998;158:1789-1795.
6. Dawson DA, Grant BF, Stinson FS, et al. Effectiveness of the derived Alcohol Use Disorders Identification Test (AUDIT-C) in screening for alcohol use disorders and risk drinking in the US general population. *Alcohol Clin Exp Res.* 2005;29:844-854.
7. Smith PC, Schmidt SM, Allensworth-Davies D, et al. A single-question screening test for drug use in primary care. *Arch Intern Med.* 2010;170:1155-1160.
8. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed, text rev. (DSM-IV-TR). Arlington, Va: American Psychiatric Association; 2000.
9. Saha TD, Stinson FS, Grant BF. The role of alcohol consumption in future classifications of alcohol use disorders. *Drug Alcohol Depend.* 2007;89:82-92.
10. Vinson DC, Kruse RL, Seale JP. Simplifying alcohol assessment: two questions to identify alcohol use disorders. *Alcohol Clin Exp Res.* 2007;31:1392-1399.
11. Aertgeerts B, Buntinx F, Kester A. The value of the CAGE in screening for alcohol abuse and alcohol dependence in general clinical populations: a diagnostic meta-analysis. *J Clin Epidemiol.* 2004;57:30-39.
12. Johnson JA, Lee A, Vinson DC, et al. Use of AUDIT-based measures to identify unhealthy alcohol use and alcohol dependence in primary care: a validation study. *Alcohol Clin Exp Res.* 2012; July 26 [Epub ahead of print].
13. Center for Adolescent Substance Abuse Research. The CRAFFT Screening Tool. Boston, MA:2009 [updated 2012]. Available at: <http://www.ceasar-boston.org/clinicians/crafft.php>. Accessed January 15, 2013.
14. Knight JR, Sherritt L, Harris SK, et al. Validity of brief alcohol screening tests among adolescents: a comparison of the AUDIT, POSIT, CAGE, and CRAFFT. *Alcohol Clin Exp Res.* 2003; 27:67-734.
15. Wallace P, Cutler S, Haines A. Randomised controlled trial of gen-

- eral practitioner intervention in patients with excessive alcohol consumption. *BMJ*. 1988;297:663-668.
16. Fleming MF, Barry KL, Manwell LB, et al. Brief physician advice for problem alcohol drinkers: a randomized controlled trial in community-based primary care practices. *JAMA*. 1997;277:1039-1044.
 17. Bertholet N, Daeppen JB, Wietlisbach V, et al. Brief alcohol intervention in primary care reduces alcohol consumption: Systematic review and meta-analysis. *Arch Intern Med*. 2005;165:986-995.
 18. Kaner EFS, Dickinson HO, Beyer F, et al. Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database Syst Rev*. 2007(2):CD004148.
 19. Fleming MF, Mundt MP, French MT, et al. Brief physician advice for problem drinkers: long-term efficacy and benefit-cost analysis. *Alcohol Clin Exp Res*. 2002;26:36-43.
 20. Cuijpers P, Riper H, Lemmers L. The effects on mortality of brief interventions for problem drinking: a meta-analysis. *Addiction*. 2004;99:839-845.
 21. U.S.Preventive Services Task Force. Screening and behavioral counseling interventions in primary care to reduce alcohol misuse: recommendation statement. *Ann Intern Med*. 2004;140:554-556.
 22. Saitz R, Alford DP, Bernstein J, et al. Screening and brief intervention for unhealthy drug use in primary care settings: randomized clinical trials are needed. *J Addict Med*. 2010;4:131-136.
 23. Field CA, Baird J, Saitz R, et al. The mixed evidence for brief intervention in emergency departments, trauma care centers, and inpatient hospital settings: what should we do? *Alcohol Clin Exp Res*. 2010;34:2004-2010.
 24. DiClemente CC, Prochaska JO. Toward a comprehensive, trans-theoretical model of change: stages of change and addictive behaviors. In: Miller WR, Heather N, eds. *Treating Addictive Behaviors*. New York, NY:Plenum Press;1998:3-24.
 25. Mason P, Butler CC. *Health Behavior Change: A Guide for Practitioners*. 2nd ed. London, UK:Elsevier; 2010.
 26. Miller WR, Rollnick S. *Motivational Interviewing: Preparing People for Change*. 2nd ed. New York, NY: Guilford Press;2002.
 27. Hettema J, Steele J, Miller WR. Motivational interviewing. *Ann Rev Clin Psych*. 2005;1:91-111.
 28. Rollnick S, Butler CC, Kinnersley P, et al. Motivational interviewing. *BMJ*. 2010;340:c1900.
 29. Rosner S, Hackl-Herrwerth A, Leucht S, et al. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev*. 2010;(12):CD001867.
 30. Swift R, Oslin DW, Alexander M, et al. Adherence monitoring in naltrexone pharmacotherapy trials: a systematic review. *J Stud Alcohol Drugs*. 2011;72:1012-1018.
 31. Pettinati HM, Silverman BL, Battisti JJ, et al. Efficacy of extended-release naltrexone in patients with relatively higher severity of alcohol dependence. *Alcohol Clin Exp Res*. 2011;35:1804-1811.
 32. Mann K, Leher P, Morgan MY. The efficacy of acamprosate in the maintenance of abstinence in alcohol-dependent individuals: results of a meta-analysis. *Alcohol Clin Exp Res*. 2004;28:51-63.
 33. Rosner S, Hackl-Herrwerth A, Leucht S, et al. Acamprosate for alcohol dependence. *Cochrane Database Syst Rev*. 2010(9):CD004332.
 34. Maisel NC, Blodgett JC, Wilbourne PL, et al. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? *Addiction*. 2012;October 17 [Epub ahead of print].
 35. Azrin NH. Improvements in the community-reinforcement approach to alcoholism. *Behav Res Ther*. 1976;14:339-348.
 36. Azrin NH, Sisson RW, Meyers R, Godley M. Alcoholism treatment by disulfiram and community reinforcement therapy. *J Behav Ther Exp Psychiatr*. 1982;13:105-112.
 37. Keane TM, Foy DW, Nunn B, et al. Spouse contracting to increase antabuse compliance in alcoholic veterans. *J Clin Psychol*. 1984;40:340-344.
 38. Arbaizar B, Diersen-Sotos T, Gomez-Acebo I, et al. Topiramate in the treatment of alcohol dependence: a meta-analysis. *Actas Espanolas de Psiquiatria*. 2010;38:8-12.
 39. Johnson BA. Update on neuropharmacological treatments for alcoholism: scientific basis and clinical findings. *Biochem Pharmacol*. 2008;75:34-56.
 40. Johnson BA, Roache JD, Javors MA, et al. Ondansetron for reduction of drinking among biologically predisposed alcoholic patients: a randomized controlled trial. *JAMA*. 2000;284:963-971.
 41. Johnson BA, Ait-Daoud N, Seneviratne C, et al. Pharmacogenetic approach at the serotonin transporter gene as a method of reducing the severity of alcohol drinking. *Am J Psychiatr*. 2011;168:265-275.
 42. Pettatini HM, Oslin D, Lampman KM, et al. A double-blind, placebo-controlled trial combining sertraline and naltrexone for treating co-occurring depression and alcohol dependence. *Am J Psychiatr*. 2010;167:668-675.
 43. Anton RF, Myrick H, Wright TM, et al. Gabapentin combined with naltrexone for the treatment of alcohol dependence. *Am J Psychiatr*. 2011;168:709-717.
 44. Myrick H, Malcolm R, Randall PK, et al. A double-blind trial of gabapentin versus lorazepam in the treatment of alcohol withdrawal. *Alcohol Clin Exp Res*. 2009;33:1582-1588.
 45. Elkashef A, Kahn R, Yu E, et al. Topiramate for the treatment of methamphetamine addiction: a multi-center placebo-controlled trial. *Addiction*. 2012;107:1297-1306.
 46. Colfax GN, Santos GM, Das M, et al. Mirtazapine to reduce methamphetamine use: a randomized controlled trial. *Arch Gen Psychiatr*. 2011;68:1168-1175.
 47. Mason BJ, Crean R, Goodell V, et al. A proof-of-concept randomized controlled study of gabapentin: effects on cannabis use, withdrawal and executive function deficits in cannabis-dependent adults. *Neuropsychopharmacology*. 2012;37:1689-1698.
 48. Gray KM, Carpenter MJ, Baker NL, et al. A double-blind randomized controlled trial of N-acetylcysteine in cannabis-dependent adolescents. *Am J Psychiatr*. 2012;169:805-812.
 49. Farrell M, Wodak A, Gowing L. Maintenance drugs to treat opioid dependence. *BMJ*. 2012;344.
 50. Pinto H, Maskrey V, Swift L, et al. The SUMMIT trial: a field comparison of buprenorphine versus methadone maintenance treatment. *J Subst Abuse Treat*. 2010;39:340-352.
 51. Marsch LA. The efficacy of methadone maintenance interventions in reducing illicit opiate use, HIV risk behavior and criminality: a meta-analysis. *Addiction*. 1998;93:515-532.
 52. Sees KL, Delucchi KL, Masson C, et al. Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: a randomized controlled trial. *JAMA*. 2000;283:1303-1310.
 53. Clausen T, Anchersen K, Waal H. Mortality prior to, during and after opioid maintenance treatment (OMT): a national prospective cross-registry study. *Drug Alcohol Depend*. 2008;94:151-157.
 54. Clark RE, Samnaliev M, Baxter JD, et al. The evidence doesn't justify steps by state Medicaid programs to restrict opioid addiction treatment with buprenorphine. *Health Affairs*. 2011;30:1425-1433.
 55. Center for Substance Abuse Treatment. *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction: Treatment Improvement Protocol (TIP) Series 40*. Rockville, Md: Substance Abuse and Mental Health Services Administration; 2004.
 56. Fudala PJ, Bridge TP, Herbert S, et al. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. *N Engl J Med*. 2003;349:949-958.
 57. Fiellin DA. Buprenorphine: effective treatment of opioid addiction starts in the office. *Am Fam Physician*. 2006;73:1513.
 58. Minozzi S, Amato L, Vecchi S, et al. Oral naltrexone maintenance treatment for opioid dependence. *Cochrane Database Syst Rev*. 2011;(4):CD001333.
 59. Krupitsky E, Nunes EV, Ling W, et al. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. *Lancet*. 2011;377:1506-1513.



Visit us @ jfpponline.com

THE JOURNAL OF
FAMILY
PRACTICE