INTRODUCTION

Substance use disorders (SUD) are commonly found in primary care settings, although screening and assessment are often overlooked, and evidence-based treatments available to primary care providers are infrequently used. A study of more than 450,000 patients screened in a variety of health care settings found that 23% of patients had current alcohol or drug problems, yet less than 20% of those with a substance use disorder nationally receive any treatment. Although SUD are associated with a wide range of medical problems, historically the treatment of...
SUD has been separate from medical care. This separation has impeded care coordination for patients with multiple problems and adequate addiction medicine education for medical providers. This article focuses primarily on alcohol and opioid issues, including the overlap of SUD and opioid prescribing for chronic noncancer pain.

**SUD ASSESSMENT AND DIAGNOSIS**

Assessment of SUD in primary care can be challenging. The presentation of patients with SUD can be varied and may include obvious signs such as intoxication and withdrawal, or more subtle signs such as poor medication or appointment adherence, problems with sleep, unstable housing, or legal issues. To further complicate assessment, patients may see real or perceived consequences to disclosing their substance use problems, as may be seen in the patient prescribed opioids for pain, or they may have concerns that disclosure could affect their medical care or benefits. Provider vigilance and persistence are warranted because of the impact substances can have on a patient’s overall health.

**Approach to Assessing Patients for Substance Use**

A nonjudgmental and compassionate approach to assessing patients for substance use disorder is essential to promote an open and honest dialogue. When patient attitudes and comfort in alcohol screening have been studied, most patients were comfortable with and in favor of screening and guidance about their use. However, patients with positive alcohol screening or current problematic alcohol and drug use were more likely to feel embarrassed by alcohol questions or less comfortable talking about it, indicating the deeply vulnerable position these patients are likely experiencing around their substance use. Despite that, one study found that 75% of the primary care patients who screened positive for alcohol misuse show motivation to change, and motivation to change increased as the severity of alcohol misuse increased. It can be less threatening to focus initially on past use and problems, because this allows the provider an opportunity to demonstrate empathy and understanding about the difficulty of behavior change before asking for disclosure about more recent use. Taking a supportive and motivational approach, and putting aside any negative assumptions when assessing patients for substance use problems, will support their readiness to make change.

**Screening**

The United States Preventive Services Task Force recommends that all adults aged 18 years or older be screened for alcohol misuse, with the goal of identifying both patients with alcohol use disorder and those who drink more than healthy limits. Unhealthy alcohol use covers a spectrum of use from drinking more than the amount recommended (Box 1) to severe alcohol use disorders. There is no specific recommended frequency around screening patients for alcohol use, but it can be done yearly, or as clinically indicated. Although there is no evidence supporting universal screening for problems with other drugs, it is generally recommended to screen all new patients and those with demographic or clinical risks, such as male sex, behavioral problems, family members with substance use problems, those with symptoms of a psychiatric disorder, or medical issues potentially related to drug use (Box 2). In pregnancy, expert opinion recommends universal screening for drug and alcohol use early in prenatal care. Because of the stigmatization associated with substance use in pregnancy, well-validated instruments for this population are necessary to assure
appropriate sensitivity (Box 3). The National Institute on Alcohol Abuse and Alcoholism (NIAAA) also recommends screening adolescents 14 to 18 by asking them questions about their use of substances and their friends’ use of substances (see Box 3).

Assessing for SUD

In all cases, a positive screen for a substance demands further assessment. The main strategy for this in alcohol use disorders is to determine if a patient has unhealthy use or a mild use disorder versus a moderate to severe use disorder, because that will impact treatment decisions. Unfortunately, there is not a quick and comprehensive way to determine if a patient has a substance use disorder outside of reviewing the DSM-5 criteria with them (Box 4). Although scales like the AUDIT-C can measure severity, and higher scores are associated with alcohol dependence, it cannot make the formal diagnosis and may result in underdiagnosis. In addition, there are no such scales appropriate for drug use. Although there are clinically significant time limitations in a primary care setting, obtaining the correct diagnosis is critical.

Drugs and alcohol use can affect every system of the body, so for all patients screening positive for unhealthy use or a substance use disorder, a physical examination, medical history, and psychiatric history are crucial (Box 5). Regular use of drugs or alcohol also carries with it several safety concerns, including suicide, which increased 10-fold in people with a substance use disorder and should be assessed. Withdrawal syndromes are also common and have been defined for alcohol, cannabis, opioids, sedative-hypnotics, and stimulants, according to the DSM-5. Special attention should be given to alcohol, benzodiazepine, and barbiturate withdrawal symptoms, which can occur within hours after last use and can lead to seizures, delirium tremens, and death.

ALCOHOL USE DISORDERS

An initial approach to alcohol screening in primary care is outlined in Fig. 1. Once a person has screened positive and been found to have unhealthy drinking or an alcohol

Box 1
Healthy drinking limits

Healthy men less than 65 years old
• ≤4 drinks in a day and
• ≤14 drinks in a week
All healthy women and healthy men older than 65 years old
• ≤3 drinks in a day and
• ≤7 drinks in a week
Abstinence for selected populations
• Pregnant
• Medication interactions
• Health conditions with contraindications
• Less than 18 years old


---

Fig. 1

Addiction Disorders

1099
Box 2
Screening tests for drug and alcohol use validated in primary care settings

Single-Item Alcohol Screener
“How many times in the past year have you had 5 (4 in women) or more drinks in a day?”

Scoring and Notes
- Positive response: any answer >0 or difficulty identifying how often
- Sensitivity: 82%, specificity: 79% \(^\text{59}\)
- Easy to remember and quick.

AUDIT-C (Alcohol Use Disorders Identification Test-Consumption)
1. How often do you have a drink containing alcohol?
   a: Never  b: Monthly or less  c: 2–4 times a month  d: 2–3 times a week  e: 4 or more times per week
2. How many standard drinks containing alcohol do you have on a typical day?
   a: 1 or 2  b: 3 or 4  c: 5 or 6  d: 7 or 9  e: 10 or more
3. How often do you have 6 or more drinks on one occasion?
   a: Never  b: Less than monthly  c: Monthly  d: Weekly  e: Daily or almost daily

Scoring and Notes
- Scoring: a = 0, b = 1, c = 2, d = 3, e = 4 \(^\text{60}\)
  - Positive response indicates unhealthy alcohol use
    - Men: >4, Sensitivity: 85%, specificity: 89%
    - Women: >3, Sensitivity: 73%, specificity: 91% \(^\text{61}\)
  - Scores >7 suggest alcohol dependence \(^\text{9}\)

Single-Item Drug Screener
“How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”

Scoring and Notes
- Positive response: any positive answer
- Sensitivity: 100%, specificity: 74% \(^\text{45}\)

Other Screeners
- AUDIT: 10 items. Alcohol screener. Positive score: \(\geq 8\) for risky drinking. Sensitivity: 57%–97%, specificity: 78%–96% \(^\text{62}\)
- DAST (Drug Abuse Screening Test): 10-, 20-, and 28-item varieties. Validated in addiction treatment centers. Positive 10-item score: \(\geq 2\) for risky drinking. Sensitivity: 80%, specificity: 88% \(^\text{63}\)
use disorder, there are several options for further treatment. Brief interventions are appropriate for all levels of alcohol use disorders, although additional treatment will likely be needed for those with a moderate to severe alcohol use disorder. Additional treatments in a primary care setting may include pharmacotherapy, motivational interviewing, and referrals to mutual help groups. Continuing to engage the patient through regular follow-up is important for patients who are both actively drinking and in recovery, as relapse is common.11

**Brief Interventions**

Brief intervention is an evidence-based approach to discussions of alcohol use in primary care and is recommended for all adults 18 years of age and old who engage in risky or hazardous drinking (see Box 1).7 Lower levels of alcohol use are considered

---

**Box 3**

**Screeners for special populations**

<table>
<thead>
<tr>
<th>Screeners for special populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>T-ACE (Tolerance, Annoyed, Cut-down, Eye opener)—Alcohol Screener64–67</td>
</tr>
<tr>
<td>4 items</td>
</tr>
<tr>
<td>• Recommended by the American College of Obstetrics and Gynecology.</td>
</tr>
<tr>
<td>• Asks about use in a more indirect way then the AUDIT–C, which may lead to more honest results.</td>
</tr>
<tr>
<td>AUDIT–C—Alcohol Screener65</td>
</tr>
<tr>
<td>3 items</td>
</tr>
<tr>
<td>4P’s Plus© (Parents, Partner, Past, Pregnancy)—Alcohol and Drug Screener68</td>
</tr>
<tr>
<td>5 items</td>
</tr>
<tr>
<td>• Developed for pregnant women.</td>
</tr>
<tr>
<td>• This test is copyrighted and may not be reproduced in any form without permission.</td>
</tr>
<tr>
<td>CRAFFT (Car, Relax, Alone, Forget, Family/friends, Trouble)—Alcohol and Drug Screener for adolescents and young adults69</td>
</tr>
<tr>
<td>6 items</td>
</tr>
<tr>
<td>• Studied in pregnant young adults ages 17–25.</td>
</tr>
<tr>
<td>Teenagers</td>
</tr>
<tr>
<td>2-question drug and alcohol screener70</td>
</tr>
<tr>
<td>1. “In the past year, on how many days have you had more than a few sips of beer, wine, or any drink containing alcohol?”</td>
</tr>
<tr>
<td>2. “If your friends drink, how many drinks do they usually drink on an occasion?”</td>
</tr>
<tr>
<td>• Any positive response requires further assessment.</td>
</tr>
<tr>
<td>• Recommended by the NIAAA and the American Academy of Pediatrics.</td>
</tr>
<tr>
<td>• Targets any use.</td>
</tr>
</tbody>
</table>
safe, and observational studies have associated low-level drinking with reduced cardiovascular risk, although causality is not clearly established. Brief intervention has been found to reduce weekly alcohol consumption rates, increase adherence to recommended drinking limits, and reduce health care utilization. In a meta-analysis of 7 trials it was found that participants had 3.6 fewer drinks per week, and 12% of participants had fewer heavy drinking episodes at 12 months. For patients with moderate to severe alcohol use disorders (corresponding to alcohol dependence in DSM-IV), brief interventions on their own have not been found effective. However, brief interventions can be used to help promote successful engagement in evidence-based treatment of this subgroup of patients, including adherence to alcohol use disorder pharmacotherapy, mutual help group attendance, or participation in specialty treatment programs.

Brief interventions can vary greatly in their components and time, but typically include multiple short encounters providing feedback, discussing safe amounts, assessing readiness for change, discussing goals, and arranging follow-up (Fig. 2, Box 6). There are a variety of evidence-based psychosocial approaches that are effective in alcohol use disorders. Although it is not typically feasible in a primary care setting to provide regular and extended therapy using these approaches, they can be used to tailor responses to harmful drinking, develop rapport, and support

---

**Box 4**

**Assessing for substance use disorder in primary care**

- After a positive screening test, begin the conversation with “tell me about your alcohol (or drug) use.”
- Listen for statements indicating that the patient has or has had concerns about their substance use and reflect those concerns in order to encourage the patient to say more about possible problems.
- Listen especially for DSM-5 symptoms of a Substance Use Disorder, which include tolerance, withdrawal, using more than intended, failed efforts to cut down or quit, spending a lot of time related to use, craving, failure to fulfill important life roles, giving up important life activities, use in hazardous situations, and continued use in spite of either negative physical/psychological problems, or social/interpersonal consequences. It is usually best to elicit these symptoms through a conversation that also allows providers to express empathy for the difficulty of dealing with addiction, rather than using a formal symptom checklist.
- If the patient seems to minimize current problems, more disclosure may be elicited by asking about past problems, even as a youth (including driving issues).
- If problems occurred, ask about prior treatment or AA/NA participation.
- Often a past or current diagnosis will become obvious with this approach. If a substance use disorder diagnosis is possible but not clearly present, it may be necessary to review DSM-5 criteria specifically.
- A DSM-5 Substance Use Disorder diagnosis requires that symptoms lead to clinically significant impairment and be present within a 12-month period. Severity of a Substance Use Disorder is estimated by the number of DSM-5 symptoms, with two or three representing a mild disorder, four or five a moderate disorder, and 6 or more a severe disorder. A moderate to severe disorder most closely approximates Substance Dependence from the DSM-IV TR.
- Unlike DSM-IV TR, tolerance and withdrawal due solely to prescribed medication taken as directed do not count towards a DSM-5 Substance Use Disorder diagnosis.

self-efficacy (Box 7). No studies have assessed brief intervention in adolescents, but it has been found efficacious in pregnant populations.17

Pharmacotherapy for Alcohol Use Disorders

**Ambulatory medically supervised withdrawal**

Many patients with moderate to severe alcohol use disorders will have physical dependence. Symptoms of alcohol withdrawal can start within 6 hours of the last drink and can proceed through the early withdrawal to delirium tremens and seizures if untreated. Mild symptoms include tremors, anxiety, insomnia, headaches, loss of appetite, nausea, emesis, and diarrhea. Moderate symptoms can include elevated blood pressure and pulse, sweating, and confusion. Patients who are 5 days out from their last drink and who have no withdrawal symptoms will not need pharmacotherapy for their withdrawal. Alcohol withdrawal symptoms severity can be assessed with the CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol, Revised).18 In addition to reviewing a patient’s medical and psychiatric stability, the CIWA-Ar can be used to help assess the most appropriate treatment setting, because scores greater than 15 are best handled in inpatient facilities. Patients eligible for ambulatory
detoxification should also be medically and psychiatrically stable, have no other current substance problems, have no history of alcohol withdrawal seizures, be able to take oral medications, have family support that can monitor the patient, and be able to commit to daily medical visits. Patients should be monitored daily until their symptoms have decreased. Symptoms typically resolve after 7 days. Thiamine 100 mg daily for prevention of Wernicke syndrome, and 1 mg of folic acid daily for nutritional replacement, should be started at the beginning of their supervised withdrawal.

Medications for alcohol withdrawal with the best evidence are benzodiazepines and anticonvulsants. Benzodiazepines reduce withdrawal symptoms and are the only medications found to prevent withdrawal seizures; thus, they remain first-line treatment. There is no evidence that one benzodiazepine is better than another, although long-acting benzodiazepines like chlordiazepoxide and diazepam are thought to provide a smoother withdrawal experience. These medications can be administered in either a fixed dose schedule or a symptom-triggered schedule. Symptom-triggered approaches have been found to reduce medication use and have shorter inpatient stays.

Anticonvulsants have also been studied for ambulatory medically supervised alcohol withdrawal. For instance, gabapentin has been found to be as effective in treating alcohol withdrawal symptoms as both lorazepam and chlordiazepoxide. In addition, the gabapentin groups had less craving and less sedation by the end of treatment. For both of these studies, a fixed dose schedule was set, with maximum doses of 1200 mg daily for 3 days and tapered over 4 days.

**Medication management for relapse prevention**
Prescribing medications for moderate to severe alcohol use disorder is useful to help patients stop drinking and in relapse prevention. Medication management for alcohol use disorders is an approach to provide both medication treatment follow-up and brief
behavioral support to promote recovery by increasing medication adherence, education, and referrals to support groups (Box 8).24

When prescribing relapse prevention medications, such as naltrexone, XR-naltrexone IM, acamprosate, and disulfiram, close weekly follow-up is helpful initially. Naltrexone, an opioid antagonist that reduces cravings and peak drinking amounts, is a reasonable first choice for patients desiring to cut back or stop drinking and not taking opioids. This medication can be started while the patient is drinking or at the end of their medically supervised withdrawal.25,26 Acamprosate, working on the glutamate and GABA neurotransmitter systems, has been shown to help prevent

<table>
<thead>
<tr>
<th>Box 6</th>
<th>Aspects of brief intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basics</td>
<td>Multiple contacts: Project TrEAT (Trial for Early Alcohol Treatment) included 4 total contacts, 2 in person with a primary care provider 1 month apart, and two 5-minute calls with a nurse 2 weeks after each visit.71</td>
</tr>
<tr>
<td></td>
<td>Brief: 6- to 15-minute encounters have been the most effective.72</td>
</tr>
<tr>
<td></td>
<td>Counseling approaches can vary (see Box 6).</td>
</tr>
<tr>
<td></td>
<td>Identify and reflect positive and negative aspects of drinking.</td>
</tr>
<tr>
<td>Components</td>
<td>Providing feedback about harmful use</td>
</tr>
<tr>
<td></td>
<td>Feedback on their use should be specific to the patient and may incorporate current psychosocial or medical issues related to their use.</td>
</tr>
<tr>
<td></td>
<td>“You’re drinking more than is medically safe and it is likely contributing to your [current problem].”</td>
</tr>
<tr>
<td></td>
<td>Discussing safe amounts and explicit recommendations</td>
</tr>
<tr>
<td></td>
<td>Describing what a standard drink is can be helpful for patients to understand how much they are actually drinking.</td>
</tr>
<tr>
<td></td>
<td>“Drinking less than 14 drinks (7 for women) in a week will help you avoid some of the bad things associated with alcohol.”</td>
</tr>
<tr>
<td></td>
<td>Assessing readiness for change</td>
</tr>
<tr>
<td></td>
<td>Patients may or may not be ready to change anything about their drinking. Some patients may not be aware they have risky drinking.</td>
</tr>
<tr>
<td></td>
<td>“With what I have reviewed with you, is there anything you would like to change about your drinking?”</td>
</tr>
<tr>
<td></td>
<td>Discussing goals and explicit recommendations</td>
</tr>
<tr>
<td></td>
<td>Goals will vary depending on the patient’s interest in making change. It is helpful to take a patient-centered approach to establishing drinking goals. Goals may include everything from reducing the amount of alcohol consumed to sobriety. Goals can also include steps the patient is currently taking to make change. Identifying specific strategies to achieve those goals is helpful. This may include tracking their drinks, eating better, alternating alcoholic and nonalcoholic beverages, managing triggering situations, utilizing friends or family.</td>
</tr>
<tr>
<td></td>
<td>Arranging for follow-up</td>
</tr>
<tr>
<td></td>
<td>Follow-up has been clearly shown to be superior to a one-time intervention.72 This will provide opportunities for further assessment, and supporting and reviewing goals.</td>
</tr>
</tbody>
</table>
relapse and increase accumulated days of abstinence. Acamprosate is useful in patients with contraindications to naltrexone, such as those taking opioids. Disulfiram blocks alcohol metabolism and leads to the buildup of acetaldehyde, which is responsible for flushing, sweating, nausea, and tachycardia. Disulfiram has been found effective in preventing relapse in alcohol dependence and in patients with cocaine and

<table>
<thead>
<tr>
<th>Box 7</th>
<th>Psychosocial counseling approaches for alcohol use disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motivational Interviewing</strong></td>
<td></td>
</tr>
<tr>
<td>Motivational interviewing is a patient-centered conversation style whereby the provider's role is to guide the conversation to develop discrepancy between the patient's use and their goals and to work toward resolving that discrepancy. It avoids confrontation, or the “righting reflex,” whereby the provider wants to correct unhealthy behaviors, and instead, works to have the patient identify their own reasons for changing. It works through using an interviewing style that uses open-ended questions, affirming something positive in the patient, reflective listening in an effort to clarify what the patient is saying, and summarizing what the patient has said, which can demonstrate understanding and promote engagement. An example version of motivational interviewing called motivational enhancement therapy can be found at: <a href="http://pubs.niaaa.nih.gov/publications/ProjectMatch/match02.pdf">http://pubs.niaaa.nih.gov/publications/ProjectMatch/match02.pdf</a>.</td>
<td></td>
</tr>
<tr>
<td><strong>Harm Reduction</strong></td>
<td></td>
</tr>
<tr>
<td>Harm reduction approaches look at specific techniques a patient can take to reduce the harms they experience from their alcohol use, which often includes reducing drinking quantity. Strategies can include spacing out drinks, drinking with food in the stomach, alternating alcoholic and nonalcoholic beverages, tracking amount of alcohol drinking, and not drinking and driving. A harm reduction approach for adults can be found in Denning and Little's, <em>Practicing harm reduction psychotherapy: an alternative approach to addictions</em>.</td>
<td></td>
</tr>
<tr>
<td><strong>Cognitive Behavioral Therapy</strong></td>
<td></td>
</tr>
<tr>
<td>Cognitive behavioral therapy (CBT) emphasizes developing skills to deal with high-risk situations, cravings, triggers, and lapses. This has been done individually and in group settings. This approach makes an effort to show the patient how their thoughts relate to their behaviors in a step-wise approach, to better understand what leads to relapses. In a meta-analysis of 53 studies of adults with alcohol or drug disorders, a modest positive effect was found compared with other interventions or controls. An example can be found at: <a href="http://pubs.niaaa.nih.gov/publications/ProjectMatch/match03.pdf">http://pubs.niaaa.nih.gov/publications/ProjectMatch/match03.pdf</a>.</td>
<td></td>
</tr>
<tr>
<td><strong>12-Step Facilitation and 12-Step Programs</strong></td>
<td></td>
</tr>
<tr>
<td>Twelve-step facilitation emphasizes alcoholism as a disease and promotes and helps facilitate participation in 12-step groups like Alcoholic Anonymous (AA). Patients are encouraged to try different groups, find a sponsor, do service, and work the 12 steps. An example of this approach can be found at: <a href="http://pubs.niaaa.nih.gov/publications/ProjectMatch/match01.pdf">http://pubs.niaaa.nih.gov/publications/ProjectMatch/match01.pdf</a>.</td>
<td></td>
</tr>
<tr>
<td><strong>AA</strong></td>
<td></td>
</tr>
<tr>
<td>AA is a mutual support fellowship for people who want to stop drinking. Meetings are widely accessible, and in larger urban areas, there are meetings that will often cater to special groups, helping to reduce the anxiety around social situations. Believing in a “higher power” does not always mean believing in a deity and should not be a barrier to participation. Observational studies have shown effectiveness for this approach, with higher rates of abstinence at 12 months among military veterans participating in AA versus those in CBT (26% vs 19%).</td>
<td></td>
</tr>
</tbody>
</table>
alcohol dependence. All of these oral medication formulations are most effective in motivated patients, or patients whose adherence can be monitored. Gabapentin has also been found effective in treating alcohol dependence (especially at the 1800 mg total daily dosing) when compared with placebo by improving rates of abstinence, decreasing heavier drinking days, as well as improving sleep, cravings, and mood (Box 9).

Primary care physicians with appropriate experience, training, and support can treat patients with more significant alcohol problems. Referral to a higher level of specialty addiction treatment can be indicated for several reasons, including the need for inpatient medically supervised withdrawal, poor response to primary care treatment, complicated comorbid mental health conditions, or need for case management services.

SUBSTANCE USE DISORDER ISSUES IN CHRONIC PAIN MANAGEMENT

One of the most common and problematic issues in primary care practice is the intersection between SUD and opioid prescribing, particularly for chronic pain problems. Because SUD may present differently in the context of chronic opioid prescribing, the recognition and management of SUD must be integrated into an overall clinical approach to chronic pain management.

**Opioid Treatment Risks**

In an effort to more effectively treat chronic pain, chronic opioid therapy has become increasingly prevalent in general practice over the last decades, although evidence for long-term effectiveness is limited, with short-term trials providing evidence for reduction in pain intensity, but mixed result for functional improvement. Accompanying the increase in opioid prescribing has been worrisome trends in prescription

<table>
<thead>
<tr>
<th>Box 8 Components of a medication management visit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial visits</strong></td>
</tr>
<tr>
<td>• Review of medical evaluation, including alcohol-affected comorbidities</td>
</tr>
<tr>
<td>• Physical signs of substance use, including signs of withdrawal</td>
</tr>
<tr>
<td>• Reviewing laboratory results</td>
</tr>
<tr>
<td>• Reviewing any negative aspects of drinking</td>
</tr>
<tr>
<td>• Discussion of their diagnosis</td>
</tr>
<tr>
<td>• Interest in abstinence</td>
</tr>
<tr>
<td>• Utility of medication, including its mechanism, adverse effects, and adherence strategies</td>
</tr>
<tr>
<td>• Encourage participation in a mutual support group</td>
</tr>
<tr>
<td><strong>Follow-up visits</strong></td>
</tr>
<tr>
<td>• Assess drinking amounts</td>
</tr>
<tr>
<td>• Functional status</td>
</tr>
<tr>
<td>• Medication adherence</td>
</tr>
<tr>
<td>• Medication adverse effects</td>
</tr>
</tbody>
</table>

opioid abuse by youth and adults emergency department and addiction treatment admissions associated with prescription opioids, and opioid-related overdose deaths. These trends have led to multiple efforts to reduce the risk of opioid prescribing for noncancer pain, including development of state level prescription monitoring programs that allow providers to access records of all dispensed controlled substances, tamper-resistant formulation of opioid medications, and clinical guideline recommendations for safer opioid prescribing for noncancer pain.

**Box 9**

**Alcohol use disorder medications**

**Naltrexone**

Start 50 mg daily. Range 25–150 mg daily. Significant interaction with opioids. Avoid in active hepatitis. Well-tolerated. May be used for harm reduction as well as abstinence-based goals. Stop for 5 days before using opioids. Liver function tests should be checked at baseline and followed every few months after that. Potential adherence problems.

**XR Naltrexone IM**

380 mg every 4 weeks. Significant interaction with opioids. Avoid in active hepatitis. Nausea, fatigue, and injection site reactions common. Side effects often improve by 5 days and can be managed with over-the-counter medications. May be used for harm reduction as well as abstinence-based goals.

**Acamprosate**

Start 666 mg 3 times a day. Range: 333–666 mg 3 times a day. An alternative for patients taking opioids. Diarrhea most common side effect. Suicidal ideation rare but reported. Renal excretion, so reduce dose with CrCl 30–50 mL/min. No liver toxicity or drug interactions. Potential adherence problems.

**Disulfiram**

Start 250 mg daily. Range: 125–500 mg daily. Should have abstained from alcohol for at least 24 hours. Most effective for those committed to abstinence with good social support for observed ingestion. Avoid in severe cardiac disease and active hepatitis. Review alcohol disulfiram reaction and forgotten forms of alcohol (e.g., cologne, deodorant, cough syrups, vinegars). Several significant drug-drug interactions, including anticoagulants, isoniazid, metronidazole, and phenytoin, among others. Monitor liver function throughout.

**Topiramate**

Start 50 mg daily. Range 50–300 mg daily, divided, 2 times a day. Titrate over several weeks. Side effects include cognitive impairment, paresthesias, weight loss, headache, fatigue, dizziness, and depression. Not US Food and Drug Administration (FDA) approved for alcohol use disorder, but multiple positive trials.

**Gabapentin**

Start 900 to 1200 orally for 3 days, followed by a taper over the next 4 days for ambulatory supervised withdrawal. Range: 900–1200 mg/d (withdrawal) and 1800 mg/d (alcohol dependence), divided 3 times a day. Useful for ambulatory medically supervised withdrawal and protracted alcohol withdrawal symptoms: depression, anxiety, and insomnia. Not FDA approved for alcohol use disorder.
The use of higher doses of opioids for chronic noncancer pain is particularly problematic. Although no clinical trials comparing opioid dose levels for chronic noncancer pain have been reported, higher prescribed opioid doses have been associated with multiple complications (Box 10). Opioid dose escalation should be avoided, but mixed evidence exists about the dose limits for opioids prescribed for noncancer pain. Risks appear to increase when daily use exceeds 50 to 100 mg of morphine or the equivalent, and multiple opioid prescribing guidelines recommend avoiding doses greater than 90 to 200 mg of morphine equivalents daily.

**Approaching Patients on High-Dose Opioids**

Conversations with patients on high doses of prescribed opioids can be challenging. Patients, particularly those with a history of substance use disorder, often feel scrutinized and stigmatized as they attempt to access medical care and have their symptoms taken seriously. Providers struggle to provide pain management safely while maintaining the rapport that is the basis of primary care practice. In addition, patients may be afraid that their pain will be poorly controlled with dose tapering, or that they may experience opioid withdrawal. It is important to validate pain complaints and work with patients to improve their nonopioid medication regimens and their nonmedication approaches to chronic pain while also educating them on the risks of higher-dose therapy. Assessment of patient-attributed problems related to opioid therapy may highlight ways in which a patient might benefit from dose reduction. Patients with safety issues related to higher dose therapy, for instance, an opioid overdose or inability to take the medication as prescribed, may need more rapid tapering. However, for stable patients who are not using other drugs or taking their medication in risky ways, slower opioid tapering may be possible and can avoid opioid withdrawal. Those who have difficulty tapering due to emergent substance use disorder symptoms may require opioid use disorder treatment with methadone or buprenorphine.

**Detection and Management of Problems During Opioid Prescribing**

Safely prescribing chronic opioid therapy for noncancer pain requires procedures that integrate comprehensive pain management and detection of emergent problems,
some of which may indicate a substance use disorder. A “universal precautions” approach whereby all patients are monitored, rather than only those seen as high risk or who have manifested problems, can aid in detection of problems and reduce conflicted interactions that threaten the primary care relationship ([Box 11]).

**Fig. 3** provides a general clinical approach to detection and management of problems in patients prescribed opioids for chronic noncancer pain. In addition to the “universal precautions” approach, the development of a comprehensive chronic pain treatment plan can form the basis for monitoring adherence and identifying problems, including SUD, which may require additional treatment. Treatment plans generally require both active strategies that patients must engage in regularly on their own (eg, exercise, physical therapy, sleep hygiene) as well as medications and more passive nonmedication approaches, such as acupuncture, massage, or Transcutaneous Electrical Nerve Stimulation units. Identifying functional goals and a patient-centered plan allow more objective assessment of the benefits of opioid prescribing over time.

Problems that commonly arise during opioid prescribing include unexpected prescription-monitoring program or urine toxicology results, requests for early refills, lost or stolen prescriptions, behavioral problems in the clinic setting, and poor adherence to the chronic pain treatment plan. These problems may arise from a simple error or misunderstanding of the treatment agreement, or be caused by a new or worsening mental health problem, social instability, diversion of opioid medication, unsafe use, or a substance use disorder, all of which require assessment. Potential responses to sample problem behaviors are shown in **Fig. 3**. Appropriate responses to such problems include prompt conversations with patients and considering asking them to return between opioid dispensing visits for unscheduled urine toxicology testing and pill counts to assess for diversion. Some problems will be simple to assess, but others may require more prolonged assessment through intensification of treatment and more frequent monitoring visits. Because urine toxicology tests are potentially prone to error or misinterpretation ([Box 12]), it is recommended that opioid-prescribing decisions not be made solely on the basis of a single test, but instead considered in light of behavioral patterns and the overall clinical scenario. Some more dangerous problems, such as overdose events, may require prompt action to lower or discontinue opioids. Patients whose behavioral problems do not respond to the initial approach described above and have recurrent problems will often need their opioids discontinued for safety reasons. The Collaborative Opioid Prescribing Education program provides

<table>
<thead>
<tr>
<th>Box 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Universal precautions&quot; for opioid prescribing</td>
</tr>
</tbody>
</table>

All patients are monitored with the following components, not just those considered high risk:

- Frequency of monitoring based on risk of problems, especially past substance use disorder
- Use of opioid risk tools
- Treatment agreements describing patient and provider responsibilities during opioid therapy
- Routine urine toxicology testing
- Review of state prescription monitoring program for overlapping scheduled prescriptions

examples of language clinicians can use to effectively communicate prescribing decisions and handle difficult situations.⁴³,⁴⁴ Those with a clear diagnosis of opioid use disorder should be treated with methadone in an Opioid Treatment Program or with buprenorphine by a physician qualified to treat opioid use disorders. Methadone for the treatment of opioid use disorder is not permitted in a primary care setting and can only be provided in specially licensed and accredited Opioid Treatment Programs. Patients on high doses of opioids for pain who cannot safely be treated in primary care settings, and who cannot tolerate opioid tapering, may also need medication-assisted treatment of opioid use disorder.
Urine toxicology testing issues and pitfalls

General Considerations

Urine toxicology testing can aid in identification of SUD, monitor patients with known disorders, and monitor patients receiving opioid therapy in primary care. Tests vary greatly in sensitivity and cost, with screening assays (enzymatic immunoassay or enzyme-multiplied immunoassay technique) and point-of-care tests generally less reliable but cheaper, and confirmatory tests (gas chromatography, GC/mass spectrometry, MS) more specific and expensive. Must understand characteristics of each test to correctly interpret results, which requires good communication with laboratory medicine expertise. Never make an important clinical decision based on a single test in isolation, but instead use results in the clinical context to guide further clinical and laboratory assessment.

Opioids

Screening assay for methadone is sensitive and specific. Opioid screening tests not sensitive for oxycodone or oxymorphone unless the dose is high, so negative tests in patients taking low doses can occur; consider including a specific oxycodone assay. Fentanyl poorly detected by opioid screening assays. Confirmatory testing (GC/MS) can be complex, because opioid metabolites may be present and confusing to interpret. For instance, hydromorphone is a common metabolite, but not of oxycodone. Poppy seeds can cause a positive test. Detection window 2–4 days.

Stimulants

Cocaine screening tests are sensitive and highly specific with minimal false positive tests. Many common medications (pseudoephedrine, bupropion, trazodone, others) cross-react with amphetamine/methamphetamine screening assays, so caution is warranted in interpreting positive tests. Consider using a reflex confirmation test for all positive amphetamine/methamphetamine screening tests. Methylphenidate (ritalin) is not an amphetamine and is thus not detected on standard drug screens. Detection window 2 days for amphetamine/methamphetamine, 2–4 days for cocaine.

Cannabis

Cannabis tests may remain positive for weeks in patients who were heavy users. Some methadone programs choose not to test for cannabis because, like nicotine, no important treatment decisions will be made based on the result. Detection window 3 days (single use) to greater than 30 days (heavy daily use).

Benzodiazepines

Some more potent benzodiazepines, such as clonazepam, are present in the urine at such low concentrations that they are poorly detected in most urine drug screening assays. Diazepam and alprazolam are well detected. Sertaline can cause a false positive result. Detection window 3 days (short acting) to 3 weeks (long acting).

Alcohol

Usual screening test detection window 7–12 hours. Urine ethyl glucuronide testing is highly specific and detectable for longer, but may be too sensitive (mouthwash, hand sanitizer can cause a positive test).

Other Drugs

Many synthetic drugs, or “designer drugs,” do not have urine toxicology tests available.
TREATMENT OF OPIOID USE DISORDERS

Patients with opioid use disorders require specific medication-assisted treatment for optimal outcomes, and these disorders can be identified in primary care settings. Although there are complexities in making a clear substance use disorder diagnosis in patients prescribed opioids for chronic pain, if patients are unable to safely manage their opioid medications in the context of a comprehensive pain management plan and are unable to be weaned from their prescriptions, opioid use disorder treatment should be considered. Detoxification treatment in the setting of opioid use disorders is unlikely to be successful, although it may be a reasonable approach for patients with a mild disorder or short duration of opioid use. Rapid and ultrarapid opioid detoxification has not been shown effective. Medications for the treatment of opioid use disorders are presented in Box 13 and include the opioid antagonist naloxone, which, along with overdose education, can be prescribed to patients at risk for opioid overdose and their families and friends.

Methadone Maintenance Treatment

Methadone maintenance treatment of opioid use disorders has more than 40 years of clinical research supporting its effectiveness in reducing drug use, criminal behavior, infectious disease transmission, overdose, and death. It is superior to even richly supported detoxification programs in randomized trials, and the poor outcomes after discontinuation of methadone maintenance support recommendations for its long-term use. In contrast to opioids prescribed in the medical setting for chronic non-cancer pain, higher doses of methadone provided in Opioid Treatment Programs have been shown to improve outcomes, as has a longer duration of treatment and inclusion of moderate amounts of psychosocial treatment. Access to methadone maintenance, which is heavily regulated and frequently threatened with defunding, is largely limited to larger metropolitan areas, and its status as separate from medical settings limits physician understanding and coordination of care. Methadone maintenance programs have limited clinical flexibility, often do not have integrated medical or mental health services, and require specific signed authorization from patients to discuss their care unless it is a medical emergency.

Patients in methadone maintenance are required to attend treatment 6 days per week at the start of treatment so that medication ingestion can be observed, although patients who do well in treatment over a period of at least 3 months can become eligible for additional take-home doses, up to a full month of medication after years of successful treatment. Primary care providers can assess the stability of methadone maintenance patients by asking them how often they are required to attend treatment, as well as asking them the results of their recent urine toxicology tests. The patient should be advised to remain in treatment until their substance use has ceased and their medical, psychiatric, legal, family, and employment problems have stabilized. If methadone is tapered, it should be done slowly to avoid relapse.

Sample Test Panel for Patients on Long-term Opioids for Chronic Pain

Screening test for opioids, methadone, cocaine, benzodiazepine, barbiturate, amphetamine/methamphetamine. Suggest reflex confirmation of positive amphetamine/methamphetamine screen and a specific test for oxycodone.

Box 13
Treatments for opioid use disorders

**Methadone**

Full opioid agonist that may be used for opioid use disorder treatment only through specially licensed and accredited Opioid Treatment Programs, not through a physician prescription. Physicians may prescribe methadone for pain, although additional training specific to methadone is recommended because of increased risk of overdose when prescribed for pain. Starting doses for opioid use disorder are 10–40 mg daily and titrated every few days. Usual maintenance doses 80–120 mg daily. Requires daily observed dosing initially, but take-home doses are permitted after demonstration of stable recovery.

**Buprenorphine/Naloxone**

Partial opioid agonist that may be prescribed for opioid use disorder treatment by physicians who have completed a specific 8-hour course and obtained a federal waiver. Naloxone included to reduce intravenous abuse of buprenorphine, but is not absorbed if taken sublingually as directed. Dose range generally 8–24 mg daily. Induction requires tolerant patients to enter mild to moderate opioid withdrawal before the first dose. Similar drug use outcomes as methadone, but less effective at retaining patients in treatment. Primary care provision of buprenorphine in primary care involves development of protocols for screening, assessment, induction, monitoring, psychosocial treatment, termination, and referral.

**Buprenorphine (mono)**

Generally reserved for pregnant women, who have a higher risk if exposed to naloxone. Similar rates of neonatal abstinence syndrome in babies born to mothers on buprenorphine and methadone, but severity and duration of neonatal abstinence syndrome is lower with buprenorphine.94

**Naltrexone**

For opioid-use disorder, start 50 mg daily. Range 25–150 mg daily. Limited data of effectiveness in the United States, as adherence is low.95 Will cause withdrawal in opioid-tolerant patients, so must be preceded by successful detoxification and a naloxone challenge test. Avoid in active hepatitis. Liver function tests should be checked at baseline and followed every few months after that. There is poor evidence supporting rapid opioid detoxification with naltrexone or naltrexone combined with anesthesia or heavy sedation.47

**XR Naltrexone IM**

380 mg every 4 weeks. Limited data support effectiveness for opioid use disorders, but adherence is improved. Similar issues as oral naltrexone. Nausea, fatigue, and injection site reactions common.

**α-2 Adrenergic Agonists**

Clonidine or other α-2 adrenergic agonists can relieve some opioid withdrawal symptoms, but are far less effective than agonist or partial agonist medications.

**Naloxone with Overdose Education**

Emerging harm reduction strategy to promote emergency lay administration of the opioid antagonist naloxone.96,97 Provided to those at risk of opioid overdose and their families and friends. Education includes identification of opioid overdose and the appropriate responses, including rescue breathing, calling 911, and administration of naloxone (see stopoverdose.org).
Opioid Treatment programs can provide methadone only for the treatment of opioid use disorders and are not permitted to provide methadone for the treatment of pain. If a patient prescribed opioids for chronic pain is found to require treatment for opioid use disorder, he or she must seek treatment specifically for their substance use problem rather than requesting pain management from a methadone program. If a patient prescribed opioids for chronic pain is found to have a cocaine or methamphetamine problem, for instance, he or she may require admission to opioid use disorder treatment with methadone or buprenorphine if they cannot tolerate withdrawal of their opioids. Substance use disorder treatment programs that do not use methadone or buprenorphine will generally not admit patients with ongoing opioid or other controlled substance prescriptions.

**Buprenorphine Treatment of Opioid Use Disorders**

Buprenorphine is a partial opioid agonist that is effective for opioid use disorder treatment and can be prescribed in the medical setting by physicians who have completed a specific 8-hour training program and received a waiver from the federal government. Federal legislation, the Drug Addiction Treatment Act of 2000, was required to allow integration of opioid use disorder treatment into medical settings for the first time, as well as outlining training and record keeping requirements, and limiting the number of patients a physician may treat at one time. Gaining knowledge and experience in opioid use disorder treatment with buprenorphine can greatly assist physicians in their management of opioid prescribing for chronic pain, and it is a gratifying form of treatment. Few treatments in primary care practice can have as much positive impact on patients’ lives as buprenorphine for opioid use disorder.

Buprenorphine binds opioid receptors and activates them, but as the dose is raised, there is a ceiling effect, unlike full opioid agonists. This ceiling effect makes buprenorphine less prone to opioid overdose and thus safer than full agonists, but its activity at the opioid receptor is adequate to relieve opioid withdrawal even in highly tolerant patients. Buprenorphine also has very high affinity for opioid receptors, so that once it is on the receptor, other opioids are blocked. These features make buprenorphine an excellent choice for opioid use disorder treatment. The most commonly used form of buprenorphine in the United States also contains naloxone, which is included solely as an abuse deterrent, because it is not absorbed if the medication is taken as directed under the tongue. If a tolerant patient crushes and injects the combined buprenorphine/naloxone, the naloxone can precipitate opioid withdrawal. The high affinity of buprenorphine has implications for initiation of treatment, as patients must be in mild to moderate withdrawal before taking the first dose or risk precipitated withdrawal as buprenorphine displaces other opioids from the receptor and potentially reduces receptor activity. Scales assessing opioid withdrawal severity are available for use when inducing patients onto buprenorphine.

Multiple comparative trials have tested the relative efficacy of buprenorphine and methadone and found comparable rates of drug use during treatment. However, meta-analyses of these trials found that methadone is more effective in retaining patients in treatment, a key outcome in addiction treatment. No clear patient predictors of response to buprenorphine or methadone have been established, although patients needing more structure may benefit from a methadone program. For most patients seeking pharmacotherapy for the first time, the less restrictive structure of treatment in a physician office setting is preferred. Psychosocial services for patients on buprenorphine can consist of simple medication management and support, whereas higher levels of psychosocial treatment or cognitive behavioral therapy have not been shown more effective.
The decision to undertake training to prescribe buprenorphine in a general medical setting requires understanding of the limitations of treatment as well as the profound benefits that can occur with successful treatment (see Box 8). Prescribers can choose to take on only patients within their practice who might benefit, due to a known opioid use disorder through having difficulty with opioid pain medications and being unable to successfully taper off. Providing effective treatment for opioid use disorders can be a lifesaving and positive clinical experience.

SUMMARY AND FUTURE DIRECTIONS

Addiction disorders are common in primary care settings and can have a major impact on treatment of medical problems, including chronic pain. Evidence-based screening, brief interventions, and pharmacotherapies are available for primary care providers and can improve patient outcomes. As physicians become experienced in prescribing pharmacotherapies for addiction disorders, integration of treatment of SUD into primary care settings will become more common and new models of providing medication and psychosocial services for these patients will need development. If successful, these models hold the promise of more integrated and effective treatment for patients with addiction disorders.

REFERENCES


