Opioid Abuse

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1. Prevention

Although there are no data on primary prevention, adopt practical strategies as dictated by the clinical context.

1.1 Carefully assess patients before prescribing an opioid, and monitor patients who are taking opioids or have a history of a substance-use disorder. Warn them about the risks, including overdose.

Recommendations

- If a patient is using prescription opioids, determine:
  - Medical indication
  - Types of opioids used
  - Amount used
  - Duration of use
  - Route of administration (iv, im, po, intranasal, smoked)
  - History of nonprescription use
  - History of tolerance or withdrawal
  - Use of other medications, including sedative-hypnotics
  - History of psychiatric conditions, including depression
- Be vigilant for signs of opioid abuse or dependence whenever a patient is taking an opioid prescribed for treatment of a medical problem.
- Screen for potential predictors of misuse of opioids, including:
  - History of substance abuse or mental health diagnosis
  - Current cigarette smoking
  - Family history of substance abuse
  - History of legal problems
- Educate patients on the potential medical risks for opioid abuse, including addiction, tolerance, respiratory depression, physical withdrawal, opioid-induced hyperalgesia, and fatal overdose.
- Consider use of a written agreement or treatment contract that details parameters of treatment, including policy on aberrant behaviors, medication refills, risks and benefits of treatment, and alternative treatments.
- Consider using an instrument to screen patients with chronic pain for risk for aberrant drug behaviors.
- See module Pain.

Evidence

- A 2014 guideline from the American Pain Society and the Heart Rhythm Society on the safe prescribing of methadone recommended that all patients in whom methadone therapy is considered undergo a complete medical and behavioral risk evaluation and have an electrocardiogram to look for QTc prolongation (1).
- A 2012 guideline from the American Society of Interventional Pain Physicians for responsible opioid prescribing for patients with chronic noncancer pain recommended comprehensive history-taking and documentation before initiation of opioids, screening for opioid use, prescription-monitoring programs, and urine drug testing to monitor patients. The guideline also recommended establishing physical and psychosocial diagnoses before initiation of opioids, with establishment of treatment goals and establishment of a robust pain management agreement (2).
• A 2008 systematic review of rates of opioid misuse and abuse in patients with chronic pain on long-term opioid therapy included 79 studies. Overall, 3.27% of patients developed opioid abuse or addiction. Among patients with chronic pain and no history of drug abuse or addiction, 0.19% developed abuse or addiction (3).

• A study used data from two large insurance plans to describe trends over time in the use of long-term opioids for nonmalignant pain. Between 1997 and 2005, use of opioids increased in both plans (4). A second study using data from the same plans found that opioid use was higher among patients with history of depression (5).

• The 2010 National Survey on Drug Use and Health reported that 359,000 people aged 12 years and over were abusing or dependent on heroin in 2010 and 1,921,000 were abusing or dependent on pain relievers (6).


• A 2010 MMWR Report found that the number of ED visits related to nonmedical use of prescription opioid analgesics increased 111% between 2004 and 2008 (8).

• A retrospective study identified risk factors for ED visits among patients prescribed opioids. Headache, back pain, and history of substance use were associated with ED visits. Overall, daily opioid dose was not associated with ED visits, but patients receiving the equivalent of morphine, >120 mg/d, had twice the risk for ED visits as those patients on lower doses (9).

• A pain management program reported results of behavioral monitoring with urine toxicology screens in 122 patients. Overall, problems were identified in 43% of patients; 21% had no behavioral issues but had a positive urine toxicology screen for a nonprescribed drug, and 14% had behavioral problems but no positive urine toxicology screens (10).

• A retrospective cohort study of patients with opioid pain contracts in primary care included 330 patients representing 4% of the clinic population. Contracts were discontinued in 17% of patients because of abuse or noncompliance (11).

Rationale

• Opioid abuse, including nonmedical use of prescription opioids, is a significant public health problem.

• Fatal and nonfatal overdoses can result from pharmaceutical opioids.

• Primary care physicians frequently see patients with active, yet undiagnosed, substance-use problems.

• Specific information on a patient's opioid-use pattern can suggest the presence of an opioid-use disorder.

• Informing patients of potential medical harms from opioids and clear elucidation of treatment parameters may prevent problems related to substance abuse.

Comments

• A 2014 guideline from the U.S. Preventive Services Task Force on primary care-based behavioral interventions to prevent substance abuse among children and adolescents stated that the evidence was insufficient to determine the balance of benefits and harms of interventions (12).

• There are no evidence-based primary prevention strategies specifically designed for opioid abuse and no research estimating the risk for the development of iatrogenic opioid addiction in persons receiving prescription opioids. Opioid abuse is prevented in a medical practice by provider awareness, a detailed clinical history, patient education, and clinical vigilance.
• A 2009 structured review found inconclusive evidence for opioid-induced hyperalgesia in humans based on opioid infusion studies (13).

• Pharmaceutical opioids are a significant contributor to overdose deaths (14).

• Overdose now exceeds motor vehicle accidents as a cause of injury or death.
2. Screening

Screen patients with risk factors.  

2.1 Do not screen the general population, but consider screening patients with specific behaviors or problems.

Recommendations

- Ask patients about opioid use in the context of alcohol consumption, smoking, and seat-belt use.
- Consider screening at-risk groups, which include:
  - Patients with a history of:
    - Self-reporting a substance-use disorder
    - Using analgesics to relieve symptoms other than pain
    - Using injection drugs
    - Combining alcohol with other psychoactive drugs
    - Having care restricted or terminated over concerns about substance use
    - A pattern of seeking prescriptions from more than one physician or ED without notification of primary provider
    - Experiencing high levels of psychosocial distress
    - Selling (diversion) or stealing illicit or prescribed opioids, or forging prescriptions
    - Obviously deteriorating social and occupational functioning unrelated to the expected complications of a medical illness
  - Individuals who have a first-degree relative with a history of opioid dependence
- Obtain a urine drug screen with confirmatory analysis (to identify specific opioids, such as methadone, oxycodone, and heroin) in patients with any of the aforementioned problems or risks after thoughtful discussion and education regarding the purpose of testing.

Evidence

- A 2012 guideline from the American Society of Interventional Pain Physicians for responsible opioid prescribing for patients with chronic noncancer pain recommended comprehensive history taking and documentation before initiation of opioids, screening for opioid use, prescription-monitoring programs, and urine drug testing to monitor patients. The guideline also recommended establishing physical and psychosocial diagnoses before initiation of opioids, introducing treatment goals, and agreeing on a robust pain management plan (2).
- A 2012 evidence review for the American Society of Interventional Pain Physicians found that approximately one-third of patients with chronic pain may misuse opioids, and that rates of illicit drug use are high among patients with chronic pain, particularly among those patients who abuse opioids (15).
- A 1996 narrative comprehensive review of opioid use for chronic, nonmalignant pain identified factors indicative of an opioid-abuse problem. Specific factors included current drug or alcohol abuse, aberrant behaviors related to opioids (diversion, forging, stealing, ‘doctor shopping’ for drugs), injection of oral formulations, multiple episodes of medication ‘loss,’ and drug-related deterioration in social and occupational functioning (16).
- A study used claims data to determine risk factors for abuse among patients receiving prescription opioids. Younger age and history of mental health disorders or substance abuse were associated with opioid abuse and dependence (17).
- An epidemiologic study of veterans who used chronic opioids for noncancer pain identified the following risk factors for opioid abuse and dependence: male gender, nonopioid substance abuse, mental health disorders, younger age, and more days of prescription opioids dispensed (18).
• A retrospective study of 122 patients chronically maintained on opioids found that use of urine toxicology tests captured 17% more patients with inappropriate drug-taking behavior than use of behavioral monitoring alone (49% vs. 32%) (10).

• A twin study examining genetic, environmental, and combined influences on DSM-III substance dependence and abuse criteria found a 67% contribution of genetic factors in the development of opioid dependence or abuse in male twins (19).

Rationale
• Framing questions about opioid use in the context of personal behaviors offers a structured, nonjudgmental way to obtain relevant information on opioid use.

• The aberrant behavioral patterns listed in the specific recommendations can be associated with an active opioid-abuse problem.

• Urine drug screening can detect recent opioid use within 1 to 4 days, depending on which opioid was used.

• Having a first-degree relative with opioid dependence is associated with increased risk for having a substance-use disorder.

Comments
• Most literature devoted to screening and prediction of opioid abuse in the clinical setting focuses on pharmaceutical opioid abuse.

• A 2004 narrative review discussed drug-testing methods (20).

• Despite its clinical utility, urine drug screening has limitations, especially in terms of detection of certain synthetic opioids (e.g., oxycodone), influence of concomitant medications (e.g., antiretrovirals), intentional falsification, false-positive or -negative results, and errors in sample collection or identification.

2.2 Screen for opioid misuse and abuse with a questionnaire, structured interview instrument, or urine toxicity screen in patients with chronic pain, either before or during chronic opioid therapy.

Recommendations
• Screen patients on chronic opioid therapy for abuse using urine toxicology tests.

• Consider screening patients before or during treatment of chronic noncancer pain with opioids using one of these standard questionnaires:
  • Prescription Drug Use Questionnaire (PDUQ)
  • Physician Opioid Therapy Questionnaire
  • Screener and Opioid Assessment for Patients with Pain (SOAPP and SOAPP-R)
  • Current Opioid Misuse Measure (COMM)
  • Pain Medication Questionnaire (PMQ)
  • Opioid Risk Tool (ORT)
  • Diagnosis, Intractability, Risk and Efficacy (DIRE)

• See module Pain.

Evidence
• A 2014 guideline from the American Pain Society and the Heart Rhythm Society on the safe prescribing of methadone recommended performing a urine drug screen on all patients before initiating methadone (either for chronic pain or for addiction), and that all patients being treated for addiction and those being treated for pain who have risk factors for opioid abuse undergo urine drug screen testing “regularly” (1).
The 2010 Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain recommended urine drug screening, using either a point-of-care test or a lab test (either immunoassay or chromatography), and noted that immunoassay tests detect drugs for a longer time than chromatography.

A 2012 guideline from the American Society of Interventional Pain Physicians for responsible opioid prescribing for patients with chronic noncancer pain recommended using urine drug screening to monitor patients on opioids, and noted the expected duration of positive urine toxicology with different drugs (2).

A 2008 systematic review of tools to predict opioid misuse in patients with chronic pain included a total of 15 studies of interview tools, questionnaires, toxicology screens, and observation. Studies were methodologically weak and none of the instruments have been well validated (21).

A cohort study evaluated the ability of the Opioid Risk Tool to predict aberrant behavior in 185 consecutive patients treated in a pain clinic. Patients were classified as being low-, moderate-, or high-risk. Rates of aberrant behavior were 6% in the low-risk group and 91% in the high-risk group (22).

A study compared the ability of various risk assessment tools to predict aberrant drug-related behavior in patients in a pain practice. Clinical assessment by a psychologist had the highest sensitivity (71%) for predicting discharge from the program. SOAPP-R had sensitivity of 39% and specificity of 69%; ORT had sensitivity of 20% and specificity of 88%, and PMQ had sensitivity of 34% and specificity of 77% (23).

**Rationale**

• Early identification of patients with risk factors for opioid misuse, abuse, and dependence might help reduce the risks of opioid therapy.

2.3 Use state prescription drug-monitoring programs, if available, to identify patients with aberrant prescription drug-use patterns.

**Recommendations**

• Access state programs that monitor the prescribing of drugs to determine whether patients are obtaining opioids from multiple providers (i.e., ‘doctor shopping’).

**Evidence**

• A 2012 guideline from the American Society of Interventional Pain Physicians for responsible opioid prescribing for patients with chronic noncancer pain recommended using prescription monitoring programs if available (2).

• The Department of Justice stated that as of 2011, 37 states had operational prescription drug-monitoring programs (24).

• An observational study found that 21% of overdose deaths in West Virginia in 2006 were accompanied by evidence of ‘doctor shopping,’ which was defined as obtaining prescriptions for controlled substances from five or more providers in the year before death (25).

• An observational study examined the relationship between prescription drug monitoring programs and drug overdose in the U.S. between 1999 and 2005. Monitoring programs were not associated with lower rates of overdose or mortality from overdose (26).

**Rationale**

• Providers can make more informed decisions about initiating opioids by being aware that the patient is filling prescriptions for opioids or other controlled substances written by other providers within the state.
• Prescribing providers can counsel patients who are ‘doctor shopping’ and refer them for substance-abuse treatment.
3. Diagnosis

Use history and physical exam to distinguish opioid abuse from dependence and to identify patients with opioid withdrawal syndrome.

3.1 Use patient history to identify opioid-use disorder and opioid withdrawal syndrome.

Recommendations

- Determine the diagnostic category of the suspected opioid-use disorder by asking patients about:
  - Use of opioids, heroin, or pain killers
  - Route of administration (pills, smoking, shooting, snorting)
  - Pattern and frequency of use
  - Use of more opioid to get the same feeling they used to get at lower doses (tolerance)
  - Use of opioids to keep from getting ‘dope sick’ (withdrawal)
  - Use of other drugs or alcohol with opioids
  - Opioid use distracting them from work responsibilities or leisure activities
  - Other people with whom they use drugs
  - Other people who may be concerned about their drug use
  - Legal problems
  - Details of any previous treatment for their drug problem
- Ask patients about a history of other psychiatric disorders and the use of alcohol and other substances.
- Consider use of the Subjective Opiate Withdrawal Scale as an optional tool to augment the history and clinical exam in the assessment of the severity of opioid withdrawal.

Evidence

- Formal diagnostic criteria for opioid dependence and opioid abuse are in the DSM-5 (27).
- A study validated instruments to measure symptoms of opioid withdrawal: the 16-item Subjective Opiate Withdrawal Scale and the 13-item Objective Opiate Withdrawal Scale in opioid abusers admitted to a detoxification unit. Both scales indicated withdrawal at admission, and scores on both scales were lower after treatment with methadone (28).
- A study assessed psychiatric comorbidities in 716 opioid abusers seeking treatment with methadone. Psychiatric comorbidities were present in 47% of patients, most commonly antisocial personality disorder (25%) and major depression (16%) (29).

Rationale

- A standardized opioid withdrawal scale in conjunction with a thorough psychosocial history can provide the clinician with information to confirm the diagnosis of an opioid-use disorder and guide treatment.

Comments

- Tolerance to opioids can occur after only a few doses in opioid-naïve patients with little or no risk for addiction; however, dependence requires prolonged, repeated exposure (30).
- It is important to note that some patients, especially those patients with chronic pain, may not be forthcoming about having an opioid addiction. Such individuals may require sufficient time and patience before they admit to or recognize that they are having a problem with opioids.
3.2 Use physical exam to look for signs of opioid intoxication, which include miosis, somnolence, and respiratory depression, and of opioid withdrawal, which include rhinorrhea, tachycardia, and restlessness.

Recommendations
- Look for signs of opioid intoxication, including:
  - Miosis
  - Somnolence
  - Respiratory slowing or respiratory depression
  - Fresh puncture marks or small scabs indicating recent injection
- Look for signs associated with opioid withdrawal, including:
  - Mydriasis
  - Rhinorrhea
  - Tachycardia
  - Hypertension
  - Mild hyperthermia
  - Restlessness
  - Irritability
  - Yawning
  - Lacrimation
  - Piloerection
  - Vomiting
  - Diarrhea

Evidence
- Consensus.

Rationale
- Chronic opioid use can lead to physiologic adaptation with characteristic signs and symptoms of intoxication, tolerance, and withdrawal.

Comments
- Withdrawal signs and symptoms from heroin usually present approximately 8 to 12 hours after last use and peak at 48 to 72 hours. Untreated, grossly observable withdrawal signs can last 7 to 10 days.

3.3 Use a urine toxicology screen to detect the presence of opioids and other substances in patients with suspected opioid abuse, and use urine toxicology regularly to monitor patients on prescription opioids.

Recommendations
- Perform a urine toxicology screen to determine the presence of opioids and other substances.
- Perform a blood alcohol level.
- Consider a serum toxicology screen as an adjunct or if urine is unobtainable.
- Understand the expected detection times of different opioids in the urine:
  - Morphine: 3 to 4 days
  - Oxycodone: 1 to 3 days
  - Hydrocodone: 1 to 2 days
• Methadone: 5 to 10 days
• Hydromorphone: 1 to 2 days
• Be aware of substances which can cause false-positive urine toxicology tests:
  • Fluoroquinolones
  • Rifampin
  • Poppy seeds
• See module Pain.
• See table Lab and Other Studies for Opioid Abuse.

Evidence
• A 2014 guideline from the American Pain Society and the Heart Rhythm Society on the safe prescribing of methadone recommended performing a urine drug screen on all patients before initiating methadone (either for chronic pain or for addiction), and that all patients being treated for addiction and those being treated for pain who have risk factors for opioid abuse undergo urine drug screen testing “regularly” (1).
• The 2010 Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain recommended urine drug screening, using either a point-of-care test or a lab test (either immunoassay or chromatography), and noted that immunoassay tests detect drugs for a longer time than chromatography.
• A 2012 guideline from the American Society of Interventional Pain Physicians for responsible opioid prescribing for patients with chronic noncancer pain recommended using urine drug screening to monitor patients on opioids, and noted the expected duration of positive urine toxicology with different drugs (2).
• A 2010 structured review of opioid drug testing and foods containing poppy seeds noted that poppy seed morphine content is greatly reduced by processing and that normal consumption is safe, but that there is a possibility for false-positive drug testing (31).
• A study evaluated the effects of quinolones on results of commercially available opioid screening assays. Nine different quinolones caused false-positive results on at least one of the assays (32).
• A lab study found a 12% rate of cross-reactivity between rifampicin and opioid screens (33).
• A study evaluated the error rate of random urine toxicology testing in adolescents in a substance abuse program. Six percent of urine samples were too dilute for proper interpretation (34).

Rationale
• Lab tests can be helpful in confirming nonprescription use of opioids, diversion of opioid prescriptions, or screen for complications of opioid abuse and injection drug use.
• Testing for other drugs and alcohol abuse is advisable, as polysubstance abuse is common.

Comments
• There are no specific lab tests that will diagnose an opioid-use disorder. However, a urine or serum toxicology screen may be used to evaluate for the presence of opioids in a patient's body.
• Methadone can be distinguished from most other opioids in most drug screens, except for propoxyphene, which can be interpreted as a false-positive result for methadone.

3.4 In patients who are known opioid users, use lab tests to detect the complications of opioid abuse.

Recommendations
• Use lab tests to detect medical complications resulting from opioid misuse, including:
BUN: creatinine ratio to exclude impaired renal function
Serologic and other tests for infection, including HIV antibody, HBV surface antibody, HCV antibody, VDRL, and PPD
β-HCG if pregnancy is suspected
CBC and blood cultures if acute bacterial infection is suspected
See table Lab and Other Studies for Opioid Abuse.

Evidence
• Consensus.

Rationale
• Injection drug use is associated with an elevated risk for bloodborne infections, such as HBV, HCV, and HIV, and is also associated with bacterial endocarditis.
• Some lifestyle and sociodemographic factors, including homelessness and selling sex for drugs, may elevate the personal risk for certain people with substance dependence. Individuals who share these characteristics are more exposed to a range of infections, including STDs (e.g., gonorrhea, chlamydia, HIV, syphilis), and pulmonary infections, such as tuberculosis.
• Opioid abuse, dependence, and withdrawal in pregnant women can have adverse fetal and perinatal outcomes.

3.5 Consider other conditions that can mimic opioid intoxication or withdrawal.

Recommendations
• In patients with suspected opioid intoxication, consider:
  • Medications such as benzodiazepines, barbiturates, dextromethorphan, and tramadol
  • Alcohol intoxication
  • Diabetic ketoacidosis
  • Hepatic encephalopathy
  • Head trauma with diminished consciousness
  • Postictal state
• In patients with suspected opioid withdrawal, consider:
  • Concomitant alcohol or sedative-hypnotic withdrawal
  • Flu-like illnesses
  • Medications such as interferon α-2b and ribavirin
• See table Differential Diagnosis of Opioid Abuse.

Evidence
• Consensus.

Rationale
• It is necessary to consider conditions that mimic opioid intoxication or withdrawal to avoid precipitating an opioid overdose by starting unwarranted opioids for maintenance or detoxification. Other treatable illnesses and conditions, such as diabetes, liver failure, head trauma, epilepsy, and alcohol and sedative-hypnotic withdrawal may be life-threatening and must be diagnosed and treated.
4. Consultation

Consider obtaining appropriate consultation for help in diagnosing substance use disorders and comorbid psychiatric disorders. Obtain consultation for help in treating patients.

4.1 Consider obtaining consultation with an addiction psychiatrist or an addiction medicine specialist.

Recommendations
- Consider obtaining consultation with an addiction psychiatrist or addiction medicine specialist to define a substance-use disorder and comorbid psychiatric pathology.

Evidence
- A study assessed psychiatric comorbidities in 716 opioid abusers seeking treatment with methadone. Psychiatric comorbidities were present in 47% of patients, most commonly patients with antisocial personality disorder (25%) and major depression (16%) (29).

Rationale
- Patients with opioid dependence frequently have comorbid psychiatric disorders (‘dual diagnoses’).

Comments
- The association between psychopathology and opioid addiction is well established. Psychiatric disorders may be drug-induced, independent, or interrelated.

4.2 Obtain appropriate specialist consultation for help in treating patients, especially patients who require pharmacologic treatment and patients with opioid-use disorders and comorbid psychiatric or substance-use disorders or chronic pain.

Recommendations
- Obtain consultation with:
  - An addiction specialist, addiction psychiatrist, or opioid treatment program for patients in opioid withdrawal who meet criteria for opioid abuse or dependence, or for patients who have a comorbid substance-use disorder to initiate pharmacotherapy
  - A general psychiatrist or addiction psychiatrist if there is a complex suspected comorbid psychiatric diagnosis, such as bipolar disorder, schizophrenia, posttraumatic stress disorder, or panic disorder
  - A pain specialist if chronic pain is a concomitant problem

Evidence
- A study of 278 patients on methadone-maintenance used a structured diagnostic interview and the Addiction Severity Index at intake and 7 months later. Psychiatric comorbidity was associated with poorer psychosocial and medical status at admission and follow-up, and participants with the combination of Axis I and II comorbidity had the most severe problems (35).
- The prevalence of chronic, severe pain, defined as pain persisting for more than 6 months of moderate-to-severe intensity or significantly hindering daily activities, was experienced by 37% of patients on methadone maintenance (n=390), 65% of whom reported high levels of pain-related interference in physical and psychosocial functioning (36).
• Patients with opioid abuse or dependence require specialized treatment services, including pharmacotherapy. Comorbid psychiatric and substance use disorders require therapy that can be provided by a general psychiatrist, an addiction psychiatrist, or an opioid treatment program.

• Chronic pain is highly prevalent in the opiate abuse population, and special services from pain specialists may be needed for patients with chronic pain.

**Comments**

• Addiction specialists are typically trained in primary care specialties, such as internal medicine or family practice, and subsequently obtain further addiction training and certification from an organization, such as the American Society of Addiction Medicine, or have experience in the care of patients with addictive disorders. An addiction psychiatrist has primary training in psychiatry with additional training or experience in the care of patients with addictive disorders. The presence and impact of a comorbid psychiatric disorder (e.g., major depression, anxiety, personality disorder) should guide the clinician in selecting a referral to an addiction specialist or addiction psychiatrist.

• Although opioids are among the most effective treatments for pain, and treatment of pain is important for all patients, opioid addicts are often excluded from pain treatment for fear of worsening their opioid addiction or triggering relapse in abstinent patients.

**4.3 Consider inpatient or outpatient consultation with appropriate specialists for help in treating significant medical complications of opioid abuse and dependence.**

**Recommendations**

• Recognize that in patients with opioid abuse and dependence, communication among providers and coordinated care is particularly important.

• Consider obtaining consultation with:
  • A hepatologist or gastroenterologist for patients with HBV or HCV, cirrhosis, or end-stage liver disease
  • An HIV specialist for patients with HIV infection
  • An infectious diseases specialist for methicillin-resistant *Staphylococcus aureus*, osteomyelitis, endocarditis, or complex STDs
  • An infectious disease or pulmonary specialist for tuberculosis
  • An orthopedic surgeon for diagnosis, culture, and debridement of septic joints or osteomyelitis
  • A cardiologist for patients with valvular heart disease from subacute or acute bacterial endocarditis
  • A wound-care specialist for patients with cellulitis or venous insufficiency
  • A pain-management specialist for chronic pain
  • Others as needed

**Evidence**

• Consensus.

**Rationale**

• Patients with opioid abuse or dependence may experience multiple complex medical complications from opioids themselves or from associated injection habits, sexual risk behavior, or socioeconomic conditions. These conditions include sleep disorders, liver disease, bloodborne infections, skin and soft tissue infections, and tuberculosis.
5. Hospitalization

After emergency stabilization, consider hospitalization of patients with opioid overdose, and inpatient detoxification in patients unable to tolerate outpatient detoxification.

5.1 After emergency stabilization, hospitalize patients with opioid overdose who are unresponsive to naloxone, and patients who have associated severe medical complications that fail to resolve quickly.

Recommendations

- For patients who are unresponsive or are showing signs of suspected opioid overdose:
  - Establish an airway and administer 100% oxygen.
  - First use a bag-valve-mask, but be alert for the need to initiate endotracheal intubation if necessary for continuing respiratory depression after naloxone treatment.
  - Administer the opioid antagonist naloxone to reverse the effect of the opioid.
    - Recognize that dosing of naloxone is empirical
    - Begin with an initial dose of naloxone, 0.4 mg iv, or 0.8 mg sc
    - Look for an increase in respiratory rate, rise in systolic blood pressure, and papillary dilatation within 2 minutes of administration
    - If necessary, administer subsequent doses of naloxone, 0.4 to 2 mg, at regular intervals
    - If there is no response after 10 mg, consider another cause of respiratory depression
  - Observe the patient clinically for signs of opioid withdrawal or toxicity for at least 1 hour after administration of naloxone.
  - Pay special attention to patients presenting with opioid intoxication in combination with other CNS depressants like alcohol or benzodiazepines.
  - Be aware that patients with suspected pulmonary edema, pneumonia, endocarditis, persistent altered mental status, or respiratory depression warrant longer periods of observation in the hospital.
  - Recognize that patients who are substantially improved within 1 hour of naloxone administration may not warrant hospitalization, but require more observation if they have taken long-acting opioids.

Evidence

- A 2006 guideline from the American Psychiatric Association for the treatment of patients with substance use disorders recommended treating severe opioid overdose in an ED or inpatient setting (37).
- A 2012 narrative review of opioid overdose noted that there were 27,500 admissions for opioid overdose in 2010 in the U.S. (38).
- A 1999 narrative review of heroin overdose estimated that hospitalization rates among patients with suspected heroin overdose are approximately 3% to 7% and are mostly related to a diagnosis of noncardiogenic pulmonary edema, pneumonia, endocarditis, altered mental status, and respiratory depression (39).
- A retrospective analysis of 573 patients treated with naloxone for presumed opioid toxicity (86% heroin overdose) developed criteria for ‘safe’ discharge within 1 hour of naloxone administration based on six factors (40):
  - Patient can mobilize as usual
• Oxygen saturation on room air is >92%
• Respiratory rate is >10 breaths/min and <20 breaths/min
• Temperature is >35.0°C (94°F) and <37.5°C (99.5°F)
• Heart rate is >50 beats/min and <100 beats/min
• Glasgow Coma Scale score is 15

Rationale
• Naloxone is a high-potency opioid antagonist that competitively inhibits opiate receptors and is indicated for the reversal of acute opioid overdose.
• Naloxone administration in patients with opioid dependence may precipitate opioid withdrawal.
• Pulmonary edema, rhabdomyolysis, compartment syndrome, hypothermia, persistent altered mental status, and recurrent respiratory depression are potentially fatal complications of opioid overdose that require continuous monitoring and aggressive treatment.

Comments
• Substantial clinical improvement within 1 hour of naloxone administration is usually a strong indicator that the patient can be discharged safely; however, toxic levels of long-acting opioids can continue to cause potentially fatal respiratory depression after the acute effects of naloxone have worn off, necessitating careful observation.
• Naloxone’s duration of action is 20 to 90 minutes and the onset of action is less than 2 minutes (38).
• It is likely that most noncardiogenic, opioid-induced pulmonary edema occurs within the first few hours of overdose, which obviates the need for prolonged observation with the sole purpose of watching for delayed-onset pulmonary edema.
• The decision to discharge a patient after an overdose is ultimately up to the individual clinician and should take into account contributing psychosocial factors that also warrant clinical attention.
• Unintentional opioid overdose is a common problem among individuals with opioid dependence. In addition to the inherent unreliability of determining the relative potency of drugs obtained on the street, such factors as recent abstinence (resulting from recent detoxification, incarceration, time spent in drug treatment, or hospitalization) and use of other CNS depressants can increase the risk for an unintentional overdose (41; 42; 43; 44).
• Although controversial, use of ‘safe injection’ facilities (i.e., clinics in which addicts are allowed to inject in a medically supervised drug-treatment facility) can significantly reduce the number of overdoses among people who use injection drugs (45).
• Studies have evaluated take-home naloxone (i.e., naloxone distributed to individuals for the prevention of opioid overdose). Their findings have suggested that the use of take-home naloxone and individual training in cardiopulmonary resuscitation may help reduce fatal opioid overdoses (46; 47; 48).

5.2 Consider inpatient detoxification in an appropriate facility for patients seeking treatment who are unable to tolerate outpatient detoxification.

Recommendations
• Work with the patient, social services, or the patient’s insurance provider to seek inpatient medical detoxification in an appropriate facility if the patient has the desire to stop using opioids and is unable to tolerate outpatient detoxification.
• Inform patients that, after medical detoxification with an opioid agonist such as methadone or buprenorphine, or an α2-agonist such as clonidine, ongoing psychosocial treatment is essential to the successful management of opioid dependence.
• Advise patients against opioid detoxification treatments that involve heavy sedation or anesthesia.

• Although the decision regarding outpatient vs. inpatient detoxification is determined by multiple factors, such as individual level of psychosocial complexity, insurance constraints, and clinical judgment, when possible, refer to the American Society of Addiction Medicine Patient Placement Criteria to assist in determining whether a patient requires an inpatient stay for opioid detoxification.

• Be cautious about the risk for relapse and subsequent overdose after detoxification.

Evidence
• Mainly consensus.

• A prospective study followed 137 patients who underwent detoxification for opioid addiction. Patients who left treatment early were deemed still tolerant to opioids, and patients who completed treatment were assumed to have lost tolerance. There were three deaths in the 4 months after treatment, all in the group which had completed treatment and lost tolerance (41).

Rationale
• In patients who are medically stable, medically supervised withdrawal detoxification can be done in outpatient or inpatient facilities depending on the level of complexity.

• The American Society of Addiction Medicine Patient Placement Criteria are increasingly used by insurance providers to determine the appropriate level of care for patients with opioid dependence.

• Patients with opioid dependence are less likely to relapse if they engage in psychosocial treatment following detoxification.

• There is a high risk for relapse and overdose after detoxification.

Comments
• Rapid opioid detoxification with opioid antagonists in combination with heavy sedation or anesthesia is risky and costly, and is not supported by the evidence.
6. Therapy

Use psychosocial interventions and 12-step programs such as Narcotics Anonymous as adjuncts to therapeutic pharmacotherapy. Use drug therapy for detoxification and maintenance treatment.  

6.1 Use opioid agonists, generally methadone or buprenorphine, to treat patients with acute opioid withdrawal in both outpatient and inpatient settings.

Recommendations

- Use an opioid agonist (methadone or buprenorphine) to treat opioid withdrawal.
- Once symptoms are controlled, slowly taper the dose of the opioid agonist.
- See table Drug Treatment for Opioid Abuse.

Evidence

- A 2014 guideline from the American Pain Society and the Heart Rhythm Society on the safe prescribing of methadone recommended performing a urine drug screen and an electrocardiogram on all patients before initiating methadone, starting low doses and titrating slowly, assessing patients on methadone for adverse events and considering drug interactions, and repeating an electrocardiogram during therapy in those with baseline QTc prolongation or risk factors for QTc prolongation (1).
- A 2006 guideline from the American Psychiatric Association for the treatment of patients with substance use disorders recommended treatment of opioid withdrawal with tapered doses of methadone or buprenorphine, clonidine for acute symptoms, or clonidine plus naltrexone (37).
- A 2013 Cochrane review of tapering methadone for patients with acute opioid withdrawal included 23 trials with 2467 participants. Compared with placebo, methadone improved withdrawal symptoms and led to fewer treatment dropouts, but methadone was equivalent to comparator drugs for all outcomes (49).
- A 2009 Cochrane review of buprenorphine for opioid withdrawal included 22 studies with 1736 participants. Compared with morphine, buprenorphine had similar effects on withdrawal symptoms but led to more patients completing withdrawal treatment (RR, 1.18 [CI, 0.93 to 1.49]). Buprenorphine was more effective than clonidine or lofexidine for symptom control (50).
- A 2010 Cochrane review of opioid antagonist-induced withdrawal under heavy sedation included nine studies with 1109 participants, including eight randomized trials. The level of sedation had no effect on the intensity or duration of opioid withdrawal. Agonist-induced withdrawal under heavy sedation had a significantly higher incidence of adverse events compared with light sedation (RR, 3.21 [CI, 1.13 to 9.12]) (51).
- SAMHSA's Center for Substance Abuse Treatment has published Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction (52).

Rationale

- Discontinuation of opioid use can cause noradrenergic activation, resulting in uncomfortable autonomic arousal.
- Use of a tapering dose of an opioid agonist provides a gradual reduction in opiate receptor binding and activation, and lessens the subjective and objective intensity of opioid withdrawal.

Comments
• To prescribe methadone for the treatment of opioid dependence and withdrawal, the DEA also requires that the physician be a participant in a treatment program, such as a certified opioid treatment program methadone clinic or a free-standing medical detoxification facility. However, any physician can prescribe methadone for a patient being treated for a primary medical problem in which acute opioid withdrawal is a complicating factor.

• All clinicians must have a DEA waiver to prescribe buprenorphine for detoxification and office-based treatment of primary opioid dependence. This rule does not apply to physicians and other authorized hospital staff who administer buprenorphine or other opioid agonists to patients addicted to opioids in the hospital for the treatment of a primary medical condition.

• There usually must be evidence of opioid withdrawal or recent opioid use in order to use opiate-agonist therapy. Exceptions are recently incarcerated or pregnant patients who may be eligible for substitution therapy without recent opiate use or opiate withdrawal.

6.2 Consider use of \( \alpha_2 \)-agonists to ease the physical manifestations of acute opioid withdrawal in both outpatient and inpatient settings.

**Recommendations**

• Use the \( \alpha_2 \)-agonist clonidine to treat the autonomic manifestations of acute opioid withdrawal, especially in the outpatient setting.

• See table Drug Treatment for Opioid Abuse.

**Evidence**

• A 2006 guideline from the American Psychiatric Association for the treatment of patients with substance use disorders recommended treatment of opioid withdrawal with tapered doses of methadone or buprenorphine, clonidine for acute symptoms, or clonidine plus naltrexone (37).

• A 2009 Cochrane review of \( \alpha_2 \)-adrenergic agonists (clonidine and lofexidine) for opioid withdrawal included 24 studies with 1631 participants. \( \alpha_2 \)-adrenergic agonists were more effective than placebo at alleviating symptoms. Compared with morphine, \( \alpha_2 \)-adrenergic agonists resulted in similar control of symptoms, but patients receiving morphine were more likely to stay in treatment. Clonidine had more adverse effects than methadone (53).

• A 1999 narrative review of three randomized trials examining 194 subjects reported the utility of lofexidine as an alternative treatment to clonidine and also confirmed a lower incidence of hypotension and treatment dropout vs. clonidine (54).

**Rationale**

• Discontinuation of opioid use can cause noradrenergic activation, resulting in uncomfortable autonomic arousal.

• Use of an \( \alpha_2 \)-noradrenergic agonist stimulates adrenergic autoreceptors, resulting in a decrease in autonomic arousal and a corresponding reduction in opioid withdrawal symptoms.

**Comments**

• Because the use of opioids for opioid detoxification is restricted to specific providers and treatment programs, \( \alpha_2 \)-agonists are generally the only medications available for the treatment of opioid withdrawal in outpatient settings.

• In the management of opioid withdrawal, \( \alpha_2 \)-agonists are usually less effective than opioid agonists and are therefore typically a second-line or adjunctive (used in combination with opioid agonists) treatment.

• Lofexidine has been approved for treatment of opioid withdrawal in the UK but is not FDA-approved for opioid withdrawal in the U.S.
6.3 If the provider is appropriately credentialed, consider medication-assisted treatment with opioid agonists or partial agonists for patients with chronic opioid dependence.

Recommendations

- Consider prescribing the opioid agonists methadone or buprenorphine or the combined formulation buprenorphine-naloxone for patients with chronic opioid dependence.
- See table Drug Treatment for Opioid Abuse.

Evidence

- A 2006 guideline from the American Psychiatric Association for the treatment of patients with substance use disorders stated that treatment with methadone or buprenorphine is reasonable in patients with opioid dependence for over 1 year, and noted that treatment with naltrexone is an alternative strategy (37).
- A 2009 Cochrane review of methadone for opioid dependence compared with no drug therapy included 11 randomized trials. Patients on methadone were less likely to use heroin (RR, 0.66 [CI, 0.56 to 0.78]) than patients who were not receiving methadone (55).
- A 2008 Cochrane review of buprenorphine for maintenance therapy for heroin addiction included 24 studies with 4497 participants. Buprenorphine was superior to placebo in terms of retention in treatment (RR, 1.50 [CI, 1.19 to 1.88] for low-dose therapy), but flexible-dose buprenorphine was less effective than methadone for retention in therapy (RR, 0.80 [CI, 0.68 to 0.95]) (56).
- A 2003 Cochrane review of high- vs. low-dose chronic methadone use included 21 studies with 6004 participants. Patients receiving high-dose methadone, 60 to 100 mg, maintenance therapy had higher rates of opioid abstinence (RR, 1.59 [CI, 1.16 to 2.18]) compared with low-dose methadone. Other outcomes were better with higher-dose methadone as well (57).
- A randomized trial compared sustained-release naltrexone with oral naltrexone or placebo in 306 patients with opioid abuse who had recently undergone detoxification. After 6 months, more patients on sustained-release naltrexone remained in treatment without relapse (52.9% vs. 15.7% in the oral naltrexone group, and 10.8% in the placebo group) (58).
- A randomized trial compared sublingual buprenorphine-naloxone with placebo in 326 opiate-dependent subjects. The study was terminated early due to the clear efficacy of buprenorphine-naloxone vs. placebo. The proportion of urine samples that were negative for opioids was greater in the combined-treatment and buprenorphine groups (17.8% and 20.7%, respectively) than in the placebo group (5.8%; P<0.001 for both comparisons); the active treatment groups also reported less opiate craving (P<0.001 for both comparisons with placebo) (59).
- A randomized trial compared extended (12 weeks) with short-term (14 days) buprenorphine-naloxone in opioid-dependent youths. After 12 weeks, more patients receiving long-term therapy remained in treatment (70% vs. 20.5%, P<0.001) (60).
- A 2011 Cochrane review comparing treatment of patients using injection drugs with patients taking oral opioids to prevent HIV infection included 38 studies with 12,400 participants; most studies had high risk for bias. Treatment for opioid-dependent injection-drug users with methadone or buprenorphine was associated with reduced illicit opioid use, injecting use, sharing injecting equipment, multiple sex partners, and exchange of sex for drugs or money, and likely with reduced rates of HIV infection, although results were not pooled due to potential bias (61).

Rationale

- Methadone maintenance therapy at an appropriate daily dosage is effective in decreasing heroin use and increasing treatment retention.
Opioid Abuse

- Buprenorphine and buprenorphine-naloxone are office-based treatments for opioid dependence that perform as well as methadone.

Comments
- In the U.S., methadone for opioid addiction is dispensed through federally regulated methadone maintenance clinics.
- Methadone is a Schedule II drug. When used for the treatment of opioid dependence, methadone must be prescribed and dispensed through one of a limited number of federally regulated methadone clinics.
- Methadone is associated with a risk for respiratory depression, excessive sedation, long QTc interval, TdP, and fatal overdose. Consider electrocardiographic screening for long QTc syndrome in patients with other risk factors for long QTc interval or on high doses of methadone (62).
- Electrocardiographic screening of all patients before initiation of methadone, during treatment, and with dose increases is controversial (63). However, it is reasonable to inform patients on methadone of the risks for QTc prolongation and TdP.
- Buprenorphine and buprenorphine-naloxone are Schedule III drugs that are administered sublingually. Providers must take a federally mandated training course such as one of the courses provided by the American Academy of Addiction Psychiatry, and register for an additional DEA identification number in order to prescribe these drugs.
- Buprenorphine-naloxone is a combined formulation developed due to federal concerns about possible diversion and iv use of the monotherapy formulation. With the combination, there is less likelihood of iv use because parenteral administration of the combined formulation can precipitate withdrawal in physically dependent opioid users due to the direct antagonist action of naloxone. When administered sublingually, naloxone undergoes significant first-pass metabolism, and therefore does not exert appreciable opioid antagonism relative to parenteral administration.

6.4 Consider oral or long-acting implants of opioid antagonists in specific opioid-dependent populations.

Recommendations
- Only consider maintenance therapy with naltrexone in conjunction with psychosocial therapy in patients who are especially highly motivated to stop abusing opioids.
- Do not give naltrexone before the patient is fully detoxified or abstinent from opioids to avoid precipitating withdrawal.
- Inform patients about the risk for overdose after stopping naltrexone therapy.
- See table Drug Treatment for Opioid Abuse.

Evidence
- A 2007 systematic review of naltrexone for relapse prevention in opioid abuse included 26 randomized trials, which were generally of poor quality. Naltrexone was not clearly superior to placebo in terms of retention in treatment, but rates of drug abuse were lower with naltrexone (RR, 0.72) (64).
- A 2011 Cochrane review of oral naltrexone for opioid dependence included 13 studies involving 1158 participants. Naltrexone alone or combined with psychosocial therapy was no more effective than placebo or other treatments. No statistically significant benefit was shown in terms of retention in treatment, side effects, or relapse results at follow-up for any of the considered comparisons (65).


- A 2008 Cochrane review of oral naltrexone for opioid dependence included one study which found that high-dose naltrexone was superior to placebo. Side effects were more frequent with naltrexone than placebo (66).

- A randomized trial compared injectable diacetylmorphine, the active ingredient in heroin, with oral methadone maintenance therapy in patients refractory to treatment. Patients receiving diacetylmorphine were more likely to stay in treatment (NNT, 3) and less likely to engage in illegal activity (NNT, 5), but rates of overdose and seizure were higher (67).

**Rationale**

- Naltrexone is a pure, long-acting opioid antagonist that can block the pharmacologic effects of opioids.

- Naltrexone use is generally reserved for certain highly motivated groups, such as impaired professionals facing disciplinary action, persons facing significant loss of social status or legal action, and high-compliance patients.

**Comments**

- Data regarding the routine use of naltrexone for opioid maintenance do not support its use over buprenorphine (68).

- The rate of overdose after stopping oral naltrexone therapy was greater in heroin users who left treatment with naltrexone than in the individuals who left treatment with agonists (69).

**6.5 Include psychosocial interventions in conjunction with medical treatment.**

**Recommendations**

- Encourage participation in a 12-step group, such as Narcotics Anonymous, and individual counseling sessions, and tailor frequency and intensity of treatment to the patient's needs.

- Use contingency-management interventions, relapse prevention, general cognitive behavioral therapy, and combinations of psychosocial interventions in patients with opioid abuse or dependence, in addition to pharmacotherapy.

**Evidence**

- A 2006 guideline from the American Psychiatric Association for the treatment of patients with substance-use disorders noted that psychosocial therapies are effective components of a long-term treatment plan (37).

- A 2011 Cochrane review of pharmacologic therapy plus psychosocial treatment compared with pharmacologic treatment alone for acute opioid detoxification included 11 studies with 1592 participants. Patients receiving psychosocial and pharmacologic treatment were less likely to return to using opioids than those patients receiving pharmacologic treatment alone (RR, 0.82 [CI, 0.71 to 0.93]) (70).

- A 2011 Cochrane review of pharmacologic therapy plus psychosocial treatment compared with pharmacologic treatment alone for treatment of opioid dependence included 35 studies with 4319 participants. Psychosocial therapies added to pharmacologic treatment did not improve retention in therapy (RR, 1.03 [CI, 0.98 to 1.07]), abstinence (RR, 1.12 [CI, 0.92 to 1.37]), or other outcomes (71).

- In a study, substance-abusing patients were randomly assigned to standard treatment, standard treatment with contingency management for submitting negative toxicology screen, or standard treatment with contingency management for completing goal-related activities. Both contingency-management interventions had better outcomes than did the standard treatment, but the contingency-management intervention that reinforced submission of negative samples had the better outcome of the two (72).
Rationale

- Patients with opioid addiction may benefit from additional psychosocial intervention.
7. Patient Counseling

Provide patients with information from credible organizations on overdose prevention and the management of opioid dependence.

7.1 Provide patients and their family members with information on how to recognize an overdose, the appropriate management of opioid dependence, and the biological, psychological, and social sequelae of opioid addiction.

Recommendations

- Inform patients and families that:
  - Opioid dependence is a chronic illness that requires comprehensive and ongoing treatment.
  - The exact course of untreated opioid addiction is uncertain, but the risk for development of infectious disease, overdose, legal trouble, and psychological problems is high and almost certainly will diminish overall quality of life and total life span.
  - Overdose is associated with high-dose opioids and mixing opioids with alcohol and other drugs.
  - Family members should call 911 as soon as possible if they witness an overdose.
- Provide patients and significant others with educational information on:
  - Opioid addiction unrelated to the treatment of chronic pain from the American Academy of Addiction Psychiatry and the National Institute on Drug Abuse
  - Opioid addiction related to treatment of chronic pain from the American Academy of Pain Medicine and the American Pain Society
  - Office-based opioid treatment with buprenorphine or buprenorphine-naloxone from the Substance Abuse and Mental Health Services Administration

Evidence

- A prospective study of new-onset injection-drug users found excess mortality among this group compared with demographically similar peers in the general population, making clear the need for interventions to prevent premature deaths among young IV drug users (73).
- A study of mortality in patients with methadone treatment in Texas concluded that the scope of treatment for these patients should include on-site treatment for other medical conditions and staff counseling of new patients about the risk for death (74).
- A 2012 report described community-based overdose education programs and presented results suggesting that these programs may reduce mortality from overdose (47).

Rationale

- Referral to recognized authorities ensures the most reliable information geared towards the lay public.

7.2 Inform patients who have been prescribed opioids about the risk to themselves and to the people with whom they may share their medications.

Recommendations

- Counsel patients not to share their prescription opioids with anyone, and to secure them from children.
- Consider recommending lock boxes or other safe storage devices to patients on opioids who have at-risk family members.

Evidence

- Among respondents to the SAMHSA 2010 National Survey on Drug Use and Health who used pain relievers nonmedically, 55% received them at no cost from a family member or friend (6).
• Sixty-three percent of overdose deaths in West Virginia in 2006 were related to nonmedical use of prescription drugs (25).

• In a study of 25 patients given opioids in the ED, none stored them safely, according to subsequent home interviews (75).

**Rationale**

• A potentially fatal overdose may result when opioids are used by family members and friends of patients.

• Nonmedical use of pharmaceutical opioids can result in opioid dependence.

• Children and others in a patient's home can access and use medications that are not safely stored.
8. Follow-up

Monitor opioid use and adherence to pharmacotherapy and psychosocial counseling.

8.1 Schedule regular follow-up to inquire about adherence to treatment of opioid-use disorders.

Recommendations

- In patients with opioid-use disorders:
  - Use random urine drug screening to monitor for opioid use
  - Ask about adherence to psychosocial counseling
  - Ask about the use of opioids and other substances, including alcohol
  - Query significant others to corroborate adherence to pharmacotherapy, 12-step group attendance, and recent drug or alcohol use
  - Examine patients for signs of opioid withdrawal and abuse.

Evidence

- A 2012 guideline from the American Society of Interventional Pain Physicians for responsible opioid prescribing for patients with chronic noncancer pain recommended using urine drug screening to monitor patients on opioids and noted the expected duration of positive urine toxicology with different drugs (2).

Rationale

- Opioid-use disorders are chronic, relapsing and remitting disorders that follow a varying course, with periods of abstinence interspersed with periods of opioid misuse. Patients with these disorders must be monitored regularly.
- A minority of patients are able to successfully detoxify from opioid substitution therapy and remain opioid-free.

8.2 Consider vaccination for HAV, HBV, and tetanus for injection-drug users.

Recommendations

- Consider vaccination for HAV, HBV, and tetanus for opioid-dependent individuals, particularly patients who use injection drugs or have other indications for these vaccines.
- See module Hepatitis A.
- See module Hepatitis B.

Evidence

- A 2006 CDC guideline recommended vaccination against HAV for users of injection and noninjection illicit drugs (76).
- A 2006 CDC guideline recommended universal HBV vaccination in drug-abuse treatment and prevention settings and vaccination of individuals with risk factors for HBV, including injection-drug use, in other settings (77).
- Individuals who use injection drugs may be at increased risk for tetanus (78), and thus adhering to CDC guidelines for tetanus vaccination (79) is particularly important for this population.

Rationale

- Several CDC vaccination guidelines recommend vaccination for users of illicit drugs.
References


new


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Glossary

β-HCG  
human chorionic gonadotropin β subunit

bid  
twice daily

BUN  
blood urea nitrogen

CBC  
complete blood (cell) count

CDC  
Centers for Disease Control and Prevention

CI  
confidence interval

CKD  
chronic kidney disease

CNS  
central nervous system

CPK  
creatine phosphokinase

CrCl  
creatinine clearance

CT  
computed tomography

CV  
cardiovascular

CYP  
cytochrome P450 isoenzyme

DEA  
Drug Enforcement Administration

DSM-V  
*Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition

ED  
emergency department

EEG  
electroencephalogram

FDA  
Food and Drug Administration

HAV  
hepatitis A virus

HbA1c  
glycosylated hemoglobin

HBV  
hepatitis B virus

HCV  
hepatitis C virus
**Opioid Abuse**

**HIV**
human immunodeficiency virus

**IgM**
immunoglobulin M

**im**
intramuscular

**iv**
intravenous

**MAT**
medication-assisted treatment for opioid addiction

**MRI**
magnetic resonance imaging

**P-gp**
P-glycoprotein

**po**
oral

**PPD**
purified protein derivative

**RPR**
rapid plasma reagin

**RR**
risk ratio

**SAMHSA**
Substance Abuse and Mental Health Services Administration

**sc**
subcutaneous

**scr**
serum creatinine

**SL**
sublingual

**STD**
sexually transmitted disease

**TdP**
torsades de pointes

**tid**
three times daily

**VDRL**
Venereal Disease Research Laboratory (test)

**Terms**

**12-step program**
Self-help program requiring mastery of a set of steps to achieve and maintain abstinence, based on the program of Alcoholics Anonymous. Many addiction treatment programs use a 12-step structure or philosophy as a construct for treatment design.

**abstinence**
Nonuse of alcohol or any illicit drugs, as well as nonabuse of medications normally obtained by prescription or over the counter. Abstinence in this module does not refer to nonuse of or withdrawal from maintenance medications (methadone, buprenorphine, or naltrexone) when they are used in MAT. Compare medically supervised withdrawal.

**addiction**
Combination of the physical dependence on, behavioral manifestations of the use of, and subjective sense of need and craving for a psychoactive substance, leading to compulsive use of the substance either for its positive effects or to avoid negative effects associated with abstinence from that substance. Compare dependence.

**analgesic**
A compound that alleviates pain without causing loss of consciousness. Opioid analgesics are a class of compounds that bind to specific receptors in the CNS to block the perception of pain or affect the emotional response to pain. Such compounds include opium and its derivatives, as well as a number of synthetic compounds. Chronic administration or abuse of opioid analgesics may lead to addiction.

**Axis I**
DSM-IV-TR disorder classification composed of definitions and descriptions of major disorders (i.e., psychotic, mood, and substance-use disorders) that may require clinical attention.

**benzodiazepines**
Group of medications having a common molecular structure and similar pharmacologic activity, including antianxiety, sedative, hypnotic, amnestic, anticonvulsant, and muscle-relaxing effects. Benzodiazepines are among the most widely prescribed medications (e.g., diazepam, chlordiazepoxide, clonazepam, alprazolam, lorazepam).

**buprenorphine**
Partial opioid agonist approved by the FDA for use in detoxification or maintenance treatment of opioid addiction and marketed under the trade names Subutex® and Suboxone® (the latter also containing naloxone).

**counseling**
In MAT, a treatment service in which a trained counselor and a case manager evaluate both a patient's external circumstances and immediate treatment progress and offer appropriate advice and assistance or referral to other experts and services as needed. A major objective in MAT is to provide skills and support for a substance-free lifestyle and encourage abstinence from alcohol and other psychoactive substances. Compare psychotherapy.

**craving**
Urgent, seemingly overpowering desire to use a substance, which often is associated with tension, anxiety, or other dysphoric, depressive, or negative affective states.

**dependence**
State of physical adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, or decreasing blood level of a substance or administration of an antagonist. Compare addiction.

**detoxification (‘detox’)**
In this module, treatment for addiction to an illicit substance in which the substance is eliminated gradually from a patient's body while various types and levels of reinforcing treatment are provided to alleviate adverse physical or psychological reactions to the withdrawal process. This module avoids using this term to designate the process of dose tapering from maintenance medication because that incorrectly suggests that opioid treatment medications are toxic. Compare medically supervised withdrawal.

**diversion**
Sale or other unauthorized distribution of a controlled substance, usually for a purpose other than the prescribed and legitimate treatment of a medical or mental disorder.

**hepatitis C**
Viral disease of the liver that is the leading cause of cirrhosis in the U.S. and a particular concern in MAT because of the high incidence of the disease and spread of the infection among people who inject drugs.

**high-risk behavior**
Activity that increases the likelihood that a recovering patient in substance-abuse treatment will relapse to substance use or contract a substance use-related disorder, such as an infectious disease.

**iatrogenic opioid addiction**
Addiction resulting from medical use of an opioid (i.e., under physician supervision), usually for pain management.

**induction**
Initial treatment process of adjusting maintenance medication dosage levels until a patient attains stabilization. The goal of induction is to achieve a steady-state blood level, which provides relief of withdrawal symptoms.

**intervention**
The process of providing care to a patient or taking action to modify a symptom, effect, or behavior. Also, the process of interacting after assessment with a patient who is substance-addicted to present a diagnosis and recommend and negotiate a treatment plan. Frequently used as a synonym for treatment. Types of intervention can include crisis intervention, brief intervention, and long-term intervention.

**level of care**
The setting or combination of settings in which the appropriate intensities and types of treatment services can be provided for individual patients.

**maintenance treatment**
Dispensing of an opioid addiction medication at stable dosage levels for a period in excess of 21 days in the supervised treatment of an individual for opioid addiction (42 CFR, Part 8 § 2).

**medically supervised withdrawal**
Dispensing of a maintenance medication in gradually decreasing doses to alleviate adverse physical or psychological effects incident to withdrawal from the continuous or sustained use of opioid drugs. The purpose of medically supervised withdrawal is to bring a patient maintained on maintenance medication to a medication-free state within a target period.

**Medication-assisted treatment for opioid addiction**
Type of addiction treatment, usually provided in a certified, licensed opioid treatment program or a physician’s office-based treatment setting that provides maintenance pharmacotherapy using an opioid agonist, a partial agonist, or an antagonist medication, which may be combined with other comprehensive treatment services, including medical and psychosocial services.

**methadone**
The most frequently used opioid agonist medication. Methadone is a synthetic opioid that binds to µ opiate receptors and produces a range of µ-agonist effects similar to those of short-acting opioids such as morphine and heroin.

**methadone maintenance treatment**
Dispensing of methadone at stable dosage levels for more than 21 days in the supervised treatment of an individual for opioid addiction (42 CFR, Part 8 § 2).

**naloxone**
Short-acting opioid antagonist. Because of its higher affinity than that of opioids for µ opiate receptors, naloxone displaces opioids from these receptors and can precipitate withdrawal, but it does not activate the µ receptors, nor does it cause the euphoria and other effects associated with opioid drugs. Naloxone is not FDA-approved for long-term therapy for opioid addiction, except in the combination buprenorphine-naloxone tablet. Some programs use naloxone to evaluate an individual's level of opioid dependence.

**naltrexone**
Derivative of naloxone and the only opioid antagonist approved for use alone in long-term treatment of people with opioid addiction. Naltrexone is used primarily after medically supervised withdrawal from opioids to prevent drug relapse in selected, well-motivated patients.

**office-based treatment**
MAT provided in a physician's office or health care setting other than an opioid treatment program

**opiate receptor(s)**
Areas on cell surfaces in the CNS that are activated by opioid molecules to produce the effects associated with opioid use, such as euphoria and analgesia. Opiate receptors are activated or blocked by opioid agonist or antagonist medications, respectively, to mediate the effects of opioids on the body. µ and κ opiate receptor groups principally are involved in this activity.

**opioid**
Natural derivative of opium or synthetic psychoactive substance that has effects similar to morphine or is capable of conversion into a drug having such effects. One effect of opioid drugs is their addiction-forming or addiction-sustaining liability.

**opioid addiction**
Cluster of cognitive, behavioral, and physiologic symptoms resulting from continuation of opioid use despite significant related problems. Opioid addiction is characterized by repeated self-administration that usually results in opioid tolerance, withdrawal symptoms, and compulsive drug taking.

**opioid agonist**
Drug that has an affinity for and stimulates physiologic activity at cell receptors in the CNS normally stimulated by opioids. Methadone and L-α acetylmethadol are opioid agonists.

**opioid antagonist**
Drug that binds to cell receptors in the CNS that normally are bound by opioid psychoactive substances and that blocks the activity of opioids at these receptors without producing the physiologic activity produced by opioid agonists. Naltrexone is an opioid antagonist.

**opioid treatment program**
Substance Abuse and Mental Health Services Administration (SAMHSA)-certified program, usually consisting of a facility, staff, administration, patients, and services, that engages in supervised assessment and treatment, using methadone, buprenorphine, L-α acetylmethadol, or naltrexone, of individuals who are addicted to opioids. An opioid treatment program can exist in a number of settings, including, but not limited to, intensive outpatient, residential, and hospital settings. Services may include medically supervised withdrawal and/or maintenance treatment, along with various levels of medical, psychiatric, psychosocial, and other types of supportive care.

**pharmacotherapy**
Treatment of disease with prescribed medications.

**prevalence**
Number of cases of a disease in a population, either at a point in time (point prevalence) or over a period (period prevalence). Prevalence rate is the fraction of people in a population who have a disease or condition at one time (the numerator of the rate is the number of existing cases of the condition at a specified time, and the denominator is the total population).

**psychoactive drug**
A substance that affects the mind, thoughts, feelings, and sometimes behaviors.

**relapse**
Breakdown or setback in a person's attempt to change or modify a particular behavior; an unfolding process in which the resumption of compulsive substance use is the last event in a series of maladaptive responses to internal or external stressors or stimuli.

**retention in treatment**
Period during which a patient is able and willing to remain in therapy, which is influenced by a combination of patient and program characteristics. Retention in treatment should be considered the product of a continuing therapeutic relationship between recovering patients and their treatment providers.

**screening**
Process of determining whether a prospective patient has a substance-use disorder before admission to treatment. Screening may include observation of known presenting complaints and symptoms that are indicators of substance-use disorders. Due to lack of established disease-specific screening instruments for opioid abuse, the definition of screening in this module applies to a specific clinical context and is not a population-based assessment.

**sedative**
Medication with CNS-sedating and -tranquilizing properties. An example is any of the benzodiazepines. Most sedatives also promote sleep. Overdoses of sedatives can lead to dangerous respiratory depression.

**stabilization**
Process of providing immediate assistance (as with an opioid agonist) to eliminate withdrawal symptoms and drug craving.

**substance-use disorder**
Maladaptive pattern of drug or alcohol use manifested by recurrent, significant adverse consequences related to the repeated use of these drugs or alcohol. The substance-related problem must have persisted and occurred repeatedly during a 12-month period. It can occur sporadically and mainly be associated with social or interpersonal problems or it can occur regularly and be associated with medical and mental problems, often including tolerance and withdrawal.

**tolerance**
Condition of needing increased amounts of an opioid to achieve intoxication or a desired effect; condition in which continued use of the same amount of a substance has a markedly diminished effect.

**urine drug testing**
Most common laboratory assessment technique in addiction treatment, which involves analysis of urine samples from patients for the presence or absence of specific drugs. Originally used as a measure of program effectiveness, urine testing now is used to make programmatic decisions, monitor psychoactive substance use, adjust medication dosage, and decide whether a patient is responsible enough to receive take-home medication. Methods of urine testing vary widely.

**withdrawal syndrome (or withdrawal)**
Predictable constellation of signs and symptoms after abrupt discontinuation of or rapid decrease in use of a substance that has been used consistently for a period of time. Signs and symptoms of withdrawal are usually opposite to the direct pharmacologic effects of a psychoactive substance.
**Tables**

**Lab and Other Studies for Opioid Abuse**

<table>
<thead>
<tr>
<th>Test</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood alcohol level (serum or breathalyzer)</td>
<td>Comorbid alcohol use disorders make opioid use disorders more difficult to treat and increase the likelihood of overdose</td>
</tr>
<tr>
<td>Serologic and other studies for infection, including HIV antibody, HBV surface antibody, HCV antibody, VDRL, and PPD</td>
<td>Obtain if infection is suspected</td>
</tr>
<tr>
<td>BUN: creatinine ratio and electrolytes</td>
<td>To exclude renal dysfunction</td>
</tr>
<tr>
<td>CBC with differential</td>
<td>If infection is suspected</td>
</tr>
<tr>
<td>Urine toxicology for other drugs of abuse</td>
<td>Important to exclude comorbid addictions or abuse, especially cocaine and benzodiazepines</td>
</tr>
<tr>
<td>β-HCG</td>
<td>Obtain in women of childbearing age to test for pregnancy</td>
</tr>
</tbody>
</table>

β-HCG = human chorionic gonadotropin β subunit; BUN = blood urea nitrogen; CBC = complete blood (cell) count; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; PPD = purified protein derivative; VDRL = Venereal Disease Research Laboratory (test).
# Differential Diagnosis of Opioid Abuse

<table>
<thead>
<tr>
<th>Disease</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diseases that mimic opioid intoxication</strong></td>
<td></td>
</tr>
<tr>
<td>Opioid intoxication</td>
<td>Respiratory depression, somnolence, miosis, puncture wounds on extremities, positive urine toxicology screen for opioids</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>Pungent-smelling breath, similar to alcohol; appears intoxicated; slurred speech, slowed reflexes, confusion</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>Appears intoxicated; slurred speech, slowed reflexes, confusion</td>
</tr>
<tr>
<td>In hepatic encephalopathy, there may be an elevated serum ammonia level, a flapping hand tremor (asterixis)</td>
<td></td>
</tr>
<tr>
<td>Abuse of alcohol or sedative-hypnotic drugs</td>
<td>Appears intoxicated; slurred speech, slowed reflexes, confusion, but does not have miosis</td>
</tr>
<tr>
<td>Urine toxicology results may be helpful to detect the presence of sedative-hypnotics, and serum analysis or breathalyzer may detect the presence of alcohol use within the previous 12 hours</td>
<td></td>
</tr>
<tr>
<td>Head trauma</td>
<td>Appears intoxicated; slurred speech, slowed reflexes, confusion</td>
</tr>
<tr>
<td>Physical exam for signs of trauma, such as bruising, dried blood, or tenderness on the scalp may signal the need for further testing with a CT scan or MRI of the head</td>
<td></td>
</tr>
<tr>
<td>Epilepsy (postictal state)</td>
<td>Appears intoxicated; slurred speech, slowed reflexes, confusion</td>
</tr>
<tr>
<td>Patient may appear confused for hours after or during a seizure. Ask about seizure history or obtain neurologic evaluation with EEG monitoring to confirm a diagnosis</td>
<td></td>
</tr>
<tr>
<td><strong>Diseases that mimic opioid withdrawal</strong></td>
<td></td>
</tr>
<tr>
<td>Opioid withdrawal</td>
<td>Irritability, hypertension, tachycardia, mild hyperthermia, mydriasis, lacrimation, vomiting, diarrhea</td>
</tr>
<tr>
<td>Flu-like illness</td>
<td>Diaphoresis; elevated temperature, blood pressure, or pulse; myalgias; chills; weakness; nausea; vomiting; anorexia</td>
</tr>
<tr>
<td>Time course and exposure to illness may be useful in differentiating flu-like illnesses from opioid withdrawal. Temperature &gt;38.6°C (101.5°F) is unusual in opioid withdrawal</td>
<td></td>
</tr>
<tr>
<td>Side effects of interferon/ribavirin</td>
<td>Myalgias, low-grade temperature, nausea, anorexia, chills, weakness</td>
</tr>
<tr>
<td>History of HCV infection or other diseases with ongoing or recent treatment using interferon/ribavirin</td>
<td></td>
</tr>
</tbody>
</table>

CT = computed tomography; EEG = electroencephalogram; HbA1c = glycosylated hemoglobin; HCV = hepatitis C virus; MRI = magnetic resonance imaging.
<table>
<thead>
<tr>
<th>Drug or Drug Class</th>
<th>Dosing</th>
<th>Side Effects</th>
<th>Precautions</th>
<th>Clinical Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Detoxification: 8-16 mg SL on day 1. Decrease by 2-4 mg daily. Induction: 8 mg SL on day 1 and 16 mg SL on day 2. Maintenance: 4-24 mg SL qd. Usual target dose is 16 mg SL qd</td>
<td>Respiratory and CNS depression, hypotension, hepatotoxicity, nausea, constipation, biliary spasm, pruritus, dependence</td>
<td>Avoid: abrupt withdrawal, alcohol, or other CNS depressants. Caution with: severe CKD, hepatic disease, GI motility disorders, seizure disorder, pulmonary disease, elderly</td>
<td>Detoxification and maintenance</td>
</tr>
<tr>
<td>Methadone (Methadose, Dolophine)</td>
<td>Detoxification: Initially 15-30 mg po qd. Decrease by 5 mg daily until discontinued. Maintenance: Initially 20-40 mg qd. May increase to 120 mg po qd</td>
<td>Respiratory and CNS depression, QT prolongation and TdP, hypotension, nausea, constipation, biliary spasm, pruritus, urinary retention, dependence</td>
<td>■ Death due to respiratory or cardiac effects. Dispensed by certified opioid treatment programs only. Risk for abuse. Avoid: abrupt withdrawal, alcohol, or other CNS depressants. Avoid with severe pulmonary disease. Caution with: GI motility disorders, seizure disorder, elderly. Substrate of CYPs 2C19, 3A4, 2B6 and P-gp</td>
<td>Detoxification and maintenance</td>
</tr>
<tr>
<td>Clonidine (Catapres)</td>
<td>Detoxification: 0.1-0.3 mg po q4hr, not to exceed 1.2 mg total daily dose. Administer for 10-14 days</td>
<td>Hypotension, bradycardia, drowsiness, constipation, xerostomia, thrombocytopenia, rebound after withdrawal</td>
<td>Consider decreased dose with: severe hepatic disease, CKD, elderly</td>
<td>Treats the autonomic manifestations of acute opioid withdrawal</td>
</tr>
<tr>
<td>Buprenorphine/ Naloxone (Suboxone)</td>
<td>Maintenance: 4-24 mg buprenorphine component SL qd. Usual target dose is 16 mg buprenorphine component SL qd</td>
<td>Respiratory and CNS depression, insomnia, hypotension, hepatotoxicity, nausea, constipation, biliary spasm, pruritus, dependence</td>
<td>Avoid: abrupt withdrawal, alcohol, or other CNS depressants. Caution with: CKD, hepatic disease, GI motility disorders, seizure disorder, pulmonary disease, elderly</td>
<td>Maintenance</td>
</tr>
<tr>
<td>Naltrexone (ReVia)</td>
<td>25 mg po on day 1, then 50 mg po qd. May then switch to 350 mg total weekly dose, given in 3 divided doses (100 mg, 100 mg, 150 mg)</td>
<td>Nausea, abdominal pain, increased CPK, CNS side effects</td>
<td>■ Hepatic injury with excessive dosing. Avoid with severe hepatic disease. May need to decrease dose with: CKD, mild-moderate hepatic disease</td>
<td>Maintenance for highly motivated patients. Must be fully detoxified and abstinent from opioids</td>
</tr>
</tbody>
</table>

■ = black box warning; CKD = chronic kidney disease; CNS = central nervous system; CPK = creatine phosphokinase; CYP = cytochrome P450 isoenzyme; GI = gastrointestinal; P-gp = P-glycoprotein; po = oral; q12hr = every 12 hours; qd = once daily; SL = sublingual; TdP = torsades de pointes.

PIER provides key prescribing information for practitioners but is not intended to be a source of comprehensive drug information.