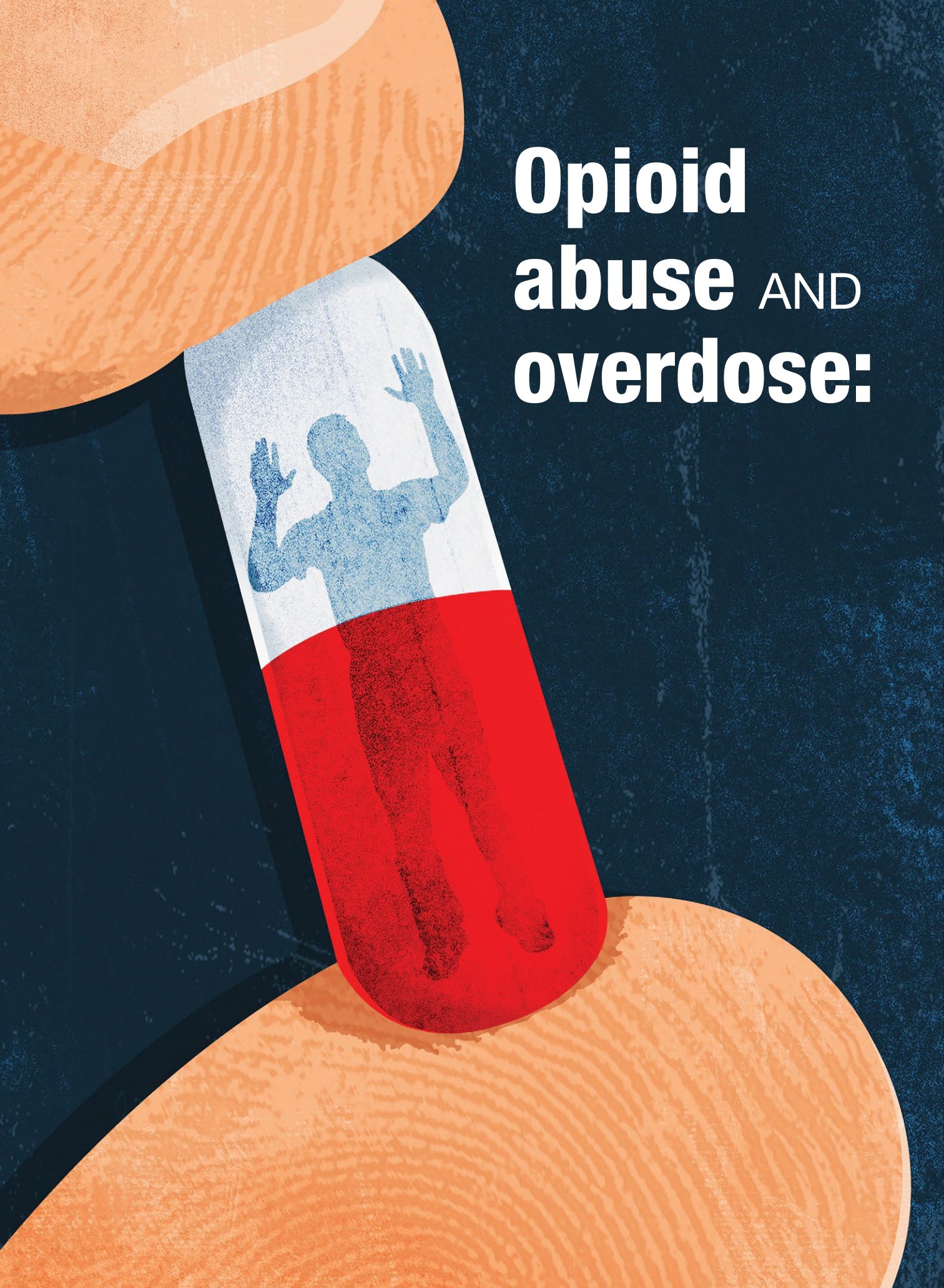


Opioid abuse AND overdose:



Keep your patients safe

Identify patients at risk, ensure an accurate evaluation, and treat the underlying disorder

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Opioid abuse and overdose are large and growing problems, and in recent years the numbers have been staggering. Overdose deaths related to opioids increased from 28,647 in 2014 to 33,091 in 2015 (*Figure, page 10*).¹ More than 2 million individuals in the United States had opioid use disorder in 2015,² and approximately 80% of them received no treatment,³ even though effective treatment could reduce the scope of abuse.^{4,5}

Although psychiatrists typically are not the primary prescribers of opioid medications, they often treat psychiatric disorders in patients with chronic pain who take prescription opioids. A recent study found that, despite representing only 16% of the adult population, adults with mental health disorders receive more than one-half of all opioid prescriptions distributed each year in the United States.⁶ Therefore, psychiatrists must be aware of risk assessment strategies for patients receiving opioids.

In this article, we provide recommendations for managing individuals with opioid use disorder, including:

- how to identify risk factors for opioid use disorder and use screening tools
- how to evaluate a patient with suspected opioid use disorder and make the diagnosis
- how to treat a patient with opioid use disorder, including a review of approved pharmaceutical agents.

Risk factors for opioid abuse and overdose

Patients with a history of mental health and/or substance use disorders or at least 3 months of prescribed opioid treatment are at risk for



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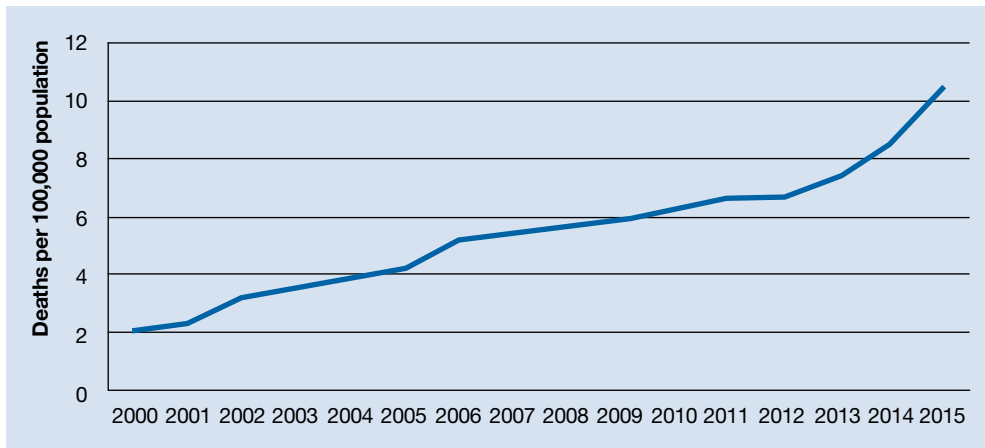
Be aware that even patients without characteristic risk factors can become dependent on opioids or be at risk for overdose



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Figure

Age adjusted rate of drug overdose deaths involving opioids, United States, 2000-2015



Source: Reference 40

opioid abuse. Those taking a high daily dose of opioids or who have a history of overdose are at risk for overdose from opioid abuse (Table 1).⁷⁻¹² Standardized tools, such as the Opioid Risk Tool, can be used to screen to assess risk for opioid abuse among individuals prescribed opioids for treatment of chronic pain.¹² However, clinicians must be aware that even patients without characteristic risk factors can become dependent on opioids and/or be at risk for an accidental or intentional overdose. For example, opioid therapy following surgical procedures, even in patients who do not have a history of opioid use, increases risk of developing opioid use disorder.¹³

Evaluation and diagnosis

DSM-5 criteria define 3 degrees of opioid use disorder, depending on how many of the following traits a patient exhibits (mild, 2 to 3; moderate, 4 to 5; and severe, ≥ 6)¹⁴:

- taking more than the initially intended quantities of opioids or for a longer period of time than intended
- continuous attempts to reduce or otherwise manage opioid use or desires to do so
 - a great deal of time using, recovering from, or acquiring opioids
 - reports of strong cravings to use opioids

- failing to meet personal objectives at home, work, or school

- continued opioid use even though it causes recurrent social problems

- reduction or elimination of activities the patient once considered important due to opioid use

- opioid use in situations where it is physically dangerous

- continued opioid use despite persistent psychological or physiologic problems despite knowing that continued use is causing or worsening those problems

- tolerance to opioids (not consequential for the diagnosis if the patient is taking opioids under appropriate medical supervision)

- withdrawal or use of opioids (or related substances) to prevent withdrawal (not consequential for the diagnosis if the patient is taking opioids under appropriate medical supervision).

Clinicians should be vigilant for symptoms of opioid use or withdrawal, such as needle marks and weight loss, during the interview (Table 2). High-risk populations that require regular screening include individuals with a history of opioid use disorder, patients taking chronic pain medication, and psychiatric patients.¹⁵ During the interview, clinicians should take a nonjudgmental approach and avoid “shame and blame.”

Table 1

Risk factors for opioid use disorder and overdose

Opioid addiction	Overdose
Male sex ⁷	High opioid dosage (daily dose >100 morphine milligram equivalents) ¹¹
Young age ^{7,12}	Sleep-apnea, hepatic or renal impairment
Psychiatric disorders (eg depression) ⁹	History of overdoses
Long-term opioid therapy (>3 months) ¹⁰	Combination of opioids with benzodiazepines
Substance use disorder (including alcohol) ^{8,9}	Long-acting or extended-release formulations (eg, methadone, fentanyl)

Table 2

Key signs and symptoms of opioid use disorder

Sign and symptom	Cause
Miosis and decreased arousal (cold clammy skin, sedation)	Opioid intoxication and opioid use disorder (pinpoint pupils may be observed in overdose)
Dilated pupils and tachycardia	Opioid withdrawal
Needle marks, scars, or necrosis near veins	Opioid use disorder
Weight loss	Opioid use disorder
Nausea, muscle aches, cramps, and/or runny nose	Opioid tolerance or withdrawal

Patients often will withhold information about drug use for various reasons.¹⁶ Therefore, collateral information from the patient's family, close friends, or a referral source is important.

Standardized scales. Various standardized scales can be used to evaluate patients for opioid withdrawal and risk for substance use disorder. Scales for assessing opioid withdrawal include:

- Clinical Opiate Withdrawal Scale
- Subjective Opiate Withdrawal Scale.

Substance use disorder screening tools include:

- Drug Abuse Screen Test-10
- Alcohol Use Disorders Identification Test
- National Institute on Drug Abuse (NIDA) Drug Screening Tool.¹⁷

Examination findings. A brief physical examination is necessary to document key findings (Table 2). Patients should undergo a urine drug screen; gas chromatography/mass spectroscopy can confirm positive results. During the examination, clinicians should look for signs and symptoms of

co-occurring substance use (eg, benzodiazepines, marijuana, alcohol, cocaine) or mental disorders (mood, anxiety, attention-deficit).¹⁸⁻²¹ Because nonprescription opioid use is associated with increased risk of suicide attempts and ideation,²² a suicide risk assessment is necessary.

Managing opioid use disorder

Detoxification is a 3-tiered approach that requires judicious prescription of medication, psychosocial support, and supervision to relieve opioid withdrawal symptoms. In both inpatient and outpatient settings, medications used for opioid detoxification include buprenorphine, clonidine, and methadone administered in doses tapered over 5 to 7 days. Appropriate detoxification increases treatment retention for continuing care.^{23,24}

Buprenorphine or buprenorphine/naloxone is the first-line option for outpatient and inpatient detoxification. Short-term detoxification schedules include starting doses between 4 and 16 mg/d, tapered over 5 to 7 days. Compared with methadone, buprenorphine has a lower risk of

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Patients often withhold information about their drug use, so seek collateral information from family, friends, or other sources



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Detoxification is a 3-tiered approach: medication, psychosocial support, and supervision

Table 3

FDA-approved medications for opioid use disorder treatment and mechanism of action

Medication	Effect
Buprenorphine, buprenorphine/naloxone (approved dose 8 to 32 mg/d; recommended dose 8 to 16 mg/d)	Mu partial agonist
Methadone (doses between 60 and 100 mg/d in methadone clinics)	Mu opioid agonist
Naltrexone (oral dose 50 to 100 mg/d; injectable dose 380 mg IM once every 4 weeks)	Mu antagonist
Naloxone nasal spray, IM or IV formulations (dose 0.4 to 2 mg for opioid overdoses only)	Mu antagonist

overdose²⁵ and abuse potential and can be given in an office-based setting. Clonidine, 0.3 to 1.2 mg/d in divided doses, is an alternative to buprenorphine and can be used in inpatient settings.²⁶

Clonidine is not as effective as buprenorphine for detoxification, but it may be used when buprenorphine is contraindicated. Clonidine may require adjuvant symptomatic treatment for insomnia (eg, trazodone, 100 mg at bedtime), anxiety (eg, hydroxyzine, 25 mg, twice a day), or diarrhea (loperamide, 2 mg/d). If a patient needs more structure and monitoring, he (she) should be referred for inpatient detoxification or to a methadone program.²⁷

Medication-assisted therapies

Detoxification alone often is not sufficient treatment. Medication-assisted therapy (MAT) is typically recommended by federal guidelines provided by the Substance Abuse and Mental Health Administration (SAMHSA) for patients with opioid use disorders.³ Patients can be directly transitioned from currently abused opioids to MAT on an outpatient basis. FDA-approved medications for MAT for opioid use disorder include buprenorphine, naltrexone (oral and long-acting injectable), and methadone (Table 3). Choice of MAT depends on several factors, including cost, patient preference, and availability of methadone programs and buprenorphine providers.²⁸

MAT should include psychosocial support²⁹⁻³³ and active monitoring with urine drug screens. Maintenance therapy with

medications is usually long-term and has been shown to have better outcomes than detoxification alone or short-term treatment.³⁴ Relapse during MAT should not be cause to discontinue treatment; instead, the patient should be referred to a higher level of care.

Some patients require individualized treatment approaches. For example, the SAMHSA has developed specific treatment improvement protocols to tailor treatments to address specific needs of adolescents.³² The American Academy of Pediatrics recommends MAT with buprenorphine in adolescents with opioid use disorder.³³ Although methadone has been approved for pregnant, opioid-dependent patients, recent data indicate buprenorphine is as effective with lower intensity of neonatal abstinence syndrome.³⁴

Buprenorphine. This long-acting (half-life of 24 to 42 hours) opioid partial agonist is approved for treating opioid use disorder in office-based settings according to the Drug Abuse Treatment Act of 2000. Buprenorphine is administered in doses of 8 to 16 mg/d in film or tablet form (sublingual or buccal) and is available in various formulations (Table 4, page 14). It is well tolerated; constipation and unpleasant taste are the most common adverse effects. Physicians are required to have a federal waiver to obtain the Drug Enforcement Administration license to prescribe buprenorphine for opioid use disorder in an office setting.

Buprenorphine reduces or eliminates cravings and withdrawal symptoms and

continued on page 14



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Maintenance therapy with medications has better outcomes than detoxification alone or short-term treatment

Table 4

FDA-approved buprenorphine and buprenorphine/naloxone formulations

Brand name	Dosage strengths	Administration route
Subutex (tablets) only generic equivalent	Buprenorphine, 2 mg	Sublingual
Suboxone (tablets) and generic equivalents ^a	Buprenorphine, 2 mg/naloxone, 0.5 mg buprenorphine, 8 mg/naloxone, 2 mg	Sublingual
Suboxone (films) and generic equivalents ^a	Buprenorphine, 2 mg/naloxone, 0.5 mg buprenorphine, 4 mg/naloxone, 1 mg buprenorphine, 8 mg/naloxone, 2 mg buprenorphine, 12 mg/naloxone, 3 mg	Sublingual
Zubsolv (tablets) ^a	Buprenorphine, 1.4 mg/naloxone, 0.36 mg buprenorphine, 2.9 mg/naloxone, 0.71 mg buprenorphine, 5.7 mg/naloxone, 1.4 mg buprenorphine, 8.6 mg/naloxone, 2.1 mg buprenorphine, 11.4 mg/naloxone, 2.9 mg	Sublingual
Bunavail (films) ^a	Buprenorphine, 1 mg/naloxone, 0.2 mg buprenorphine, 2.1 mg/naloxone, 0.3 mg buprenorphine, 4.2 mg/naloxone, 0.7 mg buprenorphine, 6.3 mg/naloxone, 1 mg	Buccal

Note: A subcutaneous 6-month implant of buprenorphine (Probuphine) was recently approved for opioid use disorder
^aThese buprenorphine products also contain naloxone

helps improve outcomes of abstinence from opioids and retention in treatment.³¹ Formulations of naloxone combined with buprenorphine reduce the risk of abuse via injection.³⁵ Buprenorphine is safe; however, overdoses can occur when it is combined with benzodiazepines and/or other opiates.

Methadone. This long-acting (half-life 8 to 59 hours), full opioid agonist is approved to treat opioid addiction in federal- and state-regulated opioid treatment programs, also known as methadone maintenance programs. These programs are highly structured and include intensive counseling, monitoring, and dispensing to reduce relapse. Methadone is administered orally either via powder, liquid concentrate, tablet, or solution of diskette. Typically, methadone is dispensed daily in doses of 60 to 100 mg, although higher doses are sometimes necessary. Patients who meet certain criteria for stability may be allowed to take home supplies of methadone.

Methadone has a “black-box” warning for overdose, QT prolongation, and risk for respiratory depression when used in combination with benzodiazepines. Because

of its long and unpredictable half-life and tissue accumulation, methadone carries a high overdose risk, particularly with rapidly titrated doses during therapy initiation.³⁵ However, most overdose deaths have occurred with methadone prescribed for pain management. When prescribed and monitored in an opioid treatment program, methadone has shown a high safety profile with respect to overdoses.³⁶

Injectable and oral naltrexone. Used for prevention of relapse to opioid dependence, naltrexone is a pure opioid antagonist that is available as an oral or IM form. Naltrexone has high affinity for the opioid receptors and in therapeutic doses provides an effective blockade for heroin or opioids. Compliance with oral naltrexone has been poor, leading to development of an IM form of naltrexone that can be administered as a single 380-mg dose once every 4 weeks for 6 months or sometimes longer. Naltrexone is also approved for alcohol dependence.

To avoid precipitated withdrawal, patients should be detoxified from opioids for 7 to 10 days before they begin naltrexone, which has no potential for

abuse. Common adverse effects include fatigue, nausea, headache, and, for the IM formulation, injection site reactions. There is a “black-box” warning for liver toxicity; therefore, baseline and periodic liver function tests are necessary.

A NIDA review reported poor compliance with oral naltrexone compared with methadone.³⁵ However, naltrexone has been shown to be effective in highly motivated patients (eg, impaired physicians) and the criminal justice population and for preventing relapse following taper from buprenorphine or methadone.^{37,38}

Treatment for opioid overdose

Naloxone is a highly effective treatment to reverse opioid overdose that is delivered via IM or IV injection or by nasal application. Naloxone has no abuse potential. In doses of 0.4 to 2 mg, naloxone reverses overdose within 2 minutes and is effective for 30 to 90 minutes.³⁹ One should call 911 as soon as possible after naloxone is administered. In several states, naloxone is available without a prescription for patients and family members to combat opioid overdoses. The CDC recommends offering naloxone to patients who have risk factors for opioid overdose.⁴⁰

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Bottom Line

The epidemic of opioid abuse and overdose has emphasized the importance of recognition and treatment of opioid use disorder. Buprenorphine/naloxone, methadone, and naltrexone formulations are approved treatments for opioid use disorder. Naloxone formulations are approved to treat opioid overdoses. Effective medication-assisted treatment should be long-term and include behavioral interventions and psychosocial support.

Related Resources

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Drug Brand Names

Buprenorphine/naloxone • Suboxone, Subutex	Naltrexone • Revia, Vivitrol Naloxone • Narcan, Evzio
Methadone • Dolophine	

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continued

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Naloxone is highly effective at reversing opioid overdose and has no abuse potential



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In several states, naloxone is available without a prescription for patients and family members to combat opioid overdoses

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