

# National Institute on Drug Abuse (NIDA) Misuse of Prescription Drugs

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# Overview

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Misuse of prescription drugs means taking a medication in a manner or dose other than prescribed; taking someone else's prescription, even if for a legitimate medical complaint such as pain; or taking a medication to feel euphoria (i.e., to get high). The term *nonmedical use* of prescription drugs also refers to these categories of misuse. The three classes of medication most commonly misused are:

- opioids—usually prescribed to treat pain
- central nervous system [CNS] depressants (this category includes tranquilizers, sedatives, and hypnotics)—used to treat anxiety and sleep disorders
- stimulants—most often prescribed to treat attention-deficit hyperactivity disorder (ADHD)

Prescription drug misuse can have serious medical consequences. Increases in prescription drug misuse<sup>1</sup> over the last 15 years are reflected in increased emergency room visits, overdose deaths associated with prescription drugs<sup>2-5</sup>, and treatment admissions for prescription drug use disorders, the most severe form of which is an addiction. Overdose deaths involving prescription opioids were five times higher in 2016 than in 1999.<sup>6</sup>

# What is the scope of prescription drug misuse?

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Misuse of prescription opioids, CNS depressants, and stimulants is a serious public health problem in the United States. Although most people take prescription medications responsibly, in 2017, an estimated 18 million people (more than 6 percent of those aged 12 and older) have misused such medications at least once in the past year.<sup>7</sup> According to results from the 2017 National Survey on Drug Use and Health, an estimated 2 million Americans misused prescription pain relievers for the first time within the past year, which averages to approximately 5,480 initiates per day. Additionally, more than one million misused prescription stimulants, 1.5 million misused tranquilizers, and 271,000 misused sedatives for the first time.

The reasons for the high prevalence of prescription drug misuse vary by age, gender, and other factors, but likely include ease of access.<sup>9</sup> The number of prescriptions for some of these medications has increased dramatically since the early 1990s.<sup>10</sup> Moreover, misinformation about the addictive properties of prescription opioids and the perception that prescription drugs are less harmful than illicit drugs are other possible contributors to the problem.<sup>11,12</sup> Although misuse of prescription drugs affects many Americans, certain populations such as youth and older adults may be at particular risk.<sup>13,14</sup>

## Adolescents and Young Adults

Misuse of prescription drugs is highest among young adults ages 18 to 25, with 14.4 percent reporting nonmedical use in the past year. Among youth ages 12 to 17, 4.9 percent reported past-year nonmedical use of prescription medications.<sup>16</sup>

After alcohol, marijuana, and tobacco, prescription drugs (taken nonmedically) are among the most commonly used drugs by 12<sup>th</sup> graders. NIDA's Monitoring the Future survey of substance use and attitudes in teens found that about 6 percent of high school seniors reported past-year nonmedical use of the

prescription stimulant Adderall® in 2017, and 2 percent reported misusing the opioid pain reliever Vicodin®.<sup>17</sup>

Although past-year nonmedical use of CNS depressants has remained fairly stable among 12<sup>th</sup> graders since 2012, use of prescription opioids has declined sharply. For example, past-year nonmedical use of Vicodin among 12<sup>th</sup> graders was reported by 9.6 percent in 2002 and declined to 2.0 percent in 2017. Nonmedical use of Adderall® increased between 2009 and 2013, but has been decreasing through 2017.<sup>17</sup> When asked how they obtained prescription stimulants for nonmedical use, around 60 percent of the adolescents and young adults surveyed said they either bought or received the drugs from a friend or relative.

Youth who misuse prescription medications are also more likely to report use of other drugs. Multiple studies have revealed associations between prescription drug misuse and higher rates of cigarette smoking; heavy episodic drinking; and marijuana, cocaine, and other illicit drug use among U.S. adolescents, young adults, and college students.<sup>18–21</sup> In the case of prescription opioids, receiving a legitimate prescription for these drugs during adolescence is also associated with a greater risk of future opioid misuse, particularly in young adults who have little to no history of drug use.<sup>14</sup>

## Older Adults



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More than 80 percent of older patients (ages 57 to 85 years) use at least one prescription medication on a daily basis, with more than 50 percent taking more than five medications or supplements daily.<sup>13</sup> This can potentially lead to health issues resulting from unintentionally using a prescription medication in a manner other than how it was prescribed, or from intentional nonmedical use. The high rates of multiple (comorbid) chronic illnesses in older populations, age-related changes in drug metabolism, and the potential for drug interactions make medication (and other substance) misuse more dangerous in older people than in younger populations.<sup>22</sup> Further, a large percentage of older adults also use over-the-counter medicines and dietary and herbal supplements, which could compound any adverse health consequences resulting from nonmedical use of prescription drugs.<sup>13</sup>

# Is it safe to use prescription drugs in combination with other medications?

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The safety of using prescription drugs in combination with other substances depends on a number of factors including the types of medications, dosages, other substance use (e.g., alcohol), and individual patient health factors. Patients should talk with their health care provider about whether they can safely use their prescription drugs with other substances, including prescription and over-the-counter (OTC) medications, as well as alcohol, tobacco, and illicit drugs. Specifically, drugs that slow down breathing rate, such as opioids, alcohol, antihistamines, CNS depressants, or general anesthetics, should not be taken together because these combinations increase the risk of life-threatening respiratory depression.<sup>4.26</sup> Stimulants should also not be used with other medications unless recommended by a physician. Patients should be aware of the dangers associated with mixing stimulants and OTC cold medicines that contain decongestants, as combining these substances may cause blood pressure to become dangerously high or lead to irregular heart rhythms.<sup>27</sup>

# What classes of prescription drugs are commonly misused?

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## Opioids

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### What are opioids?

Opioids are medications that act on opioid receptors in both the spinal cord and brain to reduce the intensity of pain-signal perception. They also affect brain areas that control emotion, which can further diminish the effects of painful stimuli. They have been used for centuries to treat pain, cough, and diarrhea.<sup>28</sup> The most common modern use of opioids is to treat acute pain. However, since the 1990s, they have been increasingly used to treat chronic pain, despite sparse evidence for their effectiveness when used long term.<sup>29</sup> Indeed, some patients experience a worsening of their pain or increased sensitivity to pain as a result of treatment with opioids, a phenomenon known as hyperalgesia.<sup>30</sup>

Importantly, in addition to relieving pain, opioids also activate reward regions in the brain causing the euphoria—or high—that underlies the potential for misuse and substance use disorder. Chemically, these medications are very similar to heroin, which was originally synthesized from morphine as a pharmaceutical in the late 19th century.<sup>31</sup> These properties confer an increased risk of substance use disorder even in patients who take their medication as prescribed.<sup>29</sup>

Overdose is another significant danger with opioids, because these compounds also interact with parts of the brain stem that control breathing. Taking too much of an opioid can suppress breathing enough that the user suffocates. An overdose can be reversed (and fatality prevented) if the compound *naloxone* is administered quickly (see "[Reversing an Opioid Overdose with Naloxone](#)").

Prescription opioid medications include hydrocodone (e.g., Vicodin<sup>®</sup>),



oxycodone (e.g., OxyContin<sup>®</sup>, Percocet<sup>®</sup>), oxymorphone (e.g., Opana<sup>®</sup>), morphine (e.g., Kadian<sup>®</sup>, Avinza<sup>®</sup>), codeine, fentanyl, and others. Hydrocodone products are the most commonly prescribed in the United States for a variety of indications, including dental- and injury-related pain.<sup>32</sup> Oxycodone and oxymorphone are also prescribed for moderate to severe pain relief.<sup>33,34</sup> Morphine is often used before and after surgical procedures to alleviate severe pain, and codeine is typically prescribed for milder pain.<sup>28</sup> In addition to their pain-relieving properties, some of these drugs—codeine and diphenoxylate (Lomotil<sup>®</sup>), for example—are used to relieve coughs and severe diarrhea.<sup>28</sup>

## How do opioids affect the brain and body?

Opioids act by attaching to and activating opioid receptor proteins, which are found on nerve cells in the brain, spinal cord, gastrointestinal tract, and other organs in the body.<sup>28</sup> When these drugs attach to their receptors, they inhibit the transmission of pain signals. Opioids can also produce drowsiness, mental confusion, nausea, constipation, and respiratory depression, and since these drugs also act on brain regions involved in reward, they can induce euphoria, particularly when they are taken at a higher-than-prescribed dose or administered in other ways than intended.<sup>28</sup> For example, OxyContin<sup>®</sup> is an oral medication used to treat moderate to severe pain through a slow, steady release of the opioid. Some people who misuse OxyContin<sup>®</sup> intensify their experience by snorting or injecting it.<sup>35</sup> This is a very dangerous practice, greatly increasing the person's risk for serious medical complications, including overdose

## **Understanding Dependence, Addiction, and Tolerance**

Dependence occurs as a result of physiological adaptations to chronic exposure to a drug. It is often a part of addiction, but they are not equivalent. Addiction involves other changes to brain circuitry and is distinguished by compulsive drug seeking and use despite negative consequences.<sup>36</sup>

Those who are dependent on a medication will experience unpleasant physical withdrawal symptoms when they abruptly reduce or stop use of the drug. These symptoms can be mild to severe (depending on the drug) and can usually be managed medically or avoided by slowly tapering down the drug dosage.<sup>37</sup>

Tolerance, or the need to take higher doses of a medication to get the same effect, often accompanies dependence. When tolerance occurs, it can be difficult for a physician to evaluate whether a patient is developing a drug problem or has a medical need for higher doses to control his or her symptoms. For this reason, physicians should be vigilant and attentive to their patients' symptoms and level of functioning and should screen for substance misuse when tolerance or dependence is present.<sup>29</sup>

**What are the possible consequences of prescription opioid misuse?**



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When taken as prescribed, patients can often use opioids to manage pain safely and effectively. However, it is possible to develop a substance use disorder when taking opioid medications as prescribed. This risk and the risk for overdose increase when these medications are misused. Even a single large dose of an opioid can cause severe respiratory depression (slowing or stopping of breathing), which can be fatal; taking opioids with alcohol or sedatives increases this risk.<sup>4,26</sup>

When properly managed, short-term medical use of opioid pain relievers—taken for a few days following oral surgery, for instance—rarely leads to an opioid use disorder or addiction. But regular (e.g., several times a day, for several weeks or more) or longer-term use of opioids can lead to dependence (physical discomfort when not taking the drug), tolerance (diminished effect from the original dose, leading to increasing the amount taken), and, in some cases, addiction (compulsive drug seeking and use) (see "[Understanding Dependence, Addiction, and Tolerance](#)"). With both dependence and addiction, withdrawal symptoms may occur if drug use is suddenly reduced or stopped. These symptoms may include restlessness, muscle and bone pain, insomnia, diarrhea, vomiting, cold flashes with goose bumps, and involuntary leg movements.<sup>31</sup>

Misuse of prescription opioids is also a risk factor for transitioning to heroin use. Read more about the relationship between prescription opioids and

heroin in NIDA's [Prescription Opioids and Heroin Research Report](#).

## How is prescription opioid misuse related to chronic pain?

Health care providers have long wrestled with how best to treat the more than 100 million Americans who suffer from chronic pain.<sup>38</sup> Opioids have been the most common treatment for chronic pain since the late 1990s, but recent research has cast doubt both on their safety and their efficacy in the treatment of chronic pain when it is not related to cancer or palliative care.<sup>29</sup> The potential risks involved with long-term opioid treatment, such as the development of drug tolerance, hyperalgesia, and addiction, present doctors with a dilemma, as there is limited research on alternative treatments for chronic pain. Patients themselves may even be reluctant to take an opioid medication prescribed to them for fear of becoming addicted.

Estimates of the rate of opioid misuse among chronic pain patients vary widely as a result of differences in treatment duration, insufficient research on long-term outcomes, disparate study populations, and different outcome measures (e.g., dependence versus OUD or addiction). One study assessing current criteria for OUD in a large number of chronic pain patients receiving opioids found that 28.1 percent had mild OUD, 9.7 percent had moderate OUD, and 3.5 percent had severe OUD (addiction).<sup>39</sup>

To mitigate addiction risk, physicians should adhere to the [CDC Guideline for Prescribing Opioids for Chronic Pain](#). Before prescribing, physicians should assess pain and functioning, consider if non-opioid treatment options are appropriate, discuss a treatment plan with the patient, evaluate the patient's risk of harm or misuse, and co-prescribe naloxone to mitigate the risk for overdose (see NIDA's webpage on [naloxone](#)). When first prescribing opioids, physicians should give the lowest effective dose for the shortest therapeutic duration. As treatment continues, the patient should be monitored at regular intervals, and opioid treatment should be continued only if meaningful clinical improvements in pain and functioning

are seen without harm.<sup>29</sup>

## CNS Depressants

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### What are CNS depressants?

CNS depressants, a category that includes tranquilizers, sedatives, and hypnotics, are substances that can slow brain activity. This property makes them useful for treating anxiety and sleep disorders. The following are among the medications commonly prescribed for these purposes<sup>40</sup>:

- **Benzodiazepines**, such as diazepam (Valium<sup>®</sup>), clonazepam (Klonopin<sup>®</sup>), and alprazolam (Xanax<sup>®</sup>), are sometimes prescribed to treat anxiety, acute stress reactions, and panic attacks. Clonazepam may also be prescribed to treat seizure disorders and insomnia. The more sedating benzodiazepines, such as triazolam (Halcion<sup>®</sup>) and estazolam (Prosom<sup>®</sup>) are prescribed for short-term treatment of sleep disorders. Usually, benzodiazepines are not prescribed for long-term use because of the high risk for developing tolerance, dependence, or addiction.
- **Non-benzodiazepine sleep medications**, such as zolpidem (Ambien<sup>®</sup>), eszopiclone (Lunesta<sup>®</sup>), and zaleplon (Sonata<sup>®</sup>), known as z-drugs, have a different chemical structure but act on the same GABA type A receptors in the brain as benzodiazepines. They are thought to have fewer side effects and less risk of dependence than benzodiazepines.
- **Barbiturates**, such as mephobarbital (Mebaral<sup>®</sup>), phenobarbital (Luminal<sup>®</sup>), and pentobarbital sodium (Nembutal<sup>®</sup>), are used less frequently to reduce anxiety or to help with sleep problems because of their higher risk of overdose compared to benzodiazepines. However, they are still used in surgical procedures and to treat seizure disorders.

### How do CNS depressants affect the brain and body?

Most CNS depressants act on the brain by increasing activity at receptors for the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). Although the different classes of CNS depressants work in unique ways, it is through their ability to increase GABA signaling—thereby increasing inhibition of brain activity—that they produce a drowsy or calming effect that is medically beneficial to those suffering from anxiety or sleep disorders.<sup>40</sup>

## What are the possible consequences of CNS depressant misuse?

Despite their beneficial therapeutic effects, benzodiazepines and barbiturates have the potential for misuse and should be used only as prescribed.<sup>40</sup> The use of non-benzodiazepine sleep aids, or z-drugs, is less well-studied, but certain indicators have raised concern about their misuse potential as well.<sup>41</sup>

During the first few days of taking a depressant, a person usually feels sleepy and uncoordinated, but as the body becomes accustomed to the effects of the drug and tolerance develops, these side effects begin to disappear. If one uses these drugs long term, he or she may need larger doses to achieve the therapeutic effects. Continued use can also lead to dependence and withdrawal when use is abruptly reduced or stopped (see "[Understanding Dependence, Addiction, and Tolerance](#)"). Because CNS depressants work by slowing the brain's activity, when an individual stops taking them, there can be a rebound effect, resulting in seizures or other harmful consequences.<sup>40</sup>

Although withdrawal from benzodiazepines can be problematic, it is rarely life threatening, whereas withdrawal from prolonged use of barbiturates can have life-threatening complications.<sup>42</sup> Therefore, someone who is thinking about discontinuing a CNS depressant or who is suffering withdrawal after discontinuing use should speak with a physician or seek immediate medical treatment.

## Stimulants

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### What are stimulants?

Stimulants increase alertness, attention, and energy, as well as elevate blood pressure, heart rate, and respiration. Historically, stimulants were used to treat asthma and other respiratory problems, obesity, neurological disorders, and a variety of other ailments. But as their potential for misuse and addiction became apparent, the number of conditions treated with stimulants has decreased.<sup>43</sup> Now, stimulants are prescribed for the treatment of only a few health conditions, including attention-deficit hyperactivity disorder (ADHD), narcolepsy, and occasionally treatment-resistant depression.<sup>44–46</sup>

### How do stimulants affect the brain and body?

Stimulants, such as dextroamphetamine (Dexedrine<sup>®</sup>, Adderall<sup>®</sup>) and methylphenidate (Ritalin<sup>®</sup>, Concerta<sup>®</sup>), act in the brain on the family of monoamine neurotransmitter systems, which include norepinephrine and dopamine. Stimulants enhance the effects of these chemicals. An increase in dopamine signaling from nonmedical use of stimulants can induce a feeling of euphoria, and these medications' effects on norepinephrine increase blood pressure and heart rate, constrict blood vessels, increase blood glucose, and open up breathing passages.<sup>47</sup>

### What are the possible consequences of stimulant misuse?

As with other drugs in the stimulant category, such as cocaine, it is possible for people to become dependent on or addicted to prescription stimulants. Withdrawal symptoms associated with discontinuing stimulant use include fatigue, depression, and disturbed sleep patterns. Repeated misuse of some stimulants (sometimes within a short period) can lead to feelings of hostility or paranoia, or even psychosis.<sup>31</sup> Further, taking high doses of a stimulant may result in dangerously high body temperature and an irregular heartbeat. There is also the potential for cardiovascular failure or

seizures.<sup>47</sup>

## Cognitive Enhancers

The dramatic increases in stimulant prescriptions over the last 2 decades have led to their greater availability and to increased risk for diversion and nonmedical use.<sup>48</sup> When taken to improve properly diagnosed conditions, these medications can greatly enhance a patient's quality of life. However, because many perceive them to be generally safe and effective, prescription stimulants such as Adderall® and Modafinil® are being misused more frequently.

Stimulants increase wakefulness, motivation, and aspects of cognition, learning, and memory. Some people take these drugs in the absence of medical need in an effort to enhance mental performance.<sup>49</sup> Militaries have long used stimulants to increase performance in the face of fatigue, and the United States Armed Forces allow for their use in limited operational settings.<sup>50</sup> The practice is now reported by some professionals to increase their productivity, by older people to offset declining cognition, and by both high school and college students to improve their academic performance.

Nonmedical use of stimulants for cognitive enhancement poses potential health risks, including addiction, cardiovascular events, and psychosis. The use of pharmaceuticals for cognitive enhancement has also sparked debate over the ethical implications of the practice. Issues of fairness arise if those with access and willingness to take these drugs have a performance edge over others, and implicit coercion takes place if a culture of cognitive enhancement gives the impression that a person must take drugs in order to be competitive.<sup>49,51</sup>



# Are prescription drugs safe to take when pregnant?

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Some prescription medications taken by a pregnant woman can cause her baby to develop dependence, which can result in withdrawal symptoms after birth, known as neonatal abstinence syndrome (NAS). This can require a prolonged stay in neonatal intensive care and, in the case of opioids, treatment with medication (see "[Sex and Gender Differences in Substance Use Disorder Treatment](#)" in NIDA's [Substance Use in Women Research Report](#)). Women should consult with their doctors to determine which medications they can continue taking during pregnancy.

Opioid pain medications require particular attention; rising rates of NAS have been associated with increases in the prescription of opioids for pain in pregnant women. NAS associated with opioid use (heroin or prescription opioids) increased fivefold from 2000 to 2012, with a higher rate of increase in

more recent years. [52.53](#)

# How can prescription drug misuse be prevented?

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## Clinicians, Patients, and Pharmacists

Physicians, their patients, and pharmacists all can play a role in identifying and preventing nonmedical use of prescription drugs.

**Clinicians.** More than 84 percent of Americans had contact with a health care professional in 2016<sup>54</sup>, placing doctors in a unique position to identify nonmedical use of prescription drugs and take measures to prevent the escalation of a patient's misuse to a substance use disorder. By asking about all drugs, physicians can help their patients recognize whether a problem exists, provide or refer them to appropriate treatment, and set recovery goals. Evidence-based screening tools for nonmedical use of prescription drugs can be incorporated into routine medical visits (see the [NIDAMED](#) webpage for resources for medical and health professionals). Doctors should also take note of rapid increases in the amount of medication needed or frequent, unscheduled refill requests. Doctors should be alert to the fact that those misusing prescription drugs may engage in "doctor shopping"—moving from provider to provider—in an effort to obtain multiple prescriptions for their drug(s) of choice.

Prescription drug monitoring programs (PDMPs), state-run electronic databases used to track the prescribing and dispensing of controlled prescription drugs to patients, are also important tools for preventing and identifying prescription drug misuse. While research regarding the impact of these programs is currently mixed, the use of PDMPs in some states has been associated with lower rates of opioid prescribing and overdose<sup>55–58</sup>, though issues of best practices, ease of use, and interoperability remain to be resolved.

In 2015, the federal government launched an initiative directed toward reducing opioid misuse and overdose, in part by promoting more cautious and responsible prescribing of opioid medications. In line with these efforts, in 2016 the Centers for Disease Control and Prevention (CDC) published its [CDC](#)

[Guideline for Prescribing Opioids for Chronic Pain](#) to establish clinical standards for balancing the benefits and risks of chronic opioid treatment.<sup>29</sup> Then, in 2017, President Trump established the President's Commission on Combating Drug Addiction and the Opioid Crisis. The commission outlined several priority areas aimed at improving the prevention and treatment of opioid addiction.

[Coordinated federal efforts](#) to reduce opioid addiction and overdose are ongoing.

Preventing or stopping nonmedical use of prescription drugs is an important part of patient care. However, certain patients can benefit from prescription stimulants, sedatives, or opioid pain relievers. Therefore, physicians should balance the legitimate medical needs of patients with the potential risk for misuse and related harms.

- **Patients.** Patients can take steps to ensure that they use prescription medications appropriately by:
  - following the directions as explained on the label or by the pharmacist
  - being aware of potential interactions with other drugs as well as alcohol
  - never stopping or changing a dosing regimen without first discussing it with the doctor
  - never using another person's prescription and never giving their prescription medications to others
  - storing prescription stimulants, sedatives, and opioids safely

Additionally, patients should properly discard unused or expired medications by following [U.S. Food and Drug Administration \(FDA\) guidelines](#) or visiting U.S. Drug Enforcement Administration collection sites.<sup>55</sup> In addition to describing their medical problem, patients should always inform their health care professionals about all the prescriptions, over-the-counter medicines, and dietary and herbal supplements they are taking before they obtain any other medications.



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- **Pharmacists.** Pharmacists can help patients understand instructions for taking their medications along with how the medication works for their condition. In addition, by being watchful for prescription falsifications or alterations, pharmacists can serve as the first line of defense in recognizing problematic patterns in prescription drug use. Some pharmacies have developed hotlines to alert other pharmacies in the region when they detect a fraudulent prescription. Along with physicians, pharmacists can use PDMPs to help track opioid-prescribing and dispensing patterns in patients.

## Medication Formulation and Regulation

Manufacturers of prescription drugs continue to work on new formulations of opioid medications, known as abuse-deterrent formulations (ADF), which include technologies designed to prevent people from misusing them by snorting or injection. Approaches currently being used or studied for use include:

- **physical or chemical barriers** that prevent the crushing, grinding, or dissolving of drug products
- **agonist/antagonist combinations** that cause an antagonist (which will counteract the drug effect) to be released if the product is manipulated
- **aversive substances** that are added to create unpleasant sensations if the drug is taken in a way other than directed
- **delivery systems** such as long-acting injections or implants that slowly release the drug over time
- **new molecular entities or prodrugs** that attach a chemical extension to a drug that renders it inactive unless it is taken orally

Several ADF opioids are on the market, and the FDA has also called for the development of ADF stimulants.<sup>56</sup> Abuse-deterrent formulations have been shown to decrease the illicit value of drugs.<sup>56</sup> Medication regulation has been shown to be effective in decreasing the prescribing of opioid medications. In 2014, the Drug Enforcement Administration moved hydrocodone products from schedule III to the more restrictive schedule II, which resulted in a decrease in hydrocodone prescribing that did not result in any attendant increases in the prescribing of other opioids.<sup>32</sup>

## Development of Safer Medications

The development of effective, non-addicting pain medications is a public health priority. A growing number of older adults and an increasing number of injured military service members add to the urgency of finding new treatments. Researchers are exploring alternative treatment approaches that target other signaling systems in the body such as the endocannabinoid system, which is also involved in pain.<sup>57</sup> More research is also needed to better understand effective chronic pain management, including identifying factors that predispose some patients to substance use disorders and developing measures to prevent the nonmedical use of prescription medications.

# How can prescription drug addiction be treated?

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Years of research have shown that substance use disorders are brain disorders that can be treated effectively. Treatment must take into account the type of drug used and the needs of the individual. Successful treatment may need to incorporate several components, including detoxification, counseling, and medications, when available. Multiple courses of treatment may be needed for the patient to make a full recovery.<sup>58</sup>

The two main categories of drug use disorder treatment are behavioral treatments (such as contingency management and cognitive-behavioral therapy) and medications. Behavioral treatments help patients stop drug use by changing unhealthy patterns of thinking and behavior; teaching strategies to manage cravings and avoid cues and situations that could lead to relapse; or, in some cases, providing incentives for abstinence. Behavioral treatments, which may take the form of individual, family, or group counseling, also can help patients improve their personal relationships and their ability to function at work and in the community.<sup>58</sup>

Addiction to prescription opioids can additionally be treated with medications including buprenorphine, methadone, and naltrexone (see "[Medications for Opioid Use Disorder](#)" below). These drugs can prevent other opioids from affecting the brain (naltrexone) or relieve withdrawal symptoms and cravings (buprenorphine and methadone), helping the patient avoid relapse. Medications for the treatment of opioid addiction are often administered in combination with psychosocial supports or behavioral treatments, known as medication-assisted treatment (MAT).<sup>59</sup> A medication to reduce the physical symptoms of withdrawal (lofexidine) is also available.

## Medications for Opioid Use Disorder

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Methadone is a synthetic opioid agonist that prevents withdrawal symptoms and relieves drug cravings. It works by acting on the same mu-

opioid receptors as other opioids such as heroin, morphine, and opioid pain medications but at less intensity and for longer duration. Methadone has been used successfully for more than 40 years to treat heroin addiction but is generally only available through specially licensed opioid treatment programs.

Buprenorphine is a partial opioid agonist—it binds to the mu-opioid receptor but only partially activates it—and can be prescribed by certified physicians, nurse practitioners, and physician assistants in an office setting. Like methadone, it can reduce cravings and is well tolerated by patients. In 2016, the U.S. Food and Drug Administration (FDA) approved the NIDA-supported development of an implantable formulation of buprenorphine that provides 6 months of sustained medication delivery; and in 2017, a month-long injectable formulation was approved. These formulations eliminate the need for daily dosing and will give patients greater ease in treatment adherence, especially if they live far from their treatment provider.

There has been a popular misconception that methadone and buprenorphine replace one addiction with another. This is not the case. In people addicted to opioids, these drugs do not produce a high but simply prevent withdrawal and craving so that they can function in life and engage with treatment while balance is restored to brain circuits that have been affected by their disorder.

Naltrexone is another type of medication, an antagonist, which prevents other opioids from binding to and activating opioid receptors. An injectable, long-acting form of naltrexone (Vivitrol®) can be a useful treatment choice for patients who do not have ready access to health care or who struggle with taking their medications regularly.

While medications are the standard of care for treating opioid use disorder, far fewer people receive medications than could potentially benefit from it. Not all people with opioid use disorder seek treatment. Even when they seek treatment, they will not necessarily receive medications. The most recent treatment admissions data available show that only 21 percent of



people admitted for prescription opioid use disorder have a treatment plan that includes medications.<sup>60</sup> However, even if the nationwide infrastructure were operating at capacity, between 1.3 and 1.4 million more people have opioid use disorder than could currently be treated with medications; this is due to limited availability of opioid treatment programs that can dispense methadone and the regulatory limit on the number of patients that physicians can treat with buprenorphine.<sup>61</sup> Coordinated efforts are underway nationwide to expand access to opioid use disorder medications, including a recent increase in the buprenorphine patient limit from 100 patients to 275 for qualified physicians who request the higher limit.<sup>62</sup>

NIDA is supporting research needed to determine the most effective ways to implement medications for opioid use disorder. For example, recent work has shown that buprenorphine maintenance treatment is more effective than tapering patients off of buprenorphine.<sup>63</sup> Also, starting buprenorphine treatment when a patient is admitted to the emergency department, such as for an overdose, is a more effective way to engage a patient in treatment than referral or brief intervention.<sup>64</sup> Finally, data have shown that treatment with methadone, buprenorphine, or naltrexone for incarcerated individuals improves post-release outcomes.<sup>65–67</sup>

For more information on medications to treat opioid use disorder, see NIDA's [Medications to Treat Opioid Use Disorder Research Report](#).

## **Reversing an Opioid Overdose with Naloxone**

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The opioid overdose-reversal drug naloxone is an opioid antagonist that can rapidly restore normal respiration to a person who has stopped breathing as a result of overdose on prescription opioids or heroin. Naloxone can be used by emergency medical personnel, first responders, and bystanders. For more information, visit NIDA's webpage on [naloxone](#).

## Treating Addiction to CNS Depressants

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Patients addicted to CNS depressants such as tranquilizers, sedatives, and hypnotics should not attempt to stop taking them on their own. Withdrawal symptoms from these drugs can be severe and, in the case of certain medications, potentially life-threatening.<sup>31</sup> Research on treating addiction to CNS depressants is sparse; however, patients who are dependent on these medications should undergo medically supervised detoxification because the dosage they take should be tapered gradually. Inpatient or outpatient counseling can help individuals through this process. Cognitive-behavioral therapy, which focuses on modifying the patient's thinking, expectations, and behaviors while increasing skills for coping with various life stressors, has also been used successfully to help individuals adapt to discontinuing benzodiazepines.<sup>68</sup>

Often CNS depressant misuse occurs in conjunction with the use of other drugs (polydrug use), such as alcohol or opioids.<sup>69</sup> In such cases, the treatment approach should address the multiple addictions.

At this time, there are no FDA-approved medications for treating addiction to CNS depressants, though research is ongoing in this area.

## Treating Addiction to Prescription Stimulants

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Treatment of addiction to prescription stimulants such as Adderall<sup>®</sup> and Concerta<sup>®</sup> is based on behavioral therapies that are effective for treating cocaine and methamphetamine addiction. At this time, there are no FDA-approved medications for treating stimulant addiction. NIDA is supporting research in this area.<sup>41</sup>

Depending on the patient, the first steps in treating prescription stimulant addiction may be to taper the drug dosage and attempt to ease withdrawal symptoms. Behavioral treatment may then follow the detoxification process (see "[Behavioral Therapies](#)" in NIDA's [Principles of Drug Addiction Treatment: A Research-Based Guide](#)).

# Where can I get further information about prescription drug misuse?

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To learn more about prescription drugs and other drugs, visit the NIDA website at [drugabuse.gov](http://drugabuse.gov) or contact the *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).

## The NIDA's website includes:

- information on drugs and related health consequences
- NIDA publications, news, and events
- resources for health care professionals
- funding information (including program announcements and deadlines)
- international activities
- links to related websites (access to websites of many other organizations in the field)
- information in Spanish (en español)

## NIDA websites and webpages

- [drugabuse.gov](http://drugabuse.gov)
- [teens.drugabuse.gov](http://teens.drugabuse.gov)
- [easyread.drugabuse.gov](http://easyread.drugabuse.gov)
- [drugabuse.gov/drugs-abuse/prescription-drugs-cold-medicines](http://drugabuse.gov/drugs-abuse/prescription-drugs-cold-medicines)
- [researchstudies.drugabuse.gov](http://researchstudies.drugabuse.gov)
- [irp.drugabuse.gov](http://irp.drugabuse.gov)

## For physician information

- NIDAMED: [drugabuse.gov/nidamed](http://drugabuse.gov/nidamed)

## Other websites

Information about prescription drug misuse is also available through the following websites:

- Substance Abuse and Mental Health Services Administration: [samhsa.gov](http://samhsa.gov)
- U.S. Drug Enforcement Administration: [dea.gov](http://dea.gov)
- Monitoring the Future: [monitoringthefuture.org](http://monitoringthefuture.org)
- Partnership for Drug-Free Kids: [drugfree.org/drug-guide](http://drugfree.org/drug-guide)

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# References

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1. Blanco C, Alderson D, Ogburn E, et al. Changes in the prevalence of non-medical prescription drug use and drug use disorders in the United States: 1991-1992 and 2001-2002. *Drug Alcohol Depend.* 2007;90(2-3):252-260. doi:10.1016/j.drugalcdep.2007.04.005
2. Center for Behavioral Health Statistics and Quality. *Treatment Episode Data Set (TEDS): 2003-2013. National Admissions to Substance Abuse Treatment Services.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2015.  
[http://www.samhsa.gov/data/sites/default/files/2013\\_Treatment\\_Episode\\_Data\\_Set\\_Na](http://www.samhsa.gov/data/sites/default/files/2013_Treatment_Episode_Data_Set_Na)
3. Center for Behavioral Health Statistics and Quality. *Drug Abuse Warning Network: 2011: Selected Tables of National Estimates of Drug-Related Emergency Department Visits.* Rockville, MD: Substance Abuse and Mental Health Services Administration
4. Jones CM, McAninch JK. Emergency Department Visits and Overdose Deaths From Combined Use of Opioids and Benzodiazepines. *Am J Prev Med.* 2015;49(4):493-501. doi:10.1016/j.amepre.2015.03.040
5. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. *Increases in Drug and Opioid Overdose Deaths—United States, 2000–2014.* Centers for Disease Control and Prevention; 2016.  
[https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm?s\\_cid=mm6450a3\\_w](https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm?s_cid=mm6450a3_w). Accessed November 7, 2017.
6. Centers for Disease Control and Prevention. Prescription Opioid Data. <https://www.cdc.gov/drugoverdose/data/prescribing.html>. Published August 31, 2018. Accessed September 18, 2018.
7. Center for Behavioral Health Statistics and Quality. *Results from the 2017 National Survey on Drug Use and Health: Detailed Tables.* Rockville (MD): SAMHSA; 2018. <https://www.samhsa.gov/data/report/2017-nsduh-detailed-tables>. Accessed October 19, 2018.
8. Centers for Disease Control and Prevention. Vital Signs: Overdoses of Prescription Opioid Pain Relievers --- United States, 1999--2008. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6043a4.htm>. Accessed

September 18, 2018.

9. Manchikanti L, Fellows B, Ailinani H, Pampati V. Therapeutic use, abuse, and nonmedical use of opioids: a ten-year perspective. *Pain Physician*. 2010;13(5):401-435.
10. Daniulaityte R, Falck R, Carlson RG. "I'm not afraid of those ones just 'cause they've been prescribed": Perceptions of risk among illicit users of pharmaceutical opioids. *Int J Drug Policy*. 2012;23(5):374-384. doi:10.1016/j.drugpo.2012.01.012
11. Webster PC. Oxycodone class action lawsuit filed. *CMAJ Can Med Assoc J*. 2012;184(7):E345-E346. doi:10.1503/cmaj.109-4158
12. Qato DM, Alexander GC, Conti RM, Johnson M, Schumm P, Lindau ST. Use of Prescription and Over-the-counter Medications and Dietary Supplements Among Older Adults in the United States. *JAMA*. 2008;300(24):2867. doi:10.1001/jama.2008.892
13. Miech R, Johnston L, O'Malley PM, Keyes KM, Heard K. Prescription Opioids in Adolescence and Future Opioid Misuse. *Pediatrics*. 2015;136(5):e1169-e1177. doi:10.1542/peds.2015-1364
14. Mack KA, Jones CM, Paulozzi LJ. *Vital Signs: Overdoses of Prescription Opioid Pain Relievers and Other Drugs Among Women—United States, 1999–2010.*; 2013:537-542. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6226a3.htm>. Accessed January 31, 2018.
15. Center for Behavioral Health Statistics and Quality. *Results from the 2017 National Survey on Drug Use and Health: Detailed Tables*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2018.
16. Miech R, Schulenberg J, Johnston L, Bachman J, O'Malley P, Patrick M. *Monitoring the Future National Adolescent Drug Trends in 2017: Findings Released*. Ann Arbor, MI: Institute for Social Research, The University of Michigan; 2017. <http://www.monitoringthefuture.org/pressreleases/17drugpr.pdf>. Accessed January 2, 2018.
17. McCabe SE, West BT, Teter CJ, Boyd CJ. Medical and nonmedical use of prescription opioids among high school seniors in the United States. *Arch*

*Pediatr Adolesc Med.* 2012;166(9):797-802.

doi:10.1001/archpediatrics.2012.85

18. Boyd CJ, Esteban S, Teter CJ. Medical and nonmedical use of prescription pain medication by youth in a Detroit-area public school district. *Drug Alcohol Depend.* 2006;81(1):37-45. doi:10.1016/j.drugalcdep.2005.05.017
19. McCabe SE, Teter CJ, Boyd CJ. Illicit use of prescription pain medication among college students. *Drug Alcohol Depend.* 2005;77(1):37-47. doi:10.1016/j.drugalcdep.2004.07.005
20. Young AM, Glover N, Havens JR. Nonmedical use of prescription medications among adolescents in the United States: a systematic review. *J Adolesc Health Off Publ Soc Adolesc Med.* 2012;51(1):6-17. doi:10.1016/j.jadohealth.2012.01.011
21. Wang R, Chen L, Fan L, et al. Incidence and Effects of Polypharmacy on Clinical Outcome among Patients Aged 80+: A Five-Year Follow-Up Study. *PloS One.* 2015;10(11):e0142123. doi:10.1371/journal.pone.0142123
22. Cotto JH, Davis E, Dowling GJ, Elcano JC, Staton AB, Weiss SRB. Gender effects on drug use, abuse, and dependence: a special analysis of results from the National Survey on Drug Use and Health. *Gen Med.* 2010;7(5):402-413. doi:10.1016/j.genm.2010.09.004
23. CDC Vital Signs: Prescription Painkiller Overdoses: A growing epidemic, especially among women. Centers for Disease Control and Prevention. <http://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/index.html>. Published March 23, 2017. Accessed March 27, 2017.
24. Ronan MV, Herzig SJ. Hospitalizations Related To Opioid Abuse/Dependence And Associated Serious Infections Increased Sharply, 2002-12. *Health Aff Proj Hope.* 2016;35(5):832-837. doi:10.1377/hlthaff.2015.1424
25. Jones CM, Paulozzi LJ, Mack KA. *Alcohol Involvement in Opioid Pain Reliever and Benzodiazepine Drug Abuse—Related Emergency Department Visits and Drug-Related Deaths—United States, 2010.* <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6340a1.htm>. Accessed September 18, 2018.
26. Pentel P. Toxicity of Over-the-Counter Stimulants. *JAMA.*



1984;252(14):1898-1903.

27. Gutstein H, Akil H. Opioid Analgesics. In: *Goodman & Gilman's the Pharmacological Basis of Therapeutics*. 11th ed. McGraw-Hill; 2006:547-590.
28. Dowell D, Haegerich TM, Chou R. *CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016.*; 2016.  
<https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm>. Accessed September 18, 2018.
29. Lee M, Silverman SM, Hansen H, Patel VB, Manchikanti L. A comprehensive review of opioid-induced hyperalgesia. *Pain Physician*. 2011;14(2):145-161.
30. Hart C, Ksir C. *Drugs, Society, and Human Behavior*. 15 edition. New York, NY: McGraw-Hill Education; 2012.
31. Jones CM, Lurie PG, Throckmorton DC. Effect of US Drug Enforcement Administration's Rescheduling of Hydrocodone Combination Analgesic Products on Opioid Analgesic Prescribing. *JAMA Intern Med*. 2016;176(3):399-402. doi:10.1001/jamainternmed.2015.7799
32. Oxycodone: MedlinePlus Drug Information.  
<https://medlineplus.gov/druginfo/meds/a682132.html>. Accessed September 18, 2018.
33. Oxymorphone: MedlinePlus Drug Information.  
<https://medlineplus.gov/druginfo/meds/a610022.html>. Accessed September 18, 2018.
34. Cicero TJ, Ellis MS. Abuse-Deterrent Formulations and the Prescription Opioid Abuse Epidemic in the United States: Lessons Learned From OxyContin. *JAMA Psychiatry*. 2015;72(5):424-430.  
doi:10.1001/jamapsychiatry.2014.3043
35. O'Brien CP, Dackis C. Principles of the Pharmacotherapy of Addictive Disorders. In: *Neurobiology of Mental Illness*. Third. Oxford University Press; 2006.
36. O'Brien CP. Drug Addiction and Drug Abuse. In: *Goodman & Gilman's the Pharmacological Basis of Therapeutics*. 11th ed. McGraw-Hill; 2006:607-

37. Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington (DC): National Academies Press (US); 2011.  
<http://www.ncbi.nlm.nih.gov/books/NBK91497/>.
38. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. *Ann Intern Med*. 2015;162(4):276-286. doi:10.7326/M14-2559
39. Hypnotics and Sedatives. In: *Goodman & Gilman's the Pharmacological Basis of Therapeutics*. 11th ed. McGraw-Hill; 2006.
40. Gunja N. The clinical and forensic toxicology of Z-drugs. *J Med Toxicol Off J Am Coll Med Toxicol*. 2013;9(2):155-162. doi:10.1007/s13181-013-0292-0
41. Sellers EM. Alcohol, barbiturate and benzodiazepine withdrawal syndromes: clinical management. *CMAJ Can Med Assoc J*. 1988;139(2):113-120.
42. Ciccarone D. Stimulant Abuse: Pharmacology, Cocaine, Methamphetamine, Treatment, Attempts at Pharmacotherapy.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3056348/>. Accessed September 18, 2018.
43. Scammell TE. Narcolepsy. *N Engl J Med*. 2015;373(27):2654-2662. doi:10.1056/NEJMra1500587
44. Santosh PJ, Sattar S, Canagaratnam M. Efficacy and tolerability of pharmacotherapies for attention-deficit hyperactivity disorder in adults. *CNS Drugs*. 2011;25(9):737-763. doi:10.2165/11593070-000000000-00000
45. Corp SA, Gitlin MJ, Altshuler LL. A review of the use of stimulants and stimulant alternatives in treating bipolar depression and major depressive disorder. *J Clin Psychiatry*. 2014;75(9):1010-1018. doi:10.4088/JCP.13r08851
46. Westfall T, Westfall D. Adrenergic Agonists and Antagonists. In: *Goodman & Gilman's the Pharmacological Basis of Therapeutics*. Vol 11. McGraw-Hill;

2006:237-295.

47. McCabe SE, West BT. Medical and Nonmedical Use of Prescription Stimulants: Results From a National Multicohort Study. *J Am Acad Child Adolesc Psychiatry*. 2013;52(12):1272-1280. doi:10.1016/j.jaac.2013.09.005
48. Schelle KJ, Faulmuller N, Caviola L, Hewstone M. Attitudes toward pharmacological cognitive enhancement—a review. *Front Syst Neurosci*. 2014;8. doi:10.3389/fnsys.2014.00053
49. Caldwell JA, Caldwell JL. Fatigue in military aviation: an overview of US military-approved pharmacological countermeasures. *Aviat Space Environ Med*. 2005;76(7 Suppl):C39-C51.
50. Hyman SE. Cognitive Enhancement: Promises and Perils. *Neuron*. 2011;69(4):595-598. doi:10.1016/j.neuron.2011.02.012
51. Tolia VN, Patrick SW, Bennett MM, et al. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. *N Engl J Med*. 2015;372(22):2118-2126. doi:10.1056/NEJMsa1500439
52. Patrick SW, Davis MM, Lehmann CU, Cooper WO. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. *J Perinatol Off J Calif Perinat Assoc*. 2015;35(8):650-655. doi:10.1038/jp.2015.36
53. National Center for Health Statistics. Ambulatory Care Use and Physician Office Visits.
54. Center for Drug Evaluation and Research. Safe Disposal of Medicines—Disposal of Unused Medicines: What You Should Know. <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely>. Accessed September 18, 2018.
55. Simon K, Worthy SL, Barnes MC, Tarbell B. Abuse-deterrent formulations: transitioning the pharmaceutical market to improve public health and safety. *Ther Adv Drug Saf*. 2015;6(2):67-79. doi:10.1177/2042098615569726
56. Maldonado R, Baños JE, Cabañero D. The endocannabinoid system and neuropathic pain. *Pain*. 2016;157 Suppl 1:S23-S32. doi:10.1097/j.pain.0000000000000428

57. National Institute on Drug Abuse. *Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition)*. Bethesda, MD: National Institutes of Health; 2012. <https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/principles-effective-treatment>. Accessed January 31, 2018.
58. Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-assisted therapies—tackling the opioid-overdose epidemic. *N Engl J Med*. 2014;370(22):2063-2066. doi:10.1056/NEJMp1402780
59. Center for Behavioral Health Statistics and Quality. *Treatment Episode Data Set (TEDS) 2002 - 2012: National Admissions to Substance Abuse Treatment Services*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014. [http://www.samhsa.gov/data/sites/default/files/TEDS2012N\\_Web.pdf](http://www.samhsa.gov/data/sites/default/files/TEDS2012N_Web.pdf).
60. Jones CM, Campopiano M, Baldwin G, McCance-Katz E. National and state treatment need and capacity for opioid agonist medication-assisted treatment. *Am J Public Health*. 2015;105(8):e55-e63. doi:10.2105/AJPH.2015.302664
61. Obama Administration Takes More Actions to Address the Prescription Opioid and Heroin Epidemic. <https://obamawhitehouse.archives.gov/the-press-office/2016/07/05/obama-administration-takes-more-actions-address-prescription-opioid-and>.
62. Fiellin DA, Schottenfeld RS, Cutter CJ, Moore BA, Barry DT, O'Connor PG. Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence: a randomized clinical trial. *JAMA Intern Med*. 2014;174(12):1947-1954. doi:10.1001/jamainternmed.2014.5302
63. D'Onofrio G, O'Connor PG, Pantalon MV, et al. Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: a randomized clinical trial. *JAMA*. 2015;313(16):1636-1644. doi:10.1001/jama.2015.3474
64. Gordon MS, Kinlock TW, Schwartz RP, Fitzgerald TT, O'Grady KE, Vocci FJ. A randomized controlled trial of prison-initiated buprenorphine: prison outcomes and community treatment entry. *Drug Alcohol Depend*. 2014;142:33-40. doi:10.1016/j.drugalcdep.2014.05.011
65. Kinlock TW, Gordon MS, Schwartz RP, O'Grady K, Fitzgerald TT, Wilson M.

A randomized clinical trial of methadone maintenance for prisoners: results at 1-month post-release. *Drug Alcohol Depend.* 2007;91(2-3):220-227. doi:10.1016/j.drugalcdep.2007.05.022

66. Lee JD, Friedmann PD, Kinlock TW, et al. Extended-Release Naltrexone to Prevent Opioid Relapse in Criminal Justice Offenders. *N Engl J Med.* 2016;374(13):1232-1242. doi:10.1056/NEJMoa1505409
67. Darker C, Sweeney B, Barry J, Farrell MF, Donnelly-Swift E. Psychosocial interventions to reduce sedative use, abuse and dependence. *Cochrane Database Syst Rev.* /CD009652/ADDICTN\_psychosocial-interventions-to-reduce-sedative-use-abuse-and-dependence. Accessed September 18, 2018.
68. Jones JD, Mogali S, Comer SD. Polydrug abuse: a review of opioid and benzodiazepine combination use. *Drug Alcohol Depend.* 2012;125(1-2):8-18. doi:10.1016/j.drugalcdep.2012.07.004