# Title: NIDA-NIH

### Learn more from the National Institute on Drug Abuse:
**https://nida.nih.gov/research-topics/opioids#opioid-use-disorder**

## What are opioids?

Opioids are a class of natural, semi-synthetic, and synthetic drugs that include both prescription medications and illegal drugs like heroin. Prescription medications such as oxycodone (OxyContin®), hydrocodone (Vicodin®), morphine, codeine, fentanyl, and others are mainly used for the treatment of pain. They can also help treat cough or diarrhea. However, like illegal opioids, prescription opioids can be addictive, particularly if they are misused.

**Natural opioids**, such as morphine, codeine, opium, and thebaine are made from the seed pods of the opium poppy plant. These natural substances are also known as opiates.

**Semi-synthetic opioids**, such as heroin and the pain relievers oxycodone, hydrocodone, and oxymorphone, are made in laboratories by chemically processing natural opioids.

**Synthetic opioids,** such as fentanyl are manufactured entirely in laboratories, with no natural ingredients.[1]

Opioids differ in their strength, or potency. For example, fentanyl is 50 to 100 times more potent than morphine.[2] This means that even small doses of fentanyl can be fatal. Fentanyl can be even more dangerous when it is mixed with other drugs. This can happen without the knowledge of the person taking them.[3]

How do opioids work?

After they are taken, opioids enter the bloodstream and travel through the body and to the brain. They bind to specific molecules called opioid receptors on certain nerve cells in the brain, the spinal cord, and throughout the body.[4,5]

These receptors normally interact with naturally occurring molecules in the body to regulate essential functions. They help control pain, regulate breathing (respiration), and help with stress responses.[6] For example, opioid receptors are found on nerve cells that send pain signals from the body to the brain. When opioid drugs bind to these receptors, they trigger changes in nerve cells that can stop the transmission of pain signals in the spinal cord. They also dull the perception of pain in the brain.[5] That's why opioids are effective pain medications.

Additionally, opioid receptors are found in brain regions collectively called the reward system. The body's own opioid-like signaling molecules bind to those receptors. In response to natural rewards, such as food and social interactions, they trigger brain processes that make us feel good and make us want to repeat the healthy behaviors that help us survive.[7]

# How do opioids make people feel?

The main effects of opioids are pain relief and feelings of happiness and relaxation. They can also cause changes in thinking, including difficulty concentrating or making decisions.[7] How soon these effects begin depends on the opioid used and how it is taken. For example, fentanyl acts faster than morphine, and opioids act faster when injected or inhaled than when taken by mouth.[8]

Taking too a high a dose of opioids, or taking opioids over longer periods of time, can lead to harmful or even deadly effects. See, "What are the health risks of using opioids?"

What are the health risks of using opioids?

**Opioids are addictive.** People can quickly lose control over their opioid use and need to keep using them to feel "normal."

**High doses can lead to overdose.** Opioids can slow breathing to life-threatening levels. As a result, not enough oxygen reaches the brain. This can cause severe brain damage or death.[6] This is what happens during an opioid overdose.

**Opioid use, even as prescribed by a health care provider or only for a short time, can lead to negative health effects.**

- Opioid medications may have unpleasant effects, particularly when people take them for a longer time. These include constipation, nausea and vomiting, headache, dizziness, and sleepiness or sleep problems.[8,9]
- Depending on the dose and how long people use them, opioids can cause cardiovascular changes, such as slower heart rate, low blood pressure, heart failure, and cardiac arrest.[10]
- Opioids can impair the immune system, increasing risk of infection.[11]
- Opioid use, particularly in high doses or for a long period of time, can cause changes in a person's body that can actually make them more sensitive to pain.[12,13]

- Opioid use also has been associated with mental disorders like depression or sexual dysfunction.[15,16,17]

When using opioids to treat acute or chronic pain, these potential risks may need to be weighed against the health risks associated with untreated or under-treated pain.[18]

**People who inject opioids are at an increased risk of diseases caused by viruses such as hepatitis C or human immunodeficiency virus (HIV).** They also may develop bacterial infections that cause inflammation of the heart's inner lining (endocarditis).[10]

**Taking opioids with other drugs raises the likelihood of harm.** Health risks associated with opioids, including risk of overdose, can be even greater when a person uses more than one drug.[19]

**Fentanyl is often added to illicit drugs and illegally manufactured counterfeit pills.** These pills may look exactly like prescription medications such as oxycodone or benzodiazepines, but really contain fentanyl. Deadly doses of illicit fentanyl can also be mixed into or sold as other drugs, such as heroin or cocaine.[3,20,21]

What is an overdose?

An opioid overdose occurs when a person takes a higher drug dose than their body can handle. Opioids affect the brain centers that control breathing. When a person takes a high dose of an opioid, breathing can slow to life-threatening levels.[6]

Several signs can indicate that a person is experiencing an overdose and requires immediate medical attention:

- Unconsciousness or inability to wake up.
- Slow or shallow breathing or difficulty breathing.
- Discolored, purplish skin, especially the nails or lips.
- Small, constricted "pinpoint" pupils that don't react to light.

People can overdose without knowing that they have taken dangerously high opioid doses. For example, deadly doses of illicit fentanyl can be mixed into or sold as other drugs, such as heroin, cocaine, or counterfeit pills.[3,20,21]

What should I do if I think someone is overdosing?

- If you suspect someone is overdosing, **call 911**.
- Use naloxone (e.g., Narcan®, Kloxxado®, Zimhi®, RiVive®) or nalmefene (Opvee®) if it is available. These overdose reversal medications are life-saving tools that can be

given to anyone who is, or may be, experiencing an opioid overdose. Naloxone and nalmefene are available as nasal sprays and can be carried and administered by anyone. Naloxone is available over the counter, without a prescription.

- Try to keep the person awake and breathing.
- For more information, see, "What to Do if You Think Someone is Overdosing" on the U.S. Centers for Disease Control and Prevention (CDC) website.

## Opioids and the overdose crisis

Opioids are involved in the majority of deaths in the drug overdose crisis in the United States. However, the types of opioids involved have changed over time.

- Misuse of prescription opioids led to the first opioid public health crisis starting in the 1990s.[22]
- Beginning in 2010, overdose deaths increasingly involved heroin.[23,24]
- A third wave, driven by illegally produced synthetic opioids such as fentanyl, started in 2013.[24]
- Overdose deaths often involve multiple drugs, and people are often not aware that illegal drugs contain hidden ingredients. For example, stimulants like cocaine and methamphetamine are often sold mixed with opioids, including fentanyl.[25,26] In recent years, more than half of people who died from an overdose after taking fentanyl had taken a stimulant such as methamphetamine.[27] Heroin or counterfeit prescription pills may also contain fentanyl.[3]
- Overdose deaths among adolescents have risen sharply in recent years because more counterfeit pills contain fentanyl.[28,3]
- The veterinary tranquilizer xylazine—"tranq"—is increasingly involved in overdose deaths. It is typically found in combination with other drugs, such as illicitly manufactured fentanyl.[29,30]
- New psychoactive substances and designer drugs have become more common in recent years and may be added to other drugs without a buyer knowing it. These emerging drugs may also contribute to the overdose crisis.
- Overdose deaths may also involve the intentional use of multiple drugs.[31] Taking more than one drug at once increases the risk of overdose because the combined effects are often stronger and more unpredictable.[19]

## Are opioids addictive?

Yes, opioids are addictive. Opioids promote brain activity that can lead to changes in mood and thinking, including making people feel happy and relaxed.[7] A person may keep taking opioids to try to repeat that experience. However, repeated use can cause brain changes that motivate a person to continue using opioids, even if they experience harmful effects.[7,24]

- Repeated opioid use can also lead to **dependence**, where a person's body adapts to the presence of the opioid. As a result of dependence, the body can only function normally when taking the drug. Dependence makes it harder to quit using drugs.
- If a person stops taking an opioid, they may experience **withdrawal** symptoms such as muscle aches, abdominal cramps, agitation, anxiety, nausea and vomiting, chills, diarrhea, and more.[32,33] People may continue to use opioids to avoid withdrawal symptoms.
- When a person's body adapts to a drug, it also may respond less and less to the drug. This is known as **tolerance**. As a result, a person may need to take a larger opioid dose or take it more often to achieve the same effects. This puts them at greater risk of negative health effects.[34] This can also occur with prescription opioids, even when taken as prescribed by a health care provider.

Health professionals look at a person's withdrawal symptoms and tolerance level, among other factors, to determine if a person has an opioid addiction—a severe opioid use disorder.

## What is opioid use disorder?

Opioid use disorder is a complex, chronic, and treatable medical condition. A person who has been diagnosed with opioid use disorder or another substance use disorder has a pattern of two or more symptoms and behaviors related to their substance use.
The *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5)—a reference text professionals use to diagnose substance use disorders—lists these as:[35]

- Consuming the drug in larger amounts or for longer than intended.
- Persistently wanting to cut down or regulate drug use.
- Spending a great deal of time obtaining, using, or recovering from the effects of the drug.
- Experiencing a strong desire to use the drug (craving).

- Failing to fulfill major obligations at work, school, or home because of drug use.
- Continuing drug use even if it causes significant social or interpersonal problems.
- Reducing or stopping other activities because of drug use.
- Repeatedly using the drug in situations when it is unsafe.
- Continuing drug use even when knowing that it causes physical or psychological problems.
- Developing tolerance.
- Experiencing withdrawal symptoms when stopping drug use.

In 2023, about 5.7 million people in the United States had opioid use disorder.[36]

Treating opioid use disorder

Opioid use disorder is a treatable chronic medical condition. Treatment options include medications and behavioral therapy.

**Medications** are the standard of care for opioid use disorder.[37] Medications approved by the U.S. Food and Drug Administration include methadone, buprenorphine, and naltrexone. Research has shown these medications can reduce the risk of return to drug use and of overdose death. They help people remain in treatment and live a normal life.[38]

The medication lofexidine has been approved for treatment of withdrawal symptoms. It has been shown to reduce craving and risk of return to drug use.[39,40]

**Behavioral therapy** for opioid use disorder is most effective when offered with medication therapy. Various types of behavioral therapy can help people stay on medication treatment. These treatments also can address problems that are not treated with these medications, such as coexisting mental health problems.[41]

Opioid use during pregnancy

Opioid use and untreated opioid use disorder during pregnancy can harm the health of both a pregnant person and their baby.[42]

**Pregnant people** with untreated opioid use disorder who do not receive appropriate prenatal care are at increased risk of serious and potentially fatal pregnancy complications.

**Babies** exposed to opioids before birth have a higher risk of health problems that include premature birth and low birth weight. They also may experience withdrawal symptoms after

birth, such as irritability, crying, tremors, or poor feeding. This is known as neonatal opioid withdrawal syndrome (NOWS).[43]

Medications to treat opioid use disorder during pregnancy

Medications for opioid use disorder are safe and effective for pregnant people. Treatment helps prevent opioid withdrawal symptoms and reduces the risk of returning to opioid use. Medications also help a pregnant person to get prenatal care and stay in addiction treatment programs, leading to better pregnancy outcomes for both a pregnant person and their baby.[44]

Breastfeeding is safe for people taking medications for opioid use disorder and their infants. Breastfeeding helps mother and infant to bond, and it can lessen the severity of neonatal opioid withdrawal syndrome and improve a baby's health outcomes. Breast milk contains only minimal amounts of the medications for opioid use disorder that a person may be taking.[45,44]

NIDA supports research on opioids and the overdose crisis

NIDA is funding hundreds of research projects with the goal of finding scientific solutions to help end the opioid and overdose crisis. Studies seek to understand how opioids affect the brain and body and influence our behavior. Researchers are also looking for better ways to prevent and treat opioid misuse, opioid use disorder, and overdose; reduce associated harms; and help people recover.

NIDA plays a leading role in the National Institutes of Health HEAL (Helping to End Addiction Long-term®) Initiative, an effort to develop new scientific solutions to the overdose epidemic, including opioid and stimulant use disorders, and the crisis of chronic pain.