SAMHSA
Substance Abuse and Mental Health Services Administration

SAMHSA
Overdose Prevention and Response

TOOLKIT

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INTRODUCTION

OVERDOSES IN THE UNITED STATES

Overdose deaths remain at historically high levels in the United States. The Centers for Disease Control and Prevention (CDC) estimates that over 108,000 people died from overdose in 2022.[1] Most of these deaths involved opioids. Although illicitly manufactured fentanyl has been a significant driver of deaths, other drugs in the illicit drug supply have become increasingly lethal and unpredictable. For example, overdose deaths involving illicit stimulants such as cocaine and methamphetamine—often in combination with opioids—have also risen.[2] In addition, xylazine, an active ingredient in a non-opioid sedative approved by FDA for use in animals, but not approved for use in humans, is increasingly added as an adulterant to the illicit drug supply. Given these realities, it is important that everyone has access to accurate and timely information about overdose risk and prevention—understanding what to look for and how to respond when an overdose occurs can help save lives. Evidence-based interventions are available—knowing when and how to use them can help end the overdose crisis.

TOOLKIT PURPOSES AND AUDIENCES

The primary purpose of this Toolkit is to educate a broad audience on overdose causes, risks, and signs, as well as the steps to take when witnessing and responding to an overdose. It provides clear, accessible information on opioid overdose reversal medications, such as naloxone. This Toolkit serves to complement, not replace, training on overdose prevention and response. It is also intended to augment the use of other overdose prevention tools for community engagement and planning, as well as enhance provider education across multiple practice areas.

Overdose education and response tools have the greatest impact when focused on people who use drugs because they are most likely to witness and respond to an overdose.[3] However, it is important to recognize that anyone could witness an overdose—whether on the street, at work, at home, in a clinical setting, or in a school. This Toolkit is therefore available for everyone to provide basic knowledge on how to recognize and respond to an overdose.

Some audiences may benefit from tailored information, guidance, and resources. Therefore, this Toolkit also includes sections for specific audiences, including people who use drugs (and their family members or caregivers) in Appendix 1; people who use prescription opioids in Appendix 2, practitioners, and health systems in Appendix 3, and first responders in Appendix 4. Appendix 5 of this Toolkit also includes information and links to resources on policy and systems considerations for planning community overdose prevention and response initiatives.

OVERDOSE BASICS: OPIOIDS

Opioids are powerful substances that activate opioid receptors, which are present in cells throughout the body and are especially concentrated in the brain. This activation leads to chemical changes that block the experience of pain and produce euphoric effects, often described as an intense sensation of warmth or well-being. Medical practitioners have prescribed opioid medications for the treatment of acute and chronic pain, severe cough, and diarrhea for hundreds of years. Under the supervision of a medical provider, prescription opioid medications can be effective and safe to use for certain types of conditions.[4] Common names for prescription opioids include morphine, codeine, oxycodone, hydrocodone, fentanyl, and hydromorphone.

Prescription opioids are also shared, sold, and used illicitly outside of a medical setting or a practitioner's supervision. Behaviors that put a person at greater risk of overdose include using prescription opioids for reasons not intended by the prescription and altering their form of ingestion, such as crushing, snorting, smoking, or injecting. People who share their prescribed opioids with family or friends may not realize that doing so places their friend or family member at risk for overdose. Drugs that are sold or purchased on the street are unregulated, meaning that their potency and content are unknown, and may include lethal amounts of drugs. Drugs that are sold on the street also may be combined with other active or inactive ingredients that affect their potency and effect. It is important to understand that illicitly manufactured fentanyl or other illicit opioids are often found in counterfeit pills, which are made to look like prescription drugs. They may also be added to other illicit drugs such as methamphetamine or cocaine. As a result, individuals using unregulated drugs may be exposed to fentanyl or other synthetic opioids unknowingly—further increasing risk for an overdose.

In addition, people who use opioids, whether prescribed or illicit, can experience other negative side effects. For example, opioids can reduce saliva, often leading to a dry mouth, and cause constipation in some people. When people take a high dose of opioids for more than a week, the opioid receptors in their bodies can become used to that amount. This phenomenon, called *tolerance*, happens with many substances and medications, not just opioids. It is the body's way of adjusting to a specific dose or amount and means that an increasingly higher dose will be needed to experience the same effects. The body's adjustment to dose is part of an expected phenomenon known as physical *dependence*. Physical dependence includes both a tolerance and a withdrawal component. *Withdrawal* can happen when a person suddenly stops taking an opioid or sharply reduces the amount to which their body has become tolerant. During withdrawal, the person experiences unpleasant symptoms, such as vomiting, diarrhea, severe abdominal cramping, runny eyes, runny nose, and severe anxiety. Withdrawal from opioids is usually not fatal, but people can become extremely dehydrated during withdrawal—which can lead to death.[5] Physical dependence also does not automatically mean that the person has an opioid addiction or are not in recovery from an opioid use disorder. For example, people taking opioids for cancer pain or individuals taking methadone or buprenorphine for the treatment of an opioid use disorder may experience withdrawal if they abruptly stop taking or significantly reduce the dose of these medications. This is only a manifestation of physical dependence and does not mean that they meet other diagnostic criteria for an opioid use disorder.

FENTANYL IS A STRONG, SYNTHETIC OPIOID that can be prescribed by a practitioner or obtained from unregulated sources when it is made illicitly. In some cases, fentanyl is also mixed with other illicit drugs, such as cocaine or methamphetamine. A person using that drug may not know they are also taking fentanyl or how much fentanyl they are taking. Fentanyl is now common in the illicit drug supply, and in recent years has become more common than heroin. Synthetic opioids, primarily illicitly manufactured fentanyl, are involved in most drug overdose deaths in the U.S.

OVERDOSE BASICS: STIMULANTS AND OTHER DRUGS

Stimulant use, in particular methamphetamine use, has been on the rise in the United States since 2009.[6] The rise in overdose deaths involving stimulants and opioids represents the most recent dimension of the ongoing overdose crisis.[7]This follows successive surges in overdoses related to prescription opioids, then heroin, and illicit fentanyl. Many deaths from stimulant drugs also involve an opioid, suggesting that some people may be buying unregulated stimulant drugs without knowing they contain fentanyl; however, patterns of stimulant use also have been changing, with a noted increase in people reporting use of both stimulants and opioids.[8,9,10,11,12]

People can experience an overdose of methamphetamine or cocaine without opioid involvement, which is referred to as *overamping*. Overamping often affects multiple organs at the same time.[13] People might present with cardiac symptoms, such as chest pains or heart palpitations, or appear to be experiencing a stroke. Some people experience psychiatric symptoms, such as agitation, delirium, or trauma. A lack of sleep, poor diet, or dehydration can increase the risk of overamping. Cocaine overdoses, in particular, are more likely to cause seizures, heart attacks, and strokes.

If stimulant overdose or overamping is suspected, seek medical assistance as quickly as possible. Although there is no available medication that can reverse stimulant overdose, as naloxone reverses opioid overdose, there are prescription medications and medical treatment that can manage acute symptoms.

HOW OVERDOSE OCCURS

An *overdose* occurs when someone takes more of a drug than their body can handle. In an overdose, the substances or medications that a person has taken can overpower the brain and other organs, preventing them from functioning normally. For example, an opioid overdose causes breathing to slow or even stop, depriving cells of the brain and heart of life-sustaining oxygen. This slowed or stopped breathing is called *respiratory depression*, which occurs because the opioids affect the breathing center in the brainstem. Without intervention, overdose can lead to death.

OVERDOSE RISK CONSIDERATIONS

Overdose risk in each individual increases or decreases depending on individual factors and community context. In ***Figure 1*** below are some key examples, not an exhaustive list, of individual and community-generated risk factors.

Figure 1. Risk Considerations

INDIVIDUAL RISK FACTORS

- Taking an amount of a drug that is greater than your tolerance level. This may include using drugs after a recent period of abstinence, which may decrease previous tolerance levels.
- Returning to drug use after leaving jail/prison or healthcare setting where a medication for opioid use disorder was not provided or taken.
- Returning to drug use before receiving another injection of naltrexone, an FDA-approved medication for opioid use disorder, since the opioid blockage effect of naltrexone will have worn off and prior tolerance levels will have decreased.
- Taking a drug that is much stronger than what you are used to taking.
- Using a drug when you have underlying lung or heart conditions that leave you unable to tolerate lower levels of oxygen, such as asthma or sleep apnea.
- Using a similar drug to the one with which you have experienced a prior overdose.
- Combining different drugs—for example, opioids with other sedating substances such as benzodiazepines or alcohol.
- Using drugs alone without notifying someone who can respond using an overdose reversal medication.

COMMUNITY CONTEXT

- Due to clinic closure or inadequate access to health system providers to address pain treatment or OUD treatment, switching from prescription opioids to unregulated street-purchased opioids that have unknown contents and potency.
- Not having access to drug checking tools to test illicit drugs for contents prior to use.

- Not having easy and timely access to opioid overdose reversal medications.
- Not checking for prescriber or pharmacist error, or misunderstanding instructions that can lead to taking a medication more often or at a higher dose than was intended.
- Using a substance or taking a medication obtained from an unregulated source and not knowing its contents.
- Using drugs in an unfamiliar or stressful environment, which can reduce awareness of and access to overdose prevention tools.

OVERDOSE PREVENTION

OVERDOSE PREVENTION AND HARM REDUCTION

It is important to distinguish that overdose prevention involves actions before, during, and after acute overdose. Overdose prevention includes taking steps to reduce the risk of overdose in the first place, responding to an overdose by administering naloxone or other opioid overdose reversal medications, and referring the person to harm reduction services and supports. Harm reduction services and supports can include syringe services programs, drug checking, and providing medications for opioid use disorder (MOUD), as well as the provision of or linkages to other evidence-based treatments for substance use disorders (SUDs) and prevention, screening, referral, and treatment services for infectious diseases such as HIV and viral hepatitis, and wound care.

HARM REDUCTION is an evidence-based, practical, and transformative approach that incorporates public health strategies—including prevention, risk reduction, and health promotion—to empower people who use drugs (PWUD) and their families with the choice to live healthier, self-directed, and purpose-filled lives. Harm reduction centers the lived and living experience of PWUD, especially those in underserved communities, in these strategies and the practices that flow from them.

Understanding the risk factors involved in overdose can help individuals take informed steps to mitigate them.

1. Consider personal risk for overdose: The level of risk and strategies for prevention differ depending on whether you are taking a prescription medication as prescribed by your practitioner, are a patient receiving long-term pain management, or are obtaining and using illicit opioids.
2. Gather more information: Ask your prescriber and pharmacist questions. If you are taking prescription opioids for a medical condition, be sure to understand the medications you are taking by reviewing the potential interactions with other medications or substances and confirming the prescribed dosage. If you are using illicit opioids obtained on the street, consult a trusted source such as a harm reduction provider, practitioner, or pharmacist for overdose prevention information. Everyone who takes opioids or knows someone who does should learn the signs of an overdose and how to respond.
3. Take action: Empower yourself to take steps to reduce your risk of overdose. Obtain an opioid overdose reversal medication such as naloxone or nalmefene, as well as fentanyl and xylazine test strips.

Information on treatment services available in or near your community can be obtained from your state health department, your state alcohol and drug agency, or SAMHSA's FindTreatment.gov at https://findtreatment.gov/. You also can call SAMHSA's National Helpline at 1-800-662-HELP (4327) or text 435748 (HELP4U) for 24/7, 365-day-a-year free and confidential treatment referral. The 988 Suicide and Crisis Lifeline may also be helpful for people experiencing a mental health or substance use crisis that does not require an acute medical intervention. For more information, see the Resources section at the end of this Toolkit.

TREATMENT AS PREVENTION

Effective treatment of SUDs can reduce the risk of overdose and help those who have experienced an overdose make positive changes and attain a healthier life. Opioid use disorder (OUD) is a chronic disease, much like diabetes, high blood pressure, or heart disease. Evidence-based treatment for OUD includes the use of medications approved by the U.S. Food and Drug Administration (FDA). Three medications for opioid use disorder (MOUDs) are approved by the FDA to treat OUD: buprenorphine, methadone, and naltrexone. Methadone and buprenorphine in particular have been associated with significant reductions in risk for overdose death.[4,14,15,16] Research has demonstrated that all three MOUDs are safe to use for months, years, or even a lifetime in supporting recovery from OUD; integrating counseling and psychosocial support with MOUD treatment may have additional benefits for some patients. MOUDs normalize brain chemistry, block the euphoric effects of opioids, relieve cravings (methadone and buprenorphine), and normalize body functions without the negative and euphoric effects of the substance used.[17] All providers who prescribe controlled medications can also prescribe buprenorphine for OUD (or refer for methadone treatment as this can only be provided in special Opioid Treatment Programs). Naltrexone is not a controlled medication and can be prescribed by any provider as long as it falls within their scope of practice.

There currently are no FDA-approved medications for the treatment of stimulant use disorder. However, contingency management is a proven, effective behavioral intervention to support recovery in people with stimulant use disorder and as a complement to MOUD for individuals with OUD.

OPIOID OVERDOSE REVERSAL MEDICATIONS

ROLE OF OPIOID OVERDOSE REVERSAL MEDICATIONS (OORM)

OORMs are life-saving medications that reverse the effects of an acute opioid overdose and restore breathing. They are available to the public by prescription, through standing orders or without a prescription/"over-the-counter" at pharmacies and other retail outlets, or at no charge from local community-based organizations. Training is typically not required to obtain OORM and, when widely offered and used, OORM can reduce overdose fatality rates.[18,19]

The most known and used OORM is **naloxone**. Naloxone is FDA-approved and has been used for decades by emergency medical service (EMS) providers and lay people to reverse opioid overdose and resuscitate individuals who have experienced an overdose involving opioids. There are two primary ways naloxone can be administered. It can be given intranasally through a device that sprays the medication into the person's nose. It is also available as an injection into a person's muscle—typically the butt, shoulder, or thigh. Different FDA-approved naloxone products are available in different doses. Products may come in kits compiled by harm reduction or other community organizations, which may include two doses of the medication, syringes for administering intramuscular[1] naloxone if the medication is to be injected, gloves, a plastic face shield to support rescue breathing, and information on local resources; these harm reduction organization-provided kits have not been reviewed or approved by FDA.[20]

Another FDA-approved OORM is called **nalmefene**. This medication reverses the effects of opioids and can treat symptoms of an acute overdose. It remains in the body for significantly longer than naloxone, with a half-life of 11 hours compared to naloxone's half-life of 1.5 to 2 hours. Research has shown that this longer half-life can lead to extended withdrawal symptoms in people who are tolerant on opioids—however, how this affects a real-world overdose is unknown.[21] Injectable nalmefene was approved by FDA in 1995; however, nalmefene nasal spray was only recently approved in 2023 and does not yet have the same extensive field experience as naloxone. Please note:

- Everyone should keep an OORM on hand, but especially those who use opioids or other drugs or have friends or family members who use opioids or other drugs.
- If someone is having a medical emergency that is not an opioid overdose – such as a heart attack or diabetic coma- giving them naloxone and nalmefene will generally not have any effect or cause them additional harm.
- Brief education on how to administer naloxone can be obtained from the provider of the naloxone kit or online at http://prescribetoprevent.org or www.getnaloxonenow.org. Speak with your pharmacist or harm reduction provider to understand the products available to you and any training considerations.
- Over-the-counter naloxone products have directions for use on the Drug Facts Label of the product.

[1] Naloxone can also be administered intravenously or subcutaneously

OORMS AVAILABLE TO THE PUBLIC

OORM	Brand	Formulation	Dosage	Availability	Considerations
Naloxone	N/A	Adaptable Nasal Spray	2 mg/ml	Rx, community naloxone distribution, harm reduction organizations	Assembly required to attach nasal spray adapter to needle-less syringe. Not approved by FDA. Possible to titrate to meet the needs of the patient and facilitate a gentler overdose reversal with potential for less severe withdrawal in people with opioids in their body.
Naloxone	RiVive ™	Single-use Nasal Spray	3 mg	Rx, OTC, community naloxone distribution, harm reduction organizations	Lower dose can facilitate a gentler overdose reversal with less severe withdrawal in people with opioids in their body.
Naloxone	Narcan, generic	Single-use Nasal Spray	4 mg/ 0.1 ml	Rx, OTC, community naloxone distribution, harm reduction organizations	May cause withdrawal symptoms in people who have opioids in their body.
Naloxone	N/A	Single-dose Vial Intramuscular Injection; can also be given intravenously or subcutaneously	0.4 mg/ml	Rx, community naloxone distribution, harm reduction organizations	Has been studied and used in the real world to reverse overdoses for decades; cheapest naloxone available; easy to use.
Naloxone	Zimhi®	Intramuscular or subcutaneous Auto-Injection	5 mg/ml	Rx, community naloxone distribution, harm reduction organizations	Accessible product format that auto-injects the medication; high dose compared to other products; may cause severe withdrawal symptoms in people with opioids in their body.
Naloxone	Kloxxado®	Single-use Nasal Spray	8mg/0.1 ml	Rx, community naloxone distribution, harm reduction organizations	High dose compared to other products; may cause severe withdrawal symptoms in people with opioids in their body.
Nalmefene	Opvee	Single-use Nasal Spray	2.7 mg/0.1 ml	Rx, community naloxone distribution, harm reduction organizations	Longer lasting than naloxone but may cause severe extended withdrawal in people with opioids in their body.

Table 1. List of OORM brands, dosages, their efficacy, and possible side effects.

OORM Q&A

IS ANY NALOXONE BETTER THAN NO NALOXONE?

Yes, in the event of an overdose, administer any naloxone available. When stored under appropriate conditions, the shelf life of naloxone is 18-24 months for injectables, and 36-48 months for a nasal spray. It is important to check the expiration date of naloxone and replace it at regular intervals. However, studies show naloxone's stability remains at a usable standard even after multiple years of storage. While it may become less effective over time, research indicates that it does not cause harm if used past its expiration date.[20,21,22,23] No research is yet available on the long-term shelf life of nalmefene.[24]

CAN NALOXONE TREAT ANY OVERDOSE?

All OORMs are effective in reversing opioid overdose, including overdose caused by fentanyl. OORMs can be used in both youth and adult populations to reverse opioid-involved overdose. Use naloxone even if you are not sure what drugs someone took. OORM may be less effective if someone has used multiple different drugs, especially those that also have a sedating effect on the body, such as alcohol or benzodiazepines. Xylazine, an active ingredient in a sedative approved by FDA for use in animals, but not humans, is increasingly being mixed into the unregulated drug supply. These drugs may make overdose reversal even more challenging. If the person is still unresponsive after the first dose, a second dose can be administered. Wait 2-3 minutes before giving a second dose of naloxone.

WHERE CAN I GET AN OORM?

Naloxone is available in all 50 states, territories, and Tribal Nations and communities. Ask your doctor, pharmacist, or other medical provider about naloxone, especially if you or someone you know is using opioids. Narcan in the 4mg nasal spray is now available for purchase over the counter in certain retail outlets with other products becoming available over-the-counter (e.g., RiVive™ 3mg naloxone nasal spray).

There are multiple options to obtain an OORM at no charge. Ask your local health department for more information or visit a harm reduction program. Many state and local health departments and behavioral health agencies now offer naloxone in public places through a vending machine, street-outreach, at fairs and festivals, or other local events. Some programs even offer naloxone delivery by mail or will deliver it to you. Keep an eye out for a "NaloxBox"—an emergency naloxone kit that can sometimes be found alongside public defibrillators.

THERE ARE SO MANY KINDS OF OORM, HOW DO I DECIDE WHICH TO GET?

Preference for an OORM is individual and can depend on familiarity with and accessibility of different products, which varies by program or pharmacy retail outlet. The major difference between each product is the strength, concentration, cost, and how it is administered. When presented with options, consider:

1. All OORM have been approved by the FDA to reverse opioid overdose. They all act quickly to reverse an opioid overdose and restore breathing, and there is no difference in effectiveness between a nasal spray and a muscular injection.[25]
2. The higher the dose, the more likely and more severely someone who has developed tolerance to opioids will experience symptoms of withdrawal upon awakening.[26] Withdrawal symptoms are flu-like and can include muscle pain, sweating, gastrointestinal distress, and heightened anxiety. A person who responds to a low dose of naloxone will typically wake up slowly and gently, similar to coming out of anesthesia after surgery. More naloxone can always be administered if needed.
3. If you are comfortable using a needle and syringe, learn how to use intramuscular naloxone. It is significantly more affordable than nasal spray products and provides the standard dose used by EMS providers.

XYLAZINE IS A NON-OPIOID SEDATIVE THAT IS APPROVED BY FDA FOR ANIMAL USE, BUT NOT FOR PEOPLE. Xylazine is increasingly added to other drugs such as cocaine, heroin, or fentanyl to enhance the effect or increase street value. Effects of xylazine include difficulty breathing, dangerously low blood pressure, sedation, slowed heart rate, and skin lesions. A person who has taken xylazine may appear to have symptoms of opioid overdose. If you are providing first aid to a person who does not respond to naloxone, continue providing rescue breaths until EMS arrive.

It is important to note that people who use drugs are those who both experience overdose and also witness and reverse the most overdoses. Experiences of withdrawal, particularly when severe, can be traumatic and may result in people who use drugs avoiding or leaving medical care settings due to their withdrawal symptoms. As a result, it is critical for decision-makers and organizations that work in this area to support choice and interest in particular products when purchasing and distributing OORM.[27]

DO I NEED TO GIVE MORE NALOXONE FOR A FENTANYL OVERDOSE?

Giving more than one dose of naloxone and using higher dose products may not be necessary when responding to a known fentanyl overdose.[28] An overdose may appear to need additional doses if other sedating drugs are present in the person's body, such as alcohol, benzodiazepines, or xylazine; however, rapidly giving more naloxone or using a stronger,

more concentrated OORM will not necessarily speed up the reversal process. Multiple studies have found that despite the presence of fentanyl, more doses were not associated with improved outcomes.[29,30,31,32]

Administering a second dose too quickly after the first dose of an OORM may make it appear that multiple doses were needed. However, in some cases, waiting 2-3 minutes before administering a second dose and ensuring that effective rescue breaths are being provided would have been sufficient to reverse the overdose. Taking time to consider the effects of putting someone into withdrawal is compassionate and potentially lifesaving. Extreme experiences of withdrawal can be painful, dangerous, and traumatizing, leading to negative feelings towards naloxone and people who use it. Fear of withdrawal may prevent someone from seeking needed care or hiding their drug use to avoid having naloxone administered.[33,34]

RESPONDING TO AN OVERDOSE

RECOGNIZE THE SIGNS OF AN OVERDOSE

The following are signs and symptoms of an opioid overdose:

- Unconsciousness or inability to awaken.
- Slow or shallow breathing or difficulty breathing such as choking sounds or a gurgling/snoring noise from a person who cannot be awakened.
- Fingernails or lips turning blue/purple. For lighter skinned people, the skin tone may turn bluish purple; for darker skinned people, skin tone may turn pale/grayish or ashen.
- Pinpointed pupils or pupils that don't react to light.

OVERDOSE RESPONSE STEPS

1. Check for a response.
2. Give naloxone or other OORM.
3. Call 911 and support the person's breathing. Administer rescue breaths or place the person in the recovery position.
4. Wait for EMS to arrive.

If an overdose is suspected, try first to wake the person up by calling the person's name. If this doesn't work, rub your knuckles on the person's upper lip or center of the chest.

IF THE PERSON DOES NOT RESPOND OR YOU ARE NOT SURE WHAT TO DO NEXT, CALL 911.

AN OVERDOSE NEEDS IMMEDIATE MEDICAL ATTENTION. If you suspect an overdose or are not sure what to do next, call 911. When the call connects, all you have to say is "someone is unresponsive and not breathing." Be sure to give a specific address and/or description of your location. After calling 911, follow the dispatcher's instructions.

DON'T LET STIGMA STOP YOU FROM SAVING A LIFE.

There is no "type" of person who experiences OUD or opioid overdose. Research has shown that women, older people, and those without obvious signs of OUD are undertreated with naloxone and, as a result, have a higher death rate. Use OORMs any time someone shows symptoms of overdose.

STEP 1 – ADMINISTER AN OPIOID OVERDOSE REVERSAL MEDICATION.

Naloxone and nalmefene are antidotes for opioid overdose. If overdose is suspected and the person is unresponsive, give an OORM as quickly as possible and then call 911. Naloxone and nalmefene do not cause harm if given to a person who is not experiencing opioid overdose.

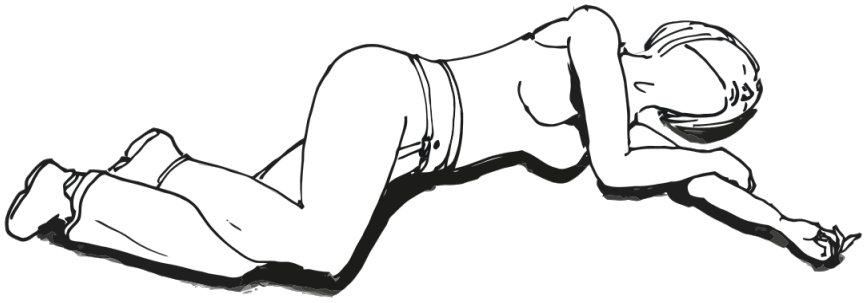
If the person does not start breathing or otherwise respond **after 2-3 minutes**, administer a second dose of naloxone or nalmefene. Continue to give doses every 2-3 minutes until the person starts breathing.

BREATH IS LIFE.

The goal of overdose reversal is to restore breathing. Breathing is more important than waking up.

STEP 2 – SUPPORT THE PERSON'S BREATHING.

If you can, provide rescue breaths. When a person overdoses, they stop breathing and this can quickly cause damage to the brain and other organs. Giving oxygen through rescue breathing saves lives—in fact, early administration of oxygen may help prevent the need to use an OORM.[14,15] You may use a medical oxygen delivery device, if available.



If you do not have training in rescue breathing and chest compressions, follow the instructions of the 911 operator.

When breathing returns, gently place the person in the recovery position (see ***Figure 2***). Roll the person onto their side with the top leg bent to support the position.

STEP 3 – WAIT FOR EMERGENCY MEDICAL SERVICES TO ARRIVE

Naloxone wears off after 30-90 minutes and overdose symptoms may return. Encourage the person to receive treatment from EMS and/or go to an emergency department.[1,20]

Know your rights! Familiarize yourself with your state's Good Samaritan Laws. These laws provide limited immunity from certain civil or criminal consequences of drug use or rendering assistance in response to drug use in the event of an overdose.

Visit here for additional information on your state's Good Samaritan Laws: https://www.networkforphl.org/resources/legal-interventions-to-reduce-overdose-mortality-overdose-good-samaritan-laws/.

POST-OVERDOSE TREATMENT CONSIDERATIONS

When people who have developed physical dependence on opioids are given naloxone or another OORM, they may start to breathe again, but they may also develop signs and symptoms of opioid withdrawal. These signs and symptoms may include body aches, diarrhea, fast heart rate, fever, runny nose, sneezing, gooseflesh, sweating, yawning, nausea or vomiting, nervousness, restlessness, or irritability, shivering or trembling, abdominal cramps, weakness, tearing, insomnia, opioid craving, dilated pupils, and increased blood pressure. These symptoms are uncomfortable and can be quite miserable, but they are generally not life threatening. Offer the person options for treatment, peer support, and harm reduction resources (e.g., contacts for the nearest harm reduction organization, fentanyl testing strips, OORM).

If the patient is receiving prescription opioids for pain management, help them contact their prescribing provider to discuss pain treatment options. For patients with OUD, an evidence-based, first line treatment for OUD is buprenorphine, which may help relieve withdrawal symptoms and can be prescribed by any Drug Enforcement Administration (DEA)-registered practitioner in accordance with their state laws. Methadone also is a highly effective treatment for OUD but is available only in special Opioid Treatment Programs (OTPs). Injectable naltrexone is an FDA-approved medication for the treatment of OUD but does not have the same withdrawal-relieving properties as buprenorphine or methadone.

WHAT IF THE PERSON DOES NOT WANT FURTHER MEDICAL CARE?

If the person declines further medical care, assess whether the person understands the risks and benefits of that decision, then offer to stay with the person to monitor for the possible return of opioid overdose signs and symptoms. Stay with the person for at least 4 hours from the last dose of naloxone. If you cannot stay with the person, leave them with a friend or family member. Be sure that whoever remains with the person has access to OORM in case

988 IS THE SUICIDE & CRISIS LIFELINE. Trained crisis counselors who respond to calls, texts, and chats are prepared to help anyone who needs support for a suicidal, mental health and/or substance use crisis. Sometimes a call to 988 requires the dispatch of EMS and/or police. However, if a person is experiencing an overdose and is breathing slowly or not breathing, they require immediate medical attention. Calling 911 is the best next step.

overdose symptoms return. Use the 988 Crisis Lifeline as a resource for both the person who experienced the overdose and the responder to help them develop a safety plan to prevent a future overdose event.

Surviving an overdose can be a traumatic experience. Provide support, understanding, and empathy to the person.

The risk of a fatal overdose remains high even a year after a non-fatal opioid overdose event.

DOS AND DON'TS WHEN RESPONDING TO AN OVERDOSE

There are important things to keep in mind to help protect a person's safety when they experience an overdose. The most effective intervention is opioid overdose reversal medications, such as naloxone. You should prioritize giving an opioid overdose reversal medication in accordance with the dos and don'ts below. Avoid actions that may cause further harm to the person.

DO attend to the person's breathing and cardiovascular needs by performing rescue breathing and/or chest compressions. Rescue breathing can be lifesaving itself. If you have access to it, administering supplemental oxygen can also be helpful.

DO administer an opioid overdose reversal medication if the person is not breathing. Give an additional dose if there is no response within 2-3 minutes of each dose.

DO put the person in the "recovery position" on their side, if you must leave them unattended for any reason, or if their breathing has returned but they are still not fully awake. In this case, monitor breathing closely.

DON'T slap or forcefully try to stimulate the person; it will only cause further injury. If you cannot wake the person by shouting or rubbing your knuckles on the sternum (center of the chest or rib cage), the person may be unconscious.

DON'T put the person into a cold bath or shower. This increases the risk of falling, drowning, or going into shock.

DON'T inject the person with any substance (e.g., saltwater, milk, stimulants). The only safe and appropriate treatment is an opioid overdose reversal medication.

DON'T try to make the person vomit drugs that may have been swallowed. Choking or inhaling vomit into the lungs can cause a fatal injury.

APPENDIX 1: PEOPLE WHO USE DRUGS

Anyone who uses drugs may experience an overdose, but some factors increase or decrease risk. Harm reduction strategies can reduce the risk of overdose and support people in achieving self-determined goals related to their drug use, which may or may not include abstinence.

Table A- 1: Risk factor and associated harm reduction strategy

Overdose Risk Factor	Harm Reduction Strategy to Reduce Risk of Overdose
You experience a recent period of not taking any opioids, such as an emergency department stay, jail, or detox, or you are starting to use opioids again after a period of non-use or administration of an opioid antagonist such as naloxone.	• Never use drugs alone, tell a friend or call 988 to talk about overdose risk with a professional or peer counselor. • Start with the lowest possible amount of drug. • Use or consume drugs slowly and observe their effects. • Test unregulated drugs purchased on the street for fentanyl. • **If you took medications such as methadone or buprenorphine while incarcerated but then stopped, starting to use street drugs upon release increases risk of overdose.**
You are using any kind of drug.	• **Start low and go slow.** Start with a low dose and only increase gradually. • **Do not use alone.** Use with a trusted person who is alert and can respond in the event of overdose or let a trusted person know to check on you. Look up a local "never use alone" hotline. • **Stagger your use.** If you are using with a group, be sure that someone is alert and can respond in the event of overdose. • **Avoid using drugs, including opioids, with alcohol.** Taking opioids in combination with alcohol and/or other depressant medications like benzodiazepines or tranquilizers can greatly increase the risk of overdose. • **Always carry an OORM.** Be familiar with signs of an overdose and be prepared to respond with an OORM. See earlier section on OORM and responding to an overdose. • **Test it.** Using test strips or other drug checking equipment to determine the presence of fentanyl and other drugs can help you decide how to use a drug to reduce risk for overdose. • **Listen to your body.** Overall health can impact overdose risk. Rest, eat, and hydrate.[15,16]
You are changing your method of administration of an opioid, altering the opioid by crushing it, or taking opioids differently from how they were prescribed.	• If you obtain unregulated opioids on the street, consider the increased risk of switching between different types and strengths of opioids, and test drugs to know the contents. • Your risk of overdose increases when injecting or smoking opioids as compared to snorting or swallowing them. You can reduce risk by using alternatives to injecting or smoking. • Crushing or otherwise manipulating prescription opioids can make the dose unpredictable, and risk of overdose increases if you snort instead of swallowing a drug.

For more resources and harm reduction strategies created with and for people who use drugs, visit https://harmreduction.org/.

APPENDIX 2: PEOPLE WHO TAKE PRESCRIPTION OPIOIDS

Opioids are effective at treating certain pain and other medical conditions under the supervision of a medical provider; however, their use can still place people at risk for physical dependence, opioid use disorder, and overdose.

Table A- 2: Prescription opioid medications for pain treatment

Overdose Risk Factor	Harm Reduction Strategy
You are new to prescription opioids.	• Take all prescription medications as instructed by your medical provider or doctor. • Start with the lowest possible dose. • Go slowly. Only increase your dose if a lower dose is not effective and in consultation with your prescriber. • Talk to your prescriber, pharmacist, or a harm reduction program provider about risk reduction strategies. • If you have a history of a SUD, talk to your prescriber about alternatives to prescription opioids or an accountability plan to accompany the prescription. If you are concerned about a negative, rather than helpful, reaction from your prescriber, consider bringing a trusted person or advocate with you. • Make a plan to dispose of excess medications that you do not use. • Crushing or otherwise manipulating prescription opioids can make the dose unpredictable, and risk of overdose increases if you snort instead of swallow a drug. • **Avoid mixing your medication with alcohol or other sedating drugs.** Mixing opioids with alcohol and/or other depressant medications like benzodiazepines or tranquilizers can greatly increase the risk of overdose. • **Always carry an OORM.** Be familiar with signs of an overdose and be prepared to respond. • Listen to your body. Overall health can impact overdose risk. Rest, eat, and hydrate.[15,16]
You are taking opioids for long-term management of chronic pain.	• Take all prescription medications as instructed by your medical provider or doctor. • Discuss non-opioid medications and non-medication treatments with your medical provider or doctor. • Plan for tolerance changes over time and prepare for its impact on pain experience. • Talk to your medical provider or doctor about any changes to medications and treatment for other conditions. • Make a plan to dispose of excess medications that you do not use. • Crushing or otherwise manipulating prescription opioids can make the dose unpredictable, and risk of overdose increases if you snort, inject, smoke, or rectally administer instead of swallowing a drug. • **Avoid mixing your medication with alcohol** or other sedating drugs. Mixing opioids with alcohol and/or other depressant medications like benzodiazepines or tranquilizers can greatly increase the risk of overdose. • **Always carry OORM.** Be familiar with signs of an overdose and be prepared to respond. • Listen to your body. Overall health can impact overdose risk. Rest, eat, and hydrate.[13,17]

For more information, visit Prescribe to Prevent at https://prevent-protect.org/. Compiled by prescribers, pharmacists, public health workers, lawyers, and researchers working on overdose prevention and naloxone access, this nongovernmental site provides healthcare providers with resources to educate patients on naloxone and overdose risk reduction.

APPENDIX 3: PRACTITIONERS & HEALTH SYSTEMS

Research shows that people at risk of overdose frequently interact with the health system.[35] Whether they are prescribed opioids or obtain them from an illicit source, they may seek medical attention for various needs. Moreover, they may have been treated for a previous nonfatal overdose. Healthcare providers can support people at risk of overdose and are uniquely positioned to significantly impact overdose prevention and response efforts in their community.

IF YOU ARE A MEDICAL PROVIDER:

- Use every interaction with a patient as an opportunity to discuss medication management and substance use, create an open dialogue about opioids and overdose risk, screen for substance use, and offer support.
- Create a practice of open dialogue with patients, encouraging them to share their questions and concerns about opioids. Respond to their questions and concerns using non-judgmental and non-stigmatizing language, sharing factual information, seeking understanding of the patient's goals and experiences, refraining from lecturing or patronizing, and approaching the interaction through a lens of shared decision-making.
- If a patient screens positive for and/or discloses substance use, assess for a potential diagnosis of a SUD and related treatment needs in a nonjudgmental manner. Not all patients are ready for or desire treatment. You can direct patients to local harm reduction programs e.g., syringe service program, offer linkage to treatment that includes MOUD, prescribe buprenorphine, or refer to local support groups (e.g., recovery community organizations).
- Familiarize yourself with addiction developmental theories, risk and protective factors, and the role Adverse Childhood Experiences and trauma play in risk for substance use disorders.
- Understanding the Stages of Change/Transtheoretical Model and Motivational Interviewing (MI) can also help providers engage with patients. MI is a practical technique for patient engagement across many chronic health conditions, including SUD. With awareness of what causes or contributes to substance use and SUDs, providers can challenge their assumptions about a person and treat them with greater compassion, dignity, and respect.
- Practice trauma-informed care and consider the possibility that a patient might feel stress during an appointment. This may prevent them from opening up about their needs.
- Integrate peer recovery specialists into the medical team.

IF YOU ARE A PRESCRIBER OF OPIOIDS:

- Practice proper opioid stewardship by familiarizing yourself with the CDC's latest opioid prescribing guidelines.
- Provide this Toolkit to patients and direct them to where they can learn more about the risks and benefits of opioid use, whether prescribed or obtained illicitly.
- Prescribe an OORM when you prescribe an opioid and encourage patients to have it on hand.
- Seek out education on medications for OUD, such as buprenorphine and methadone.

Federally funded continuing medical education courses are available at no charge at https://pcssnow.org/ and https://attcnetwork.org/.

OPIOID STEWARDSHIP

The CDC developed guidelines to improve communication between prescribers and patients about the risks and benefits of opioid therapy for acute, sub-acute, and chronic pain; improve the safety and effectiveness of pain treatment; and reduce the risks associated with opioid therapy including opioid use disorder, overdose, and death.[36] The 12 recommendations for prescribing opioids for adults with acute, sub-acute, or chronic pain are directed toward healthcare providers in the outpatient setting and are organized into four overarching categories: 1) determining whether or not to initiate opioids for pain, 2) selecting opioids and determining opioid dosages, 3) deciding duration of initial opioid prescription and conducting follow up, 4) and assessing risk and addressing potential harms of opioid use.[36]

For patients receiving opioids for pain treatment, each clinic visit is an important opportunity to reevaluate treatment goals, consider whether the functional benefits are outweighing the risks of opioids, whether the dose needs to be reduced, if the role of opioids or non-opioid treatment options should be reconsidered in the treatment plan, whether a transition to a

different opioid treatment option such as buprenorphine is appropriate, or whether a referral to an OTP may be beneficial if a patient has an underlying OUD. When a patient assessment identifies potentially harmful behaviors (e.g., high-volume use of opioids; taking opioids in combination with alcohol, benzodiazepines, or other respiratory depressants; using illicit opioids where contents of substances cannot be confirmed), providers may offer education that can reduce that person's risk for overdose. The patient may benefit from education on harm reduction strategies to reduce their unique risk factors such as testing drugs, not using alone, or carrying an OORM. Decrease opioid prescribing when risks outweigh benefits, and the patient is able to consider and access alternatives to pain management. Risk reduction messaging may also include information about other respiratory depressant medications a patient takes. For example, benzodiazepines, anti-seizure medications, and many other psychiatric medications are depressants. Letting patients know that mixing these substances with opioids or taking more than prescribed in combination with opioids may increase overdose risk. OORM may be prescribed alongside any opioid. It is also advisable to suggest that the patient create an "overdose plan" to share with friends, partners, and/or caregivers. Such a plan should contain information on the signs of overdose, how to administer an OORM or otherwise provide emergency care (i.e., calling 911).

OPIOID USE DISORDER TREATMENT

If a patient discloses opioid misuse and an assessment reveals that they have an OUD, there are medications that support treatment and reduce risk of overdose. FDA-approved, evidence-based MOUDs include methadone, buprenorphine with or without naloxone, and naltrexone. These medications can reduce opioid misuse and significantly improve quality of life. Methadone treatment for OUD can be provided only in OTPs. Buprenorphine can be prescribed by practitioners who have schedules III–V on their DEA registration, except for full time veterinarians. As of June 27, 2023, all practitioners with schedule II–V on their DEA registration will be required to complete a one-time, 8-hour training on opioid or SUD to obtain a new DEA registration or to renew their current DEA registration. Naltrexone is an injectable medication that can be prescribed and administered by any provider with prescribing authority operating within their scope of practice. For many people with OUD, psychosocial and other behavioral health treatments in conjunction with MOUD may help them achieve and sustain recovery. However, given the lethality of the illicit drug supply, medication access should not be made contingent upon participation in specific counseling or other treatment services.[38] Low barrier models of care facilitate engagement in treatment and make services easily accessible and readily available.[37] For more information on these medications and recommendations on how to reduce barriers to access, see SAMHSA's *Medication-Assisted Treatment of Opioid Use Disorder Pocket Guide* and SAMHSA's *Advisory: Low Barrier Models of Care for Substance Use Disorders* in the resources section. To identify treatment providers in your area, visit SAMHSA's Find Treatment locator or call SAMHSA's National Helpline (1-800-662-HELP [4327]) or (1-800-487-4899 TDD) or text HELP4U (435748) for 24/7 free and confidential treatment and referral in English and Spanish.

LEGAL AND LIABILITY CONSIDERATIONS

Health care professionals who are concerned about legal risks associated with OORM prescribing may be reassured that prescribing an OORM to manage opioid overdose is consistent with FDA-approved indications, resulting in no increased liability, as long as the prescriber adheres to general rules of professional conduct. Most state laws and regulations now permit practitioners to prescribe naloxone to a third party, such as a caregiver.[14] More information on state policies is available from the Prescription Drug Abuse Policy System's Naloxone Overdose Prevention Laws website or from individual state medical boards. For more information visit www.opioidprescribing.org.

APPENDIX 4: FIRST RESPONDERS

EMS providers and other first responders such as firefighters are often first on the scene of an overdose. They can create a calm environment for someone who survives an overdose. Moreover, they are critical partners in public health programs that improve patient outcomes and reduce opioid overdose rates. EMS providers and other first responders can partner with communities and harm reduction agencies to respond to community needs in multiple ways. They are critical interagency collaborators—linking data to public health action and implementing lifesaving public health interventions that bolster community-based overdose prevention efforts and serve as a connector to health services.

CARE FOR SOMEONE AFTER AN OVERDOSE

EMS providers can create a supportive environment for the person surviving an overdose, as well as their friends and family. This may include clearing the room of any law enforcement personnel, speaking in a calm tone, and avoiding use of any and all restraints. However, although EMS is a critical part of a system of care that can overall reduce opioid use and overdose, they are often underused as part of a comprehensive strategy to prevent overdoses.[38,39]

LINKAGE TO A PEER RECOVERY SPECIALIST[40]

EMS is uniquely positioned to offer life-saving resources to people after they overdose. One of those resources is ongoing engagement by someone who serves as a peer recovery specialist—a person with lived experience that allows them to guide someone else through the system of care. Most behavioral health agencies, health departments, and medical services have hired or are partnering with peer recovery specialists. EMS personnel can refer a patient to a peer recovery specialist or invite them onsite to follow up after the overdose event.

NALOXONE LEAVE BEHIND [51]

Some EMS providers leave a naloxone kit behind with the survivor. Evaluations of Naloxone Leave Behind programs show they are feasible, do not require significant effort, and can have a positive impact on community-wide naloxone distribution. Receiving a naloxone kit increased the odds a person who survives an overdose will engage a peer recovery specialist, demonstrating the importance of naloxone distribution as a connector for multiple prevention approaches.

BUPRENORPHINE INDUCTION[41]

This emerging practice involves EMS providers, with a doctor's oversight, administering buprenorphine after OORM administration. This creates a "softer landing" for people waking up from an overdose and has shown promise for encouraging treatment uptake in the short term. The patient is then linked to ongoing care with buprenorphine used as a treatment for OUD.

DATA SHARING AND COLLABORATION[42]

Data are important for understanding where and when overdoses happen. EMS data are geographically indexed and can be accessed within a short period of time. As EMS personnel are most often the first professional responders on the scene of an overdose, EMS data can inform a public health response.[43] EMS data also reflect nonfatal overdose events that may be missed by other health data because people may refuse transport to a hospital (i.e., they are treated in the field and then released). These data are incredibly useful to public health and behavioral health because they provide a more complete picture of who may not be reached in other ways with overdose prevention resources. Studies show nearly one-third of overdose decedents interacted with EMS in the year prior to their death.[44] Beyond data sharing, EMS personnel provide an important voice in coalitions or workgroups that collaborate to address substance use and overdose in a community.

For more information, see: https://www.astho.org/globalassets/report/innovations-in-overdose-response.pdf., https://www.ems.gov/resources/search/?category=opioid-epidemic, and Connecting Communities to Substance Use Services: Practical Tools for First Responders https://www.samhsa.gov/resource/ebp/connecting-communities-substance-use-services-practical-tools-for-first-responders

APPENDIX 5: POLICY & SYSTEMS CONSIDERATIONS

This section of the Toolkit outlines a public health approach to preventing overdose. This approach involves widespread education about overdose risk, making OORM such as naloxone as accessible as possible, and increasing awareness among healthcare providers.[14]

A foundation for any effective and sustainable public health intervention is community engagement, or coalition building. Genuine engagement seeks to bring together the skills, knowledge, and experiences of the community to create solutions that work for all its members. It aims to ensure that people who are most affected by challenges and inequities have a voice in creating and implementing solutions to accelerate change. For those working to end the opioid overdose crisis, this means working with community members who are most affected by the crisis, including, but not limited to, people who use drugs, people with lived experience, service providers, law enforcement, and EMS personnel.[45]

Strategies should be informed by community engagement and also selected based on the strength of their evidence-base. Evidence-based practices are interventions that are guided by the best research evidence with practice-based expertise, cultural competence, and the values of the persons receiving the services that promote individual-level or population-level outcomes. Some evidence-based and promising strategies to reduce overdose death include:

TARGETED OORM DISTRIBUTION

People who use drugs are most likely to witness and respond to an overdose with an OORM, preventing overdose death. The most effective OORM distribution strategies at a population-level prioritize people who use drugs and their loved ones. This can often be done through syringe service programs that are recommended as critical access points for communities with high opioid overdose mortality rates and low reach of other organizations.[46] Harm reduction programs, whether they are syringe service programs or not, engage people who use drugs in a nonjudgmental manner and provide direct access to needed care.

In addition, communities should consider other high-risk settings where targeted distribution of OORM can be beneficial. This can include at release from criminal justice settings, other institutional settings such as substance use treatment facilities, and schools given recent increases in overdose deaths among youth and young adults.

DRUG CHECKING

Drug checking services analyze drug samples to provide information on the contents that can help a person determine how or whether to use the drugs they have obtained. Harm reduction providers may offer drug checking services anonymously, including at mobile sites during events, and often provide test strips distributed for individual use. Drug checking can be used to detect the presence of unexpected substances, such as fentanyl and xylazine, and growing evidence suggests drug checking can change behavioral intention.[47] When aggregated, data from drug checking provides important information to the public about the illicit drug supply that may inform policy and public health efforts.[48]

PUBLIC COMMUNICATION CAMPAIGNS

Public communication campaigns about overdose using social media, radio, TV, public service announcements, billboards, and bus advertising should be rooted in positive public health messaging. Fear-based campaigns are not effective.[49] Inform the public of trends in overdose fatalities and share information on changes in the drug market that can increase overdose risk. Incorporating information from drug checking activities in your community can help people know what opioids and other drugs are in the local illicit drug supply. Ensure there is constant education on naloxone and other OORMs, including what it is and where to obtain it. This is an action step that should be incorporated into every overdose awareness campaign.

GOOD SAMARITAN LAWS

Evaluate your state's Good Samaritan laws,[50] and consider whether changes may be necessary. Incorporate "know your rights" information into overdose prevention campaigns and educational materials so the public is aware that they will not be held liable for a good faith attempt to save someone's life. Increase awareness that it is critical to call 911 when someone may be experiencing an unrelated medical emergency or needs additional medical support for an overdose.

APPENDIX 5: POLICY & SYSTEMS CONSIDERATIONS

RESOURCES

SAMHSA has developed more in-depth resources to guide community-driven, evidence-based overdose prevention and response strategic planning and implementation:

For more information about coalition building to address overdose in your community, see SAMHSA's Engaging Community Coalitions to Decrease Opioid Overdose Deaths Practice Guide: https://www.samhsa.gov/resource/ebp/engaging-community-coalitions-decrease-opioid-overdose-deaths-practice-guide-2023

For guidance on evidence based practices, see SAMHSA's Opioid Overdose Reduction Continuum of Care Approach Practice Guide: https://www.samhsa.gov/resource/ebp/opioid-overdose-reduction-continuum-care-approach-orcca-practice-guide-2023

PREVENT & PROTECT

Compiled by prescribers, pharmacists, public health workers, lawyers, and researchers working on overdose prevention and naloxone access, this nongovernmental site provides health care providers with resources to educate patients on how to reduce overdose risk and provide naloxone rescue kits to patients: https://prevent-protect.org/

NATIONAL HARM REDUCTION COALITION

Resources for evidence-based harm reduction strategies created with and for people who use drugs: https://harmreduction.org/

NEXT DISTRO

Online and mail-based harm reduction service for access to naloxone and other harm reduction supplies and collaborate with others in your community: https://nextdistro.org/

REMEDY ALLIANCE FOR THE PEOPLE

Naloxone buyer's club created to increase access and distribution of injectable naloxone for programs: https://remedyallianceftp.org/

SAMHSA

988 Suicide & Crisis Lifeline: 988 or https://988lifeline.org/

SAMHSA's National Helpline: 1-800-662-HELP (4357) or 1-800-487-4889 (TDD, for hearing impaired) or send a text to 435748 (HELP4U) for 24/7, 365-day-a-year, free and confidential treatment referral in English and Spanish https://www.samhsa.gov/find-help

FindTreatment: https://findtreatment.gov/

Single State Agencies for Substance Abuse Services: https://www.samhsa.gov/sites/default/files/ssa-directory.pdf

State Opioid Treatment Authorities: https://www.samhsa.gov/medications-substance-use-disorders/sota

SAMHSA Harm Reduction Framework: https://www.samhsa.gov/find-help/harm-reduction/framework

SAMHSA Advisory on Low Barrier Models of Care for Substance Use Disorders: Substance Abuse and Mental Health Services Administration. Low Barrier Models of Care for Substance Use Disorders. Advisory. Publication No. PEP23-02-00- 005. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2023. https://store.samhsa.gov/product/advisory-low-barrier-models-care-substance-use-disorders/pep23-02-00-005

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CENTERS FOR DISEASE CONTROL AND PREVENTION

Understanding the Epidemic: https://www.cdc.gov/drugoverdose/epidemic

Clinical Practice Guideline for Prescribing Opioids for Pain: https://www.cdc.gov/mmwr/volumes/71/rr/rr7103a1.htm

APPENDIX 5: POLICY & SYSTEMS CONSIDERATIONS

Public Health and Safety Toolkit (PHAST): https://www.cdc.gov/drugoverdose/pdf/phast-toolkit-508.pdf

Addiction Medicine Toolkit: https://www.cdc.gov/opioids/addiction-medicine/index.html

Association of State and Territorial Health Officials: https://www.astho.org/

Preventing Opioid Misuse in the States and Territories: http://my.astho.org/opioids/home

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National Institute on Drug Abuse
Advancing Addiction Science

DrugFacts

Naloxone DrugFacts

What is naloxone?

Naloxone is a medicine that rapidly reverses an opioid overdose. It is an opioid antagonist. This means that it attaches to opioid receptors and reverses and blocks the effects of other opioids. Naloxone can quickly restore normal breathing to a person if their breathing has slowed or stopped because of an opioid overdose. But, naloxone has no effect on someone who does not have opioids in their system, and it is not a treatment for opioid use disorder. Examples of opioids include heroin, fentanyl, oxycodone (OxyContin®), hydrocodone (Vicodin®), codeine, and morphine.

What are some signs of an opioid overdose?

- unconsciousness
- very small pupils
- slow or shallow breathing
- vomiting
- an inability to speak
- faint heartbeat
- limp arms and legs
- pale skin
- purple lips and fingernails

How is naloxone given?

Naloxone should be given to any person who shows signs of an opioid overdose or when an overdose is suspected. Naloxone can be given as a

nasal spray or it can be injected into the muscle, under the skin, or into the veins. Steps for responding to an opioid overdose can be found in the Substance Abuse and Mental Health Administration's (SAMHSA) *Opioid Overdose Prevention Toolkit*.

What are the different naloxone delivery systems?

Naloxone comes in two FDA-approved forms: injectable and prepackaged nasal spray. No matter what dosage form you use, it's important to receive training on how and when to use naloxone. You should also read the product instructions and check the expiration date.

First Responders Can Safely Administer Naloxone during the COVID-19 Pandemic (HHS)

- **Injectable** brands of naloxone are offered by different companies listed in the FDA Orange Book under "naloxone" (look for "injectable"). Typically, the proper dose must be drawn up from a vial. Usually, it is injected with a needle into muscle, although it also may be administered into a vein or under the skin. The FDA recently approved Zimhi™, a single-dose, prefilled syringe that can be injected into the muscle or under the skin.
    - *Note: Some people use an improvised nasal spray emergency kit not approved by the FDA that combines injectable naloxone with an attachment designed to deliver naloxone through the nose. However, this improvised intranasal device is not easy to assemble, especially when under pressure in an emergency, and requires training beforehand. Additionally, the FDA-approved naloxone devices have been shown to produce substantially higher blood levels of naloxone than the improvised nasal spray. These outcomes suggest that the approved prepackaged nasal spray technology is preferable over non-FDA-approved forms.*
- **Prepackaged Nasal Spray (generic naloxone, Narcan®, Kloxxado®),** developed as a result of NIDA-funded research, is an FDA-approved prefilled, needle-free device that requires no assembly and is sprayed into one nostril while the person lays on their back. This device can also be easier for loved ones and bystanders without formal training to use.

Is there a preferable delivery system?

All systems used by first responders deliver the stated dose of naloxone and can be highly effective in reversing an opioid overdose. Study findings released in March 2019 suggests that the FDA-approved naloxone devices deliver higher blood levels of naloxone than the improvised nasal devices.

Is Narcan® the same as naloxone?

When naloxone was first approved to reverse opioid overdoses, its brand name was "Narcan." There are now other formulations and brand names for naloxone, but many people continue to call all of these products "Narcan." However, the proper generic name is "naloxone."

Can I give naloxone to someone who has overdosed?

Yes. Families with loved ones who struggle with opioid addiction should have naloxone nearby; ask their family member to carry it; and let friends know where it is. People should still call 911 immediately in the event of an overdose.

Naloxone is being used more by police officers, emergency medical technicians, and non-emergency first responders than before. In most states, people who are at risk or who know someone at risk for an opioid overdose can be trained on how to give naloxone. Families can ask their pharmacists or health care provider how to use the devices.

What precautions are needed when giving naloxone?

Naloxone works to reverse opioid overdose in the body for only 30 to 90 minutes. But many opioids remain in the body longer than that. Because of this, it is possible for a person to still experience the effects of an overdose after a dose of naloxone wears off. Also, some opioids are stronger and might require multiple doses of naloxone. Therefore, one of the most important steps to take is to call 911 so the individual can receive immediate medical attention. NIDA is supporting research for stronger formulations for use with potent opioids like fentanyl.

People who are given naloxone should be observed constantly until emergency care arrives. They should be monitored for another 2 hours after the last dose of naloxone is given to make sure breathing does not slow or stop.

People with physical dependence on opioids may have withdrawal symptoms within minutes after they are given naloxone. Withdrawal symptoms might include headaches, changes in blood pressure, rapid heart rate, sweating, nausea, vomiting, and tremors. While this is uncomfortable, it is usually not life threatening. The risk of death for someone overdosing on opioids is worse than the risk of having a bad reaction to naloxone. Clinicians in emergency room settings are being trained to offer patients immediate relief and referral to treatment for

Tolerance vs. Dependence vs. Addiction

Long-term use of prescription opioids, even as prescribed by a doctor, can cause some people to develop a **tolerance**, which means that they need higher and/or more frequent doses of the drug to get the desired effects.

Drug **dependence** occurs with repeated use, causing the neurons to adapt so they only function normally in the presence of the drug. The absence of the drug causes several physiological reactions, ranging from mild in the case of caffeine, to potentially life-threatening, such as with heroin. Some chronic pain patients are dependent on

opioid use disorder with effective medications after an opioid overdose is reversed. NIDA offers tools for emergency clinicians here.

Side effects from naloxone are rare, but people might have allergic reactions to the medicine. Overall, naloxone is a safe medicine. But it only reverses an overdose in people with opioids in their systems and will not reverse overdoses from other drugs like cocaine or methamphetamine.

> opioids and require medical support to stop taking the drug.
>
> Drug **addiction** is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and long-lasting changes in the brain. The changes can result in harmful behaviors by those who misuse drugs, whether prescription or illicit drugs.

How much does naloxone cost?

The cost varies depending on where you get the naloxone, how you get it, and what type you get. Patients with insurance should check with their insurance company to see if this medicine is covered. Patients without insurance can check the retail costs at their local pharmacies. Some drug companies have cost assistance programs for patients unable to pay for it.

Where can I get naloxone?

Many pharmacies carry naloxone. In some states, you can get naloxone from a pharmacist even if your doctor did not write you a prescription for it. It is also possible to get naloxone from community-based distribution programs, local public health groups, or local health departments, free of charge.

Co-Prescribing Naloxone with Prescription Opioids

Research indicates that clinicians prescribing naloxone along with prescription opioids may reduce the risk of opioid-related emergency room visits and prescription opioid-involved overdose deaths. The U.S. Centers for Disease Control and Prevention recommends co-prescription of naloxone for some patients who take opioids. This recommendation was first outlined in the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain and is still present in the updated 2022 CDC Clinical Practice Guideline for Prescribing Opioids for Pain.

Points to remember

- Naloxone is a medicine that rapidly reverses an opioid overdose. It attaches to opioid receptors and reverses and blocks the effects of other opioids.
- Naloxone is a safe medicine. It only reverses overdoses in people with opioids in their systems.
- There are two FDA-approved formulations of naloxone: injectable and prepackaged nasal spray.
- Police officers, emergency medical technicians, and first responders are trained on how to give naloxone.
- In some states, friends and family members can be trained on how to give naloxone.
- Naloxone only works in the body for 30 to 90 minutes. It is possible for a person to still experience the effects of an overdose after naloxone wears off or need multiple doses if a potent opioid is in a person's system.
- In some areas, you can get naloxone from pharmacies with or without a personal prescription from community-based distribution programs, or local health departments. The cost varies depending on where and how you get it as well as what type you get.

Learn more

For more information about naloxone and opioid use disorder, visit:

- NIDA's Opioids webpage
- NIDA's Naloxone for Opioid Overdose: Life-Saving Science Policy Brief

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