

Opioid Overdose Prevention Toolkit (Updated)

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SAMHSA Opioid Overdose Prevention Toolkit

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OPIOID USE DISORDER FACTS

SCOPE OF THE PROBLEM

Opioid overdose continues to be a major public health problem in the United States. It has contributed significantly to overdose deaths among those who use or misuse illicit and prescription opioids. In fact, all U.S. overdose deaths involving opioids (i.e., unintentional, intentional, homicide, and undetermined) increased to more than 42,000 deaths in 2016.¹

WHAT ARE OPIOIDS? Opioids include prescription medications used to treat pain such as morphine, codeine, methadone, oxycodone, hydrocodone, fentanyl, hydromorphone, and buprenorphine, as well as illegal drugs such as heroin and illicit potent opioids such as fentanyl analogs (e.g., carfentanil).

Opioids work by binding to specific receptors in the brain, spinal cord, and gastrointestinal tract. In doing so, they diminish the body's perception of pain. However, opioids can also have an impact on other systems of the body, such as altering mood, slowing breathing, and causing constipation. Opioid receptor binding causes the signs and symptoms of overdose as well as the euphoric effects or "high" with opioid use.

HOW DOES OVERDOSE OCCUR? A variety of effects can occur after a person takes opioids, ranging from pleasure to nausea and vomiting, severe allergic reactions (anaphylaxis), and overdose, in which breathing and heartbeat slow or even stop.

Opioid overdose can be due to many factors. For example, overdose can occur when a patient deliberately misuses a prescription, uses an illicit opioid (such as heroin), or uses an opioid contaminated with other even more potent opioids (such as fentanyl). Overdose can also occur when a patient takes an opioid as directed but the prescriber miscalculated the opioid dose, when an error was made by the dispensing pharmacist, or when the patient misunderstood the directions for use. It can also occur when opioids are taken with other medications—for example, prescribed medications such as benzodiazepines or other psychotropic medications that are used in the treatment of mental disorders—or with illicit drugs or alcohol that may have adverse interactions with opioids. At particular risk are

individuals who use opioids and combine them with benzodiazepines, other sedative hypnotic agents, or alcohol, all of which cause respiratory depression.²

WHO IS AT RISK? Anyone who uses opioids for long-term management of chronic pain is at risk for opioid overdose, as are individuals who use heroin or misuse prescription pain relievers.³ Others at risk include those who:

- Are receiving rotating opioid medication regimens (and thus are at risk for incomplete cross-tolerance).
- Have been discharged from emergency medical care following opioid overdose.
- Need opioid pain relievers, coupled with a suspected or confirmed substance use disorder or history of non-medical use of prescription opioids or use of illicit opioids.
- Have completed opioid detoxification or are abstinent for a period of time (and presumably have reduced opioid tolerance and high risk of return to opioid use).
- Have been recently released from incarceration and have a history of opioid use disorder or opioid misuse (and presumably have reduced opioid tolerance and high risk of return to opioid use).

Tolerance develops when someone uses an opioid drug regularly so that his or her body becomes accustomed to the drug and needs a larger or more frequent dose to continue to experience the same effect.

Loss of tolerance occurs when someone stops taking an opioid after long term use. When someone loses tolerance and then takes the opioid drug again, he or she can experience serious adverse effects, including overdose, even if the amount taken had not caused problems in the past.

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STRATEGIES TO PREVENT OVERDOSE DEATHS

STRATEGY 1: Encourage providers, persons at high risk, family members, and others to learn how to prevent and manage opioid overdose. Providers should be encouraged to keep their knowledge current about evidence-based practices for the use of opioid analgesics to manage pain, as well as specific steps to prevent and manage opioid overdose.

The Substance Abuse and Mental Health Services Administration (SAMHSA) funds continuing medical education courses that are available to providers at no charge from the Providers Clinical Support System (PCSS) at <https://pcssnow.org/>.

Helpful information for laypersons on how to prevent and manage overdose is available from Prevent & Protect at <http://prevent-protect.org/>.

STRATEGY 2: Ensure access to treatment for individuals who are misusing opioids or who have a substance use disorder. Effective treatment of substance use disorders can reduce the risk of overdose and help overdose survivors attain a healthier life. Medications for opioid use disorder, as well as counseling and other supportive services, can be obtained at SAMHSA-certified and Drug Enforcement Administration-registered opioid treatment programs and in specialty substance use disorder treatment programs, as well as from physicians and other practitioners including nurse practitioners and physician assistants who are trained to provide care in office-based settings with buprenorphine and naltrexone.

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 the SAMHSA Behavioral Health Treatment Services Locator at <https://www.findtreatment.samhsa.gov>.

STRATEGY 3: Ensure ready access to naloxone. Opioid overdose-related deaths can be prevented when naloxone is administered in a timely manner. (For instructions on how to use naloxone, go to <http://prescribetoprevent.org>). Naloxone displaces opioids from receptor sites in the brain and reverses respiratory depression that usually is the cause of overdose deaths.² Naloxone is an appropriate response for all opioid overdose events, including fentanyl-involved overdoses. Multiple doses of naloxone may be required when the overdose results from ingestion of large amounts of opioids or potent opioids such as fentanyl, carfentanil, or other opioid analogs.⁴ (For more information regarding the various formulations of naloxone, see <https://www.drugabuse.gov/publications/naloxone-opioid-overdose-life-saving-science/naloxone-opioid-overdose-life-saving-science>.)

On the other hand, naloxone is not effective in treating overdoses of benzodiazepines, barbiturates, clonidine, GHB, or ketamine. It is also not effective against overdoses of stimulants, such as cocaine and amphetamines (including methamphetamine and MDMA). However, if opioids are taken in combination with other sedatives or stimulants, naloxone may be helpful.

Naloxone injection has been approved by the Food and Drug Administration (FDA) and used for more than 40 years by emergency medical services personnel to reverse opioid overdose and resuscitate

Encourage providers and others to learn about preventing and managing opioid overdose.

Ensure access to treatment for individuals who have a substance use disorder.

Expand access to naloxone.

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individuals who otherwise might have died in the absence of treatment.⁵ Naloxone comes in several forms, including injectable, intranasal, and auto-injector. Injectable naloxone is typically supplied as a kit with a minimum of two doses and two syringes.⁶ Brief education on how to administer naloxone using a syringe can be obtained from the provider of the naloxone kit or from <http://prescribetoprevent.org/>. The FDA has also approved an intranasal naloxone product (a nasal spray) and a naloxone auto-injector that delivers a therapeutic dose of naloxone in an overdose situation. The intranasal spray is a prefilled, needle-free device that requires no assembly. The auto-injector can deliver a dose of naloxone through clothing, if necessary, when placed on the outer thigh.

Prior to 2012, just six states had laws that expanded access to naloxone or limited criminal liability.⁷ By mid-2017, every state and the District of Columbia had enacted statutes that provide criminal liability protections to laypersons or first responders who administer naloxone. Forty-six states and the District of Columbia have statutes that provide civil liability protections to laypersons or first responders who administer naloxone. Thirty-seven states have statutes that offer criminal liability protections for prescribing or distributing naloxone. Forty-one states have statutes that offer civil liability protections for prescribing or distributing naloxone, and 46 states have statutes that allow naloxone distribution to third parties or first responders via direct prescription or standing order. To find relevant laws for each state, visit the Prescription Drug Abuse Policy System at <http://www.pdaps.org/>

STRATEGY 4: Encourage the public to call 911. An individual who is experiencing an opioid overdose needs immediate medical attention. An essential first step is to get help from someone with medical expertise as quickly as possible.⁸ Therefore, members of the public should be encouraged to call 911. All they have to say is “Someone is unresponsive and not breathing” and give a specific address and/or description of the location. Thirty-seven states and the District of Columbia have “Good Samaritan” statutes that prevent prosecution for possession of a controlled substance or paraphernalia if emergency assistance is sought for someone who is experiencing an overdose, including an opioid-induced overdose.⁹

STRATEGY 5: Encourage prescribers to use state prescription drug monitoring programs (PDMPs). State PDMPs have emerged as a key strategy for addressing the misuse of prescription opioids and thus preventing opioid overdoses and deaths. Specifically, prescribers can check their state’s PDMP database to determine whether a patient is filling the prescriptions provided and/or obtaining prescriptions for the same or a similar drug from multiple prescribers.

While nearly all states now have operational PDMPs, the programs differ from state to state in terms of the exact information collected, how soon that information is available to prescribers, and who may access the data. Therefore, information about the program in a particular state is best obtained directly from the Prescription Drug Abuse Policy System at <http://www.pdaps.org/>, the specific state PDMP, or the state’s board of medicine or pharmacy.

Encourage the public to call 911.

Encourage prescribers to use state prescription drug monitoring programs.

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RESOURCES FOR COMMUNITIES

Resources that may be useful to local communities and organizations include:

SAMHSA

- National Helpline: 1-800-662-HELP (4357) or 1-800-487-4889 (TDD, for hearing impaired)
- Behavioral Health Treatment Services Locator (search by address, city, or ZIP Code): <https://findtreatment.samhsa.gov/>
- Buprenorphine Treatment Practitioner Locator (search by address, city, or ZIP Code): <https://www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator>
- Single State Agencies for Substance Abuse Services: <https://www.samhsa.gov/sites/default/files/ssa-directory.pdf>
- State Opioid Treatment Authorities: <https://dpt2.samhsa.gov/regulations/smalist.aspx>
- SAMHSA Publications Ordering (all SAMHSA Store products are available at no charge): <https://store.samhsa.gov/>; 1-877-SAMHSA-7 (1-877-726-4727)

Centers for Disease Control and Prevention

- Understanding the Epidemic: <https://www.cdc.gov/drugoverdose/epidemic>
- Poisoning: <https://www.cdc.gov/homeandrecreationalafety/poisoning>

Association of State and Territorial Health Officials

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

National Association of State Alcohol and Drug Abuse Directors

- Opioids Fact Sheet (February 5, 2016): <http://nasadad.org/2016/02/opioids-fact-sheet-2016/>

Prevent & Protect

- Tools for conducting overdose prevention and naloxone advocacy, outreach, and communication campaigns: <http://prevent-protect.org/community-resources-1/>

*Resources
that may
be useful
to local
communities
and
organizations*

FIVE ESSENTIAL STEPS FOR FIRST RESPONDERS

Overdose is common among persons who use illicit opioids such as heroin and among those who misuse medications prescribed for pain such as oxycodone, hydrocodone, methadone, buprenorphine, and morphine. The incidence of opioid overdose is rising nationwide. In 2016, more than 42,000 of the drug overdose deaths in the United States involved some type of opioid, including heroin.¹

To address the problem, emergency medical personnel, health care professionals, people who use drugs, and other community members who may witness and respond to an overdose are being trained in the use of the opioid antagonist medication naloxone, which can reverse the potentially fatal respiratory depression caused by opioid overdose. (Note that naloxone has no effect on non-opioid overdoses, such as those involving cocaine, benzodiazepines, or alcohol.¹⁰)

The steps outlined in this section are recommended to reduce the number of deaths resulting from opioid overdoses.

STEP 1: EVALUATE FOR SIGNS OF OPIOID OVERDOSE

Signs of **OVERDOSE**, which often results in death if not treated, include:¹⁰

- Unconsciousness or inability to awaken.
- Slow or shallow breathing or breathing difficulty such as choking sounds or a gurgling/snoring noise from a person who cannot be awakened.
- Fingernails or lips turning blue/purple.

If an opioid overdose is suspected, stimulate the person:

- Call the person's name.
- If this doesn't work, vigorously grind knuckles into the sternum (the breastbone in middle of chest) or rub knuckles on the person's upper lip.
- If the person responds, assess whether he or she can maintain responsiveness and breathing.
- Continue to monitor the person, including breathing and alertness, and try to keep the person awake and alert.

If the person does not respond, call 911, provide rescue breathing if the person is not breathing on their own, and administer one dose of naloxone.

STEP 2: CALL 911 FOR HELP

AN OPIOID OVERDOSE NEEDS IMMEDIATE MEDICAL ATTENTION. An essential step is to get someone with medical expertise to see the person as soon as possible. If no emergency medical services (EMS) or other trained personnel is on the scene, activate the 911 emergency system immediately. 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. If appropriate, the 911 operator will instruct you to begin CPR (technique based on rescuer's level of training).

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STEP 3: ADMINISTER NALOXONE

If the person overdosing does not respond within 2 to 3 minutes after administering a dose of naloxone, administer a second dose of naloxone.

Naloxone should be administered to anyone who presents with signs of opioid overdose or when opioid overdose is suspected. Naloxone is approved by the Food and Drug Administration (FDA) and has been used for decades by EMS personnel to reverse opioid overdose and resuscitate individuals who have overdosed on opioids. Research has shown that women, older people, and those without obvious signs of opioid use disorder are undertreated with naloxone and, as a result, have a higher death rate.¹¹ Therefore, it is also important to consider naloxone administration in women and the elderly found unresponsive with opioid overdose.

Naloxone can be given by intranasal spray and by intramuscular (into the muscle), subcutaneous (under the skin), or intravenous injection.¹²

All naloxone products are effective in reversing opioid overdose, including fentanyl-involved opioid overdoses, although overdoses involving potent (e.g., fentanyl) or large quantities of opioids may require more doses of naloxone.

DURATION OF EFFECT. The duration of effect of naloxone depends on dose, route of administration, and overdose symptoms² and is shorter than the effects of some opioids. The goal of naloxone therapy should be to restore adequate spontaneous breathing, but not necessarily complete arousal.²

More than one dose of naloxone may be needed to revive someone who is overdosing. People who have taken longer acting or more potent opioids may require additional intravenous bolus doses or an infusion of naloxone.¹³

Comfort the person being treated, as withdrawal triggered by naloxone can feel unpleasant. Some people may become agitated or confused, which may improve by providing reassurance and explaining what is happening.

SAFETY OF NALOXONE. The safety profile of naloxone is remarkably high, especially when used in low doses and titrated to effect.¹⁰ When given to individuals who are not opioid intoxicated or opioid dependent, naloxone produces no clinical effects, even at high doses. Moreover, although rapid opioid withdrawal in opioid-tolerant individuals may be unpleasant, it is not life threatening.

Naloxone can be used in life-threatening opioid overdose circumstances in pregnant women.¹⁴

The FDA has approved an injectable naloxone, an intranasal naloxone, and a naloxone auto-injector as emergency treatments for opioid overdose. People receiving naloxone kits that include a syringe and naloxone ampules or vials should receive brief training on how to assemble and administer the naloxone to the victim. The nasal spray is a prefilled, needle-free device that requires no assembly and that can deliver a single dose into one nostril. The auto-injector is injected into the outer thigh to deliver naloxone to the muscle (intramuscular) or under the skin (subcutaneous). Once turned on, the currently available device provides verbal instruction to the user describing how to deliver the medication, similar to automated defibrillators. Both the nasal spray and naloxone auto-injector are packaged in a carton containing two doses to allow for repeat dosing if needed.

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FENTANYL-INVOLVED OVERDOSES. Suspected opioid overdoses, including suspected fentanyl-involved overdoses, should be treated according to standard protocols.⁴ However, because of the higher potency of fentanyl and fentanyl analogs compared to that of heroin, multiple doses of naloxone may be required to reverse the opioid-induced respiratory depression from a fentanyl-involved overdose.^{4,15,16}

Many anecdotes report more rapid respiratory depression with fentanyl than with heroin, although other reports do not reflect such rapid depression.¹⁷

Because of these effects, quicker oxygenation efforts and naloxone delivery may be warranted with fentanyl-involved overdoses compared with heroin-only overdoses. However, naloxone is an appropriate response for all opioid overdoses, including fentanyl-involved overdoses.

STEP 4: SUPPORT THE PERSON'S BREATHING

Ventilatory support is an important intervention and may be lifesaving on its own. Rescue breathing can be very effective in supporting respiration, and chest compressions can provide ventilatory support.^{18,19} Rescue breathing for adults involves the following steps:

- Be sure the person's airway is clear (check that nothing inside the person's mouth or throat is blocking the airway).
- Place one hand on the person's chin, tilt the head back, and pinch the nose closed.
- Place your mouth over the person's mouth to make a seal and give two slow breaths.
- Watch for the person's chest (but not the stomach) to rise.
- Follow up with one breath every 5 seconds.

Chest compressions for adults involve the following steps:

- Place the person on his or her back.
- Press hard and fast on the center of the chest.
- Keep your arms extended.

STEP 5: MONITOR THE PERSON'S RESPONSE

All people should be monitored for recurrence of signs and symptoms of opioid toxicity for at least 4 hours from the last dose of naloxone or discontinuation of the naloxone infusion. People who have overdosed on long-acting opioids should have more prolonged monitoring.^{2,10,13}

Most people respond by returning to spontaneous breathing. The response generally occurs within 2 to 3 minutes of naloxone administration. (Continue resuscitation while waiting for the naloxone to take effect.)^{2,10}

Because naloxone has a relatively short duration of effect, overdose symptoms may return.^{2,10,13} Therefore, it is essential to get the person to an emergency department or other source of medical care as quickly as possible, even if the person revives after the initial dose of naloxone and seems to feel better.

SIGNS OF OPIOID WITHDRAWAL. The signs and symptoms of opioid withdrawal in an individual who is physically dependent on opioids may include body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection (gooseflesh), sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, abdominal cramps, weakness, tearing, insomnia, opioid craving, dilated

FIVE ESSENTIAL STEPS FOR FIRST RESPONDERS

pupils, and increased blood pressure. These symptoms are uncomfortable, but not life threatening. After an overdose, a person dependent on opioids should be medically monitored for safety and offered assistance to get into treatment for opioid use disorder.

If a person does not respond to naloxone, an alternative explanation for the clinical symptoms should be considered. The most likely explanation is that the person is not overdosing on an opioid but rather some other substance or may be experiencing a non-overdose medical emergency.

In all cases, support of ventilation, oxygenation, and blood pressure should be sufficient to prevent the complications of opioid overdose and should be given priority if the response to naloxone is not prompt.

DO'S AND DON'TS WHEN RESPONDING TO OPIOID OVERDOSE

- DO attend to the person's breathing and cardiovascular support needs by administering oxygen or performing rescue breathing and/or chest compressions.
- DO administer naloxone and utilize a second dose, if no response to the first dose.
- DO put the person in the "recovery position" on the side, if you must leave the person unattended for any reason.
- DO stay with the person and keep the person warm.
- DON'T slap or forcefully try to stimulate the person; it will only cause further injury. If you cannot wake the person by shouting, rubbing your knuckles on the sternum (center of the chest or rib cage), or light pinching, 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 naloxone.
- 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.

NOTE: All naloxone products have an expiration date, so it is important to check the expiration date and obtain replacement naloxone as needed.

INFORMATION FOR PRESCRIBERS

Opioid overdose is a major public health problem. In 2016, more than 42,000 people died of an opioid-related overdose.¹ Overdoses are experienced by both men and women of all ages, ethnicities, and demographic and socioeconomic characteristics and involve both illicit opioids such as heroin and illicitly manufactured fentanyl and prescription opioid analgesics such as oxycodone, hydrocodone, fentanyl, and methadone.¹

Health care providers can reduce the toll of opioid overdose through:

- Opioid stewardship and implementing the opioid prescribing guidelines of the Centers for Disease Control and Prevention (CDC; <https://www.cdc.gov/drugoverdose/prescribing/guideline.html>).
- Offering risk reduction messaging and prescribing naloxone when potentially dangerous behaviors or opioid doses are identified.
- Treating opioid use disorder (OUD) when individuals screen positive for the disorder and when their substance use histories and further examination indicate a current OUD.
- Treating opioid overdose emergencies.

Federally funded Substance Abuse and Mental Health Services Administration (SAMHSA) continuing medical education courses are available at no charge at <https://pcssnow.org/> and <https://www.OpioidPrescribing.com>.

OPIOID STEWARDSHIP

The CDC developed guidelines to improve communication between prescribers and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including OUD, overdose, and death.²⁰ The 12 recommendations for prescribing opioids for adults with chronic pain

outside of active cancer, palliative, and end-of-life care are targeted toward primary care providers and are organized into three overarching categories.

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety. If these goals are not met, then the opioid therapy should be tapered and stopped and other approaches should be considered.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy as well as patient and clinician responsibilities for managing therapy.

OPIOID SELECTION, DOSAGE, DURATION, FOLLOW-UP, AND DISCONTINUATION

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual

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benefits and risks when increasing dosage to =50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to more than 90 MME/day or carefully justify a decision to titrate dosage to more than 90 MME/day.

6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three or fewer days will often be sufficient; more than 7 days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

ASSESSING RISK AND ADDRESSING HARMS OF OPIOID USE

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate these into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (more than 50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program

(PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every time a prescription is written to every 3 months.

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for use of prescribed medications as well as use of other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with OUD.

RISK REDUCTION MESSAGING, OVERDOSE PREVENTION EDUCATION, AND NALOXONE PRESCRIPTION

When potentially harmful behaviors are identified (e.g., high-volume use of opioids; taking opioids in combination with alcohol, benzodiazepines, or other respiratory depressants; using illicit opioids where contents of substance cannot be confirmed), it is important to offer education that can reduce that individual's risk for overdose. Providing basic risk reduction messaging, overdose prevention education, and a naloxone prescription can be lifesaving interventions.

Risk reduction messaging from a prescriber may include information about which other medications a patient is taking that are respiratory depressants; benzodiazepines, anti-seizure medications, and many psychiatric medications are respiratory depressants. Letting

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the patient know that mixing these substances with opioids or taking more than prescribed in combination with opioids may increase his or her risk of overdose.

Naloxone competitively binds opioid receptors and is the antidote to acute opioid toxicity. Naloxone will not reverse alcohol, benzodiazepine, or other types of toxicity because it attaches only to the opioid receptors. Community-based naloxone distribution programs have not been shown to increase drug use and have, in fact, been shown to increase treatment engagement. Most patients respond positively to naloxone prescriptions, and some report additional positive behavioral changes following overdose education and naloxone prescription.²¹ Naloxone prescriptions could be (1) a naloxone kit containing naloxone vials, syringes, and needles; (2) intranasal naloxone spray, which delivers a single dose of naloxone into one nostril via a prefilled intranasal spray; or (3) a naloxone auto-injector, which delivers a single dose of naloxone to the outer thigh via a handheld auto-injector.¹²

Patients who are candidates for naloxone include individuals:²⁰

- With a history of overdose.
- With a history of substance use disorder.
- Who are taking benzodiazepines with opioids.
- Who are at risk for returning to a high dose to which they are no longer tolerant (e.g., former inmates recently released from prison, patients leaving detoxification facilities).
- Who are taking higher dosages of opioids (more than 50 MME/day).

It may also be advisable to suggest that the at-risk patient create an “overdose plan” to share with friends, partners, and/or caregivers. Such a plan would contain information on the signs of overdose and how to administer naloxone or otherwise provide emergency care (as by calling

911). Examples of patient handouts in seven languages are available from the State of California Department of Consumer Affairs and can be found at http://www.pharmacy.ca.gov/licensees/naloxone_info.shtml.

OUD TREATMENT

If a patient has an OUD, arrange for and/or provide treatment. Treating OUD with Food and Drug Administration (FDA)-approved medications (methadone, buprenorphine with or without naloxone, and naltrexone) is an evidence-based approach. Methadone treatment for OUD can be provided only in licensed opioid treatment programs (OTPs). Buprenorphine can be prescribed by physicians, nurse practitioners, and physician assistants who have completed additional training and have obtained a waiver to prescribe this medication. Naltrexone is an injectable medication that can be prescribed by any provider with prescribing authority. It is recommended that each medication be prescribed in conjunction with behavioral and psychosocial treatment.¹⁵ For more information on these medications, see SAMHSA’s *Medication-Assisted Treatment of Opioid Use Disorder Pocket Guide* in the resources section or visit <https://store.samhsa.gov/product/Medication-Assisted-Treatment-of-Opioid-Use-Disorder-Pocket-Guide/SMA16-4892PG>. To identify treatment providers in your area, visit SAMHSA’s Behavioral Treatment Services Locator at <https://findtreatment.samhsa.gov/> or SAMHSA’s Buprenorphine Treatment Practitioner Locator at <https://www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator>.

TREATING OPIOID OVERDOSE

In the time it takes for an overdose to become fatal, it is possible to reverse the respiratory depression and other effects of opioids through respiratory support and administration of the opioid antagonist naloxone.¹⁰ Naloxone is approved by the FDA and has been used for decades to reverse overdose and resuscitate individuals who have overdosed on opioids. The routes of administration for naloxone are intravenous, intranasal, intramuscular, and subcutaneous. All naloxone products are effective in reversing opioid overdose, including fentanyl-involved opioid overdoses, although fentanyl-involved overdoses may require more naloxone.

The safety profile of naloxone is remarkably high, especially when used in low doses and titrated to effect.² If given to individuals who are not opioid intoxicated or opioid dependent, naloxone produces no clinical effects, even at high doses. Moreover, although rapid opioid withdrawal in opioid-tolerant patients may be unpleasant, it is not life threatening.

Naloxone should be part of an overall approach to known or suspected opioid overdose that incorporates the steps below.

RECOGNIZE THE SIGNS OF OVERDOSE. An opioid overdose requires rapid diagnosis. The most common signs of overdose include:¹⁰

- Unconsciousness or inability to awaken orally or upon sternal rub.
- Slow or shallow breathing or breathing difficulty such as choking sounds or a gurgling/snoring noise from a patient who cannot be awakened.
- Fingernails or lips turning blue/purple.
- Slow heartbeat and/or low blood pressure.

SUPPORT RESPIRATION. Supporting respiration is a critical intervention for opioid overdose and may be lifesaving on its own. Begin CPR (technique based on rescuer's level of training).¹⁹ Ideally, individuals who are experiencing opioid overdose should be ventilated with oxygen before naloxone is administered to reduce the risk of acute lung injury.²

ADMINISTER NALOXONE. Naloxone competitively binds opioid receptors and is the antagonist of choice for the reversal of acute opioid toxicity. Naloxone should be administered to anyone who presents with signs of opioid overdose or when opioid overdose is suspected. Naloxone can be given by injection intranasally, intramuscularly, subcutaneously, or intravenously.¹²

PREGNANT PATIENTS. Naloxone can be used in life-threatening opioid overdose circumstances in pregnant women.¹⁴

MONITOR THE PATIENT'S RESPONSE. Patients should be monitored for reemergence of signs and symptoms of opioid toxicity for at least 4 hours following the last dose of naloxone; however, patients who have overdosed on long-acting opioids require more prolonged monitoring.^{2,13}

Most patients respond to naloxone by returning to spontaneous breathing, with mild withdrawal symptoms.² The response generally occurs within 2 to 3 minutes of naloxone administration. Continue rescue breathing while waiting for the naloxone to take effect.

The duration of effect of naloxone depends on dose and route of administration and is shorter than the effects of some opioids. Patients should be observed after administration for reemergence of overdose symptoms. The goal of naloxone therapy should be restoration of adequate spontaneous breathing, but not necessarily complete arousal.²²

More than one dose of naloxone may be required to revive the patient. Those who have

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taken longer-acting opioids or opioid partial agonists may require additional doses, additional intravenous bolus doses, or an infusion of naloxone.¹³ Therefore, it is essential to get the person to an emergency department or other source of acute care as quickly as possible, even if the person revives after the initial dose of naloxone and seems to feel better.

SIGNS OF OPIOID WITHDRAWAL.

Withdrawal triggered by naloxone can feel unpleasant. Some people may become agitated or confused, which may improve by providing reassurance and explaining what is happening. The signs and symptoms of opioid withdrawal in an individual who is physically dependent on opioids may include body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection (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.²³ These symptoms are uncomfortable, but not life threatening unless vomiting and diarrhea result in extreme dehydration. After an overdose, a person dependent on opioids should be medically monitored for safety and offered treatment for OUD.

NO RESPONSE TO NALOXONE. If a patient does not respond to naloxone, an alternative explanation for the clinical symptoms should be considered. The most likely explanation is that the person is not overdosing on an opioid but rather some other substance or may even be experiencing a non-overdose medical emergency.

Support of ventilation, oxygenation, and blood pressure should be sufficient to prevent the complications of opioid overdose and should be given the highest priority if the patient's response to naloxone is not prompt.

FENTANYL-INVOLVED OVERDOSE.

Suspected opioid overdoses, including suspected fentanyl-involved overdoses, should be treated according to standard protocols.^{16,17} However, because of the higher potency of fentanyl and fentanyl analogs compared to that of heroin, larger doses of naloxone may be required to reverse the opioid-induced respiratory depression from a fentanyl-involved overdose.^{11,15,16,17}

Many anecdotal accounts report more rapid respiratory depression with fentanyl than with heroin, although other reports do not reflect such rapid depression.¹⁷

Because of these effects, quicker oxygenation efforts and naloxone delivery may be warranted compared to heroin-only overdose. However, naloxone is an appropriate response for all opioid overdoses, including fentanyl-involved overdoses.

NOTE: All naloxone products have an expiration date. It is important to check the expiration date and obtain replacement naloxone as needed.

LEGAL AND LIABILITY CONSIDERATIONS

Health care professionals who are concerned about legal risks associated with prescribing naloxone may be reassured that prescribing naloxone to manage opioid overdose is consistent with the drug's FDA-approved indication, resulting in no increased liability so long as the prescriber adheres to general rules of professional conduct. Most state laws and regulations now permit physicians to prescribe naloxone to a third party, such as a caregiver.⁸ More information on state policies is available from the Prescription Drug Abuse Policy System's Naloxone Overdose Prevention Laws web page (<http://www.pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139>) or from individual state medical boards.

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CLAIMS CODING AND BILLING

Most private health insurance plans, Medicare, and Medicaid cover naloxone for the treatment of opioid overdose, but policies vary by state. The cost of take-home naloxone should not be a prohibitive factor. Many community pharmacies stock naloxone routinely, and those that do not can always order it. If you are caring for a large population of patients who are likely to benefit from naloxone, you may wish to notify the pharmacy when you implement naloxone prescribing as a routine practice.

The codes for Screening, Brief Intervention, and Referral to Treatment (SBIRT) can be used to bill time for counseling a patient about how to recognize overdose and how to administer naloxone. Billing codes for SBIRT are as follows:

- Commercial Insurance: CPT 99408 (15 to 30 minutes), 99409 (greater than 30 minutes)
- Medicare: G0396 (15 to 30 minutes), G0397 (greater than 30 minutes)

- Medicaid: H0049 (alcohol and/or drug screening), H0050 (alcohol and/or drug screening, brief intervention, per 15 minutes)

For counseling and instruction on the safe use of opioids, including the use of naloxone outside the context of SBIRT services, the provider should document the time spent in medication education and use the E&M (Evaluation and Management) code that accurately captures the time and complexity. For example, for new patients deemed appropriate for opioid pharmacotherapy and when a substantial and an appropriate amount of additional time is used to provide a separate service such as behavioral counseling (e.g., opioid overdose risk assessment, naloxone administration training), consider using modifier–25 in addition to the E&M code.

In addition, when using an evidence-based opioid use disorder or overdose risk factor assessment tool/screening instrument, CPT Code 99420 (Administration and interpretation of health risk assessment instrument) can be used for patients with commercial insurance.

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RESOURCES FOR PRESCRIBERS

Additional information on prescribing opioids for chronic pain is available at the following websites:

- <https://www.opioidprescribing.com>: Sponsored by the Boston University School of Medicine, with support from SAMHSA, the OpioidPrescribing.org site presents course modules on various aspects of prescribing opioids for chronic pain. Continuing medical education credits are available at no charge.
- <https://pcssnow.org/>: Sponsored by the American Academy of Addiction Psychiatry in collaboration with other specialty societies and with support from SAMHSA, the Providers Clinical Support System offers multiple resources related to opioid prescribing and the diagnosis and management of OUD. The site also is the source for Drug Addiction Treatment Act of 2000 waiver education requirements.
- <https://www.drugabuse.gov/nidamed-medical-health-professionals/cmece-activities#opioids>: NIDAMED's mission is to disseminate science-based resources to health professionals on the causes and consequences of drug use and addiction, and advances in pain management. Continuing medical education credits are available at no charge.
- <https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm163647.htm>: The Risk Evaluation and Mitigation Strategy website provides physician training and patient education on OUD treatment medications as required by the FDA for extended-release and long-acting opioid analgesics.
- <http://prescribetoprevent.org>: Compiled by prescribers, pharmacists, public health workers, lawyers, and researchers working on overdose prevention and naloxone access, this privately funded site provides health care providers with resources to educate patients on how to reduce overdose risk and provide naloxone rescue kits to patients.
- <https://store.samhsa.gov/product/Medication-Assisted-Treatment-of-Opioid-Use-Disorder-Pocket-Guide/SMA16-4892PG>: SAMHSA's *Medication-Assisted Treatment for Opioid Use Disorder Pocket Guide* provides practical information for clinicians on medications to treat OUD.
- <https://store.samhsa.gov/product/SMA18-5063FULLDOC>: SAMHSA's Treatment Improvement Protocol 63: *Medications for Opioid Use Disorders* provides in-depth information for health care and addiction professionals, policymakers, patients, and families.

SAFETY ADVICE FOR PATIENTS & FAMILY MEMBERS

WHAT ARE OPIOIDS?

Opioids include prescription medications used to treat pain such as morphine, codeine, methadone, oxycodone, hydrocodone, fentanyl, hydromorphone, and buprenorphine, as well as illicit drugs such as heroin.

Opioids work by binding to specific receptors in the brain, spinal cord, and gastrointestinal tract. In doing so, they diminish the body's perception of pain. However, opioids can also have an impact on other systems of the body, such as altering mood, slowing breathing, and causing constipation. Opioid receptor binding causes the signs and symptoms of overdose as well as the euphoric effects or "high" with opioid use.

A variety of effects can occur after a person takes opioids, ranging from pleasure to nausea and vomiting, severe allergic reactions (anaphylaxis), and overdose, in which breathing and heartbeat slow or even stop.

Opioid overdose can be due to many factors. For example, overdose can occur when a patient deliberately misuses a prescription, uses an illicit opioid (such as heroin), or uses an opioid contaminated with other even more potent opioids (such as fentanyl). Overdose can also occur when a patient takes an opioid as directed but the prescriber miscalculated the opioid dose, when an error was made by the dispensing pharmacist, or when the patient misunderstood the directions for use. It can also occur when opioids are taken with other medications—for example, prescribed medications such as benzodiazepines or other psychotropic medications that are used in the treatment of mental disorders—or with illicit drugs or alcohol that may have adverse interactions with opioids. At particular risk are individuals who use opioids and combine them with benzodiazepines, other sedative hypnotic agents, or alcohol, all of which cause respiratory depression.^{2,24}

PREVENTING OVERDOSE

If you are concerned about your own use of opioids, don't wait! Talk with the health care professionals who prescribed the medications for you. If you are concerned about family members or friends, urge them to talk to whoever prescribed their medications.

Effective treatment of an opioid use disorder can reduce the risk of overdose and help a person who is misusing or addicted to opioid medications attain a healthier life. Opioid use disorder is a chronic disease, much like heart disease. An evidence-based practice for treating opioid addiction is the use of Food and Drug Administration-approved medications, along with counseling and other supportive services. These services are available at Substance Abuse and Mental Health Services Administration (SAMHSA)-certified and Drug Enforcement Administration-registered opioid treatment programs and from specialty substance use disorder treatment programs. In addition, physicians and other practitioners, including nurse practitioners and physician assistants who are trained to provide treatment for opioid addiction in office-based and other settings with medications such as buprenorphine/naloxone and naltrexone, may be available in your community. For more information, see the Resources section at the end of this toolkit.

IF YOU SUSPECT AN OVERDOSE

An opioid overdose requires immediate medical attention. An essential first step is to get help from someone with medical expertise as soon as possible. **Call 911 immediately** if you or someone you know exhibits any of the signs listed below. All you have to say is "Someone is unresponsive and not breathing." Give a specific address and/or description of your location.

SAFETY ADVICE FOR PATIENTS & FAMILY MEMBERS

Signs of **OVERDOSE**, which is a life-threatening emergency, include the following:

- The face is extremely pale and/or clammy to the touch.
- The body is limp.
- Fingernails or lips have a blue or purple cast.
- The person is vomiting or making gurgling noises.
- The person cannot be awakened from sleep or cannot speak.
- Breathing is very slow or stopped.
- The heartbeat is very slow or stopped.

Signs of **OVERMEDICATION**, which may progress to overdose, include:

- Unusual sleepiness or drowsiness.
- Mental confusion, slurred speech, or intoxicated behavior.
- Slow or shallow breathing.
- Extremely small “pinpoint” pupils.
- Slow heartbeat or low blood pressure.
- Difficulty being awakened from sleep.

WHAT IS NALOXONE?

Naloxone is an antidote to opioid overdose. It is an opioid antagonist that is used to reverse the effects of opioids. Naloxone works by blocking opioid receptor sites. It is not effective in treating overdoses of benzodiazepines, barbiturates, clonidine, GHB, or ketamine. It is also not effective in treating overdoses of stimulants such as cocaine and amphetamines (including methamphetamine and MDMA). However, if opioids are taken in combination with other sedatives or stimulants, naloxone may be helpful.

Suspected fentanyl-involved overdoses should be treated with naloxone.¹⁷ However, because of the higher potency of fentanyl and fentanyl analogs compared to that of heroin, larger doses of naloxone may be required to reverse the opioid-induced respiratory depression from a fentanyl-involved overdose.^{11,15,17} Quicker oxygenation efforts and naloxone delivery may be warranted compared to heroin-only overdose.

NALOXONE STORAGE

Store naloxone in a safe and quickly accessible place at room temperature and protected from light. Keep all medicine in a safe place where children or pets cannot reach it.

SUMMARY: HOW TO AVOID OPIOID OVERDOSE

1. Take medication only if it has been prescribed to you by your doctor. Make sure to tell your doctor about all medications you are taking.
2. Do not take more medication or take it more often than instructed.
3. Call your doctor if your pain gets worse.
4. Never mix pain medications with alcohol, sleeping pills, or any illicit substance.
5. Learn the signs of overdose and how to use naloxone to keep an overdose from becoming fatal.
6. Teach your family members and friends how to respond to an overdose.
7. Dispose of unused medication properly.

READ MORE. The Food and Drug Administration’s naloxone webpage provides more information at <https://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm472923.htm>.

RECOVERING FROM OPIOID OVERDOSE

RESOURCES FOR OVERDOSE SURVIVORS AND FAMILY MEMBERS

Survivors of opioid overdose have experienced a life-changing and traumatic event. They have had to deal with the emotional consequences of overdosing, which can involve embarrassment, guilt, anger, and gratitude, all accompanied by the discomfort of opioid withdrawal. Most need the support of family and friends to take the next steps toward recovery.

While many factors can contribute to opioid overdose, it is almost always an accident. Moreover, the underlying problem that led to opioid use—most often pain or substance use disorder—still exists and continues to require attention.¹⁴

The individual who has experienced an overdose is not the only one who has endured a traumatic event. Family members often feel judged or inadequate because they could not prevent the overdose. It is important for family members to work together to help the overdose survivor obtain the help that he or she needs.

FINDING A NETWORK OF SUPPORT

As with any health condition, it is not a sign of weakness to admit that a person or a family cannot deal with overdose and its associated issues without help. It takes real courage to reach out to others for support and to connect with members of the community to get help.

Health care providers, including those who specialize in treating substance use disorders, can provide structured, therapeutic support and feedback.

If the survivor's underlying problem is pain, referral to a pain specialist may be in order. If it is addiction, the patient should be referred to an addiction specialist for assessment and treatment by a physician specializing in the treatment of opioid addiction in a residential treatment program or in a federally certified opioid treatment program. In each case, counseling can help the individual manage his or her problems in a healthier way. The path to recovery can be a dynamic and challenging process, but there are ways to help.

In addition to receiving support from family and friends, overdose survivors can access a variety of community-based organizations and institutions, such as:

- Health care and behavioral health providers.
- Peer-to-peer recovery support groups such as Narcotics Anonymous.
- Faith-based organizations.
- Educational institutions.
- Neighborhood groups.
- Government agencies.
- Family and community support programs.

RECOVERING FROM OPIOID OVERDOSE

RESOURCES

Substance Abuse and Mental Health Services Administration (SAMHSA)

- National Helpline: 1-800-662-HELP (4357) or 1-800-487-4889 (TDD, for hearing impaired)
- Behavioral Health Treatment Services Locator (search by address, city, or ZIP Code): <https://findtreatment.samhsa.gov/>
- Buprenorphine Treatment Practitioner Locator (search by address, city, or ZIP Code): <https://www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator>
- Single State Agencies for Substance Abuse Services: <https://www.samhsa.gov/sites/default/files/ssa-directory.pdf>
- State Opioid Treatment Authorities: <https://dpt2.samhsa.gov/regulations/smalist.aspx>
- SAMHSA Publications Ordering (all SAMHSA Store products are available at no charge): <https://store.samhsa.gov>; 1-877-SAMHSA-7 (1-877-726-4727)

Centers for Disease Control and Prevention (CDC)

- Understanding the Epidemic: <https://www.cdc.gov/drugoverdose/epidemic>
- Poisoning: <https://www.cdc.gov/homeandrecreationalsafety/poisoning>
- CDC Guideline for Prescribing Opioids for Chronic Pain: <https://www.cdc.gov/drugoverdose/prescribing/guideline.html>

Faces & Voices of Recovery

- Shaping the Future of Recovery: <https://facesandvoicesofrecovery.org/>

Project Lazarus

- Learn About the Project Lazarus Model: <https://www.projectlazarus.org>

Harm Reduction Coalition

- Main Page: <http://www.harmreduction.org>

Prevent & Protect

- Tools for conducting overdose prevention and naloxone advocacy, outreach, and communication campaigns: <http://prevent-protect.org/community-resources-1/>

Prescribe to Prevent

- Prescribe Naloxone, Save a Life: <http://prescribetoprevent.org>

SAMHSA does not specifically endorse any group, and appropriateness should be determined at the local level. Many groups are appropriate for loved ones and family members. Referrals are encouraged to groups that have received explicit endorsements from those who have been intimately affected by opioid use and overdose.

- Grief Recovery After a Substance Passing is for those who have lost a loved one: <http://grasphelp.org/>.
- Learn 2 Cope is for families with loved ones who have a substance use disorder: <https://www.learn2cope.org/>.
- The International Overdose Awareness Day website has a list of worldwide events: <https://www.overdoseday.com/>.

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