

Responding to an Overdose

Go low and slow!

In most cases, a 3-4mg dose of nasal spray naloxone or 0.4mg dose of intramuscular naloxone is all that is needed to reverse an overdose (2). Using the least naloxone possible to restore independent breathing before transporting the individual for further medical monitoring and care can reduce risk of more uncomfortable withdrawal symptoms and the length of time these symptoms last.

Rescue Breathing and Chest Compressions

A dose of naloxone can take up to 2-5 minutes to take effect. It's important to supplement naloxone administration with rescue breathing and chest compressions - if you're CPR certified or being instructed by a 911 operator. This is particularly true if the person's lips or fingers have a grey or bluish tone, have gurgled or labored breathing, or do not appear to be breathing at all. Lack of oxygen can lead to long term health consequences in as little as 4 minutes.



Naloxone Dosing Considerations

Naloxone administration is a bedrock component of overdose response efforts. As stronger opioids, such as fentanyl, have increasingly dominated the available drug supply, the pharmaceutical industry has developed and marketed stronger formulations of the lifesaving drug, with the purported goal of increasing the success of overdose reversals. **There is currently no evidence that administration of higher doses of naloxone improves odds of overdose survival (1).** There are, however, a number of downsides and risks to the over-administration of naloxone that first responders, loved ones, and other community bystanders should take into account, including risk of precipitated withdrawals, which may lead to decreased post-overdose support and linkage to care.

State and Local Health Departments have a lot of purchasing power for naloxone products and are instrumental in getting this lifesaving medication out into their communities (3). People who use drugs (PWUD) are most likely to give or receive naloxone and should be core to decision making about naloxone purchasing and distributing. When possible, offer a variety of products to suit preferences and needs.

Availability and Cost-Effectiveness

There are currently at least seven different types of naloxone products available in the US. Generic 0.4mg naloxone that can be administered intramuscularly or intravenously has been around the longest and is the least costly (2). This product has been administered by lay rescuers and trained professionals for over 20 years. Narcan branded 4mg intranasal spray and several generic 4mg IN sprays are available as well.

Narcan and another IN product, RiVive, are the only naloxone products currently available without a prescription (4). Retail Narcan costs roughly \$47 for a package of two 4mg sprays. RiVive costs \$36 for the two 3mg sprays. Both products are shown to be effective doses to reverse opioid overdoses.

In the last five years, several higher-dose naloxone products have emerged, such as Kloxxado (IN, 8mg) and Zimhi (IM, 5mg). Kloxxado is twice the dose as Narcan and Zimhi is 25 times greater dose than generic IM naloxone (2).

There is also a newer product, an opioid receptor antagonist called nalmefene, the active ingredient in Opvee, an IN spray. Nalmefene is a higher potency product than naloxone. Typically, 3-4mg IN doses of naloxone can be in a person's system for 1-2 hours after administration; Opvee can last 12 hours. A two-dose package of Opvee ranges \$75-\$98.

High Dose Naloxone Pushback

Nalmefene has drawn criticism from medical professionals, as well as PWUD, for its high potency. For example, a joint statement by the American College of Medical Toxicology and American Academy of Clinical Toxicology in September 2023 urged caution and recommended that nalmefene not replace naloxone as the standard of care for overdose responses, citing concerns of prolonged precipitated withdrawal and increased need for medical observation (5). Adding to this, in 2024, a group of harm reduction experts put out a call to action based on the discussion featured at the Compassionate Overdose Response Summit & Naloxone Dosing Meeting held earlier in the year (6). The group first and foremost advocated for PWUD involvement in the research and development of opioid overdose reversal products. In addition, they called for the need for regulatory agencies and pharmaceutical manufacturers to communicate the risk and duration of withdrawal associated with higher dose and longer acting opioid antagonists, such as nalmefene. Third, the group called for the inclusion of at least two doses of an IM product containing 0.4mg or an IN product containing less than or equal to 4 mg within take-home naloxone kits, writing that there was no use for high dose and long-acting opioid antagonists in acute opioid overdose response. Finally, the group called for the emphasis of restoration of breathing, avoiding withdrawal, and compassionate post overdose care and support within overdose response educational materials and trainings. While a variety of naloxone products should be offered as they are available, it is important to prioritize PWUD voices and keep abreast of emerging research related to higher dose naloxone.

Over-Administration and the Negative Consequences of Increased Risk of Precipitated Withdrawal Symptoms

Increased dosing is more likely to cause precipitated withdrawal, as naloxone rapidly binds to opioid receptors in the brain and blocks the effects of opioids such as heroin or fentanyl.

Precipitated withdrawal is an intensely uncomfortable and often painful state characterized by the following symptoms (2):

- Body aches and abdominal cramps
- Increased heart rate (tachycardia) and increased blood pressure
- Sweating and fever
- Runny nose and sneezing
- Goose bumps, shivering, and trembling
- Diarrhea, nausea, and vomiting
- Nervousness, restlessness and irritability

Overdose Aftercare

Patience and Kindness

Coming out of an overdose can be jarring or uncomfortable.



Being patient and kind to a person who has experienced an overdose can help them feel safer, supported, and better able to make decisions about receiving care. Use short simple sentences in a calm tone, letting the person know that they received naloxone and medical support is on the way.

Know Your Good Samaritan Laws

Laws pertaining to safe reporting of overdose vary state to state, and many have changed in recent years. Being up to date on these laws and sharing them with PWUD, their loved ones and community members, can help ensure that more people will feel comfortable calling for help when an overdose occurs, staying for assistance, and seeking medical attention following an overdose emergency. This can decrease risk of further medical complications and increase access to medical care and other resources.



Conclusion

Naloxone is only effective at reversing opioid overdoses, but there is no greater risk of harm to a person who may be experiencing another health emergency or used substances that may contain unknown adulterants. Administering naloxone, providing rescue breaths, and getting a person prompt medical attention, are the best ways to help someone you suspect may be having an opioid overdose. Providing enough naloxone to reverse the overdose, 3mg intranasally or 0.4mg intramuscularly, reverses most overdoses within a 2-minute period. If further doses are required, be sure to continue to provide rescue breaths every ten seconds and allow the subsequent doses time to work. Precipitated withdrawal can be extremely uncomfortable but will subside with time. Providing a person with a minimally necessary dose of naloxone can reduce the time of discomfort and decrease stress and harm for all involved.



References

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