



# Naloxone Training

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L.A. Care Opioid Use Disorder Conference In Collaboration  
with Los Angeles County Department of Public Health  
May 18, 2024, Almansor Court, Alhambra, CA

# Disclosures

The following CME planners and faculty do not have relevant financial relationships with ineligible companies in the past 24 months:

- Leilanie Mercurio, L.A. Care PCE Program Manager, CME Planner.
- Kevin Burns, MD, MPH, L.A. Care CalAIM Medical Director, CME Planner.
- Brian Hurley, MD, MBA, FAPA, DFASAM, Medical Director, Substance Abuse Prevention and Control, County of Los Angeles, Department of Public Health, CME Planner.
- Winter Roth, PharmD, USC Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences, CME Faculty.

An ineligible company is any entity whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Commercial support was not received for this CME/CE activity.

# Learning Objectives

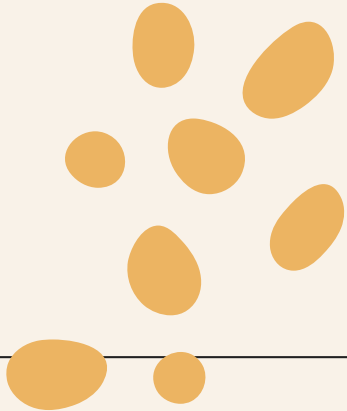
1. Identify at least two (2) signs and symptoms of an opioid overdose.
2. Specify two (2) important factors of naloxone's pharmacokinetics in the treatment of opioid overdose.
3. Demonstrate proper naloxone administration technique.
4. Compare and contrast the different opioid overdose reversal agents (dose, route, onset, and duration of action).

# Frequently Asked Questions

1. How many doses of Narcan® can be administered? Are there any adverse consequences to administering multiple doses?
2. How long does intranasal Narcan® last in someone's system?
3. Who should carry Narcan®? Can Narcan® be self-administered?
4. What is the difference between Narcan® and Kloxxado®? Is one better than the other?

# Important Definitions:

- **Opioids** – medications used for pain management (ex. oxycodone, hydrocodone, codeine, heroin, fentanyl, etc.)
- **Tolerance** – needing a higher dose of the drug to get the same effect
- **Withdrawal** – suddenly stopping or reducing the amount of drug taken, leading to unpleasant symptoms (for opioids these include diarrhea, vomiting, goosebumps, yawning, pain, and anxiety)
- **Overdose** – taking more of a substance than the body can handle, leading to impaired organ function



# Epidemiology

# Epidemiology

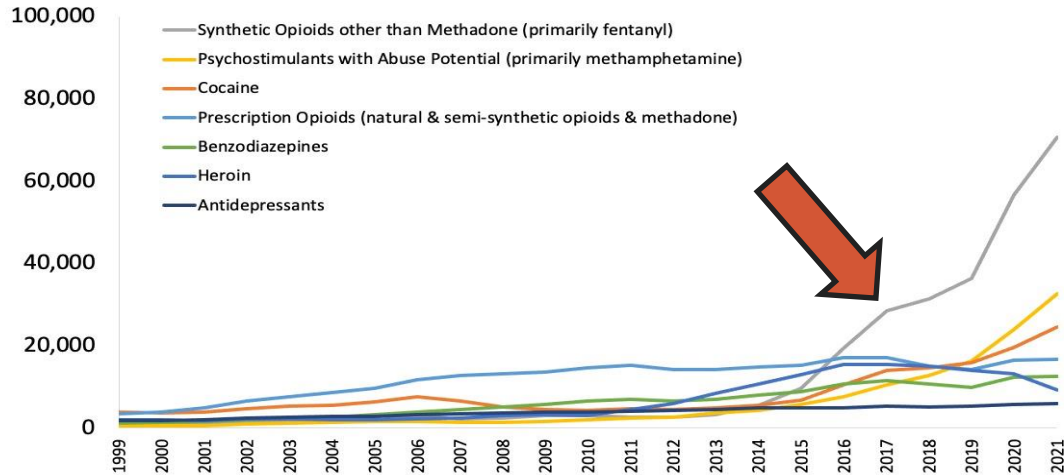
- In the last two decades, **564,000 people** died from an opioid overdose

- Drug overdose deaths  **17%** between 2021 and 2023

- ***75% of drug overdoses were opioid overdoses***
- ***88% of opioid overdoses were related to fentanyl***

# Epidemiology

Figure 2. National Drug-Involved Overdose Deaths\*, Number Among All Ages, 1999-2021



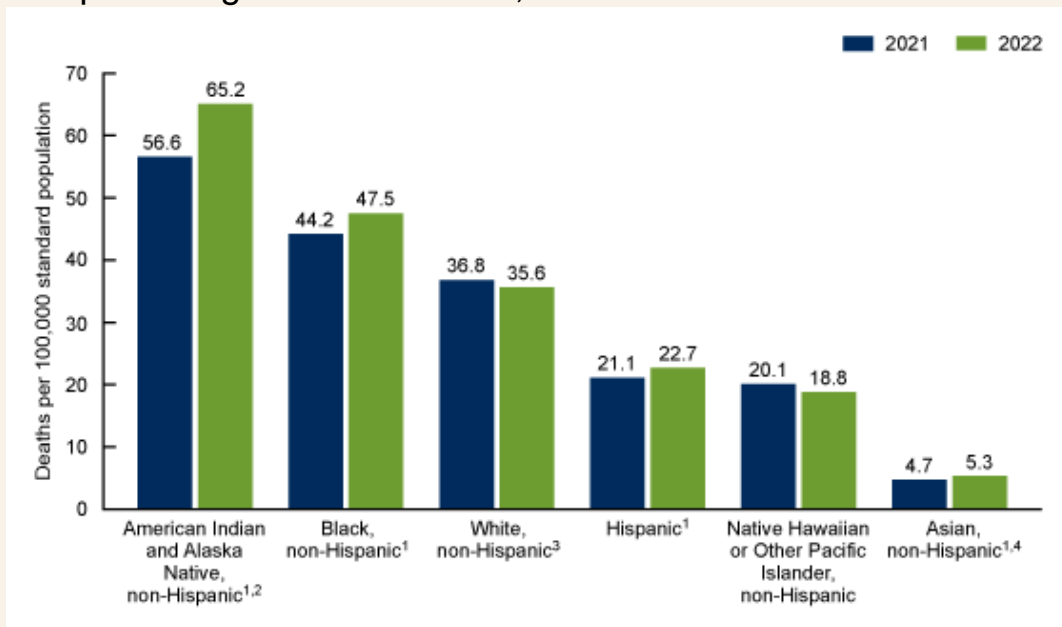
*Synthetic opioid overdose deaths increased by 60% from 2019 to 2023*

\*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.



# Overdose Disparities

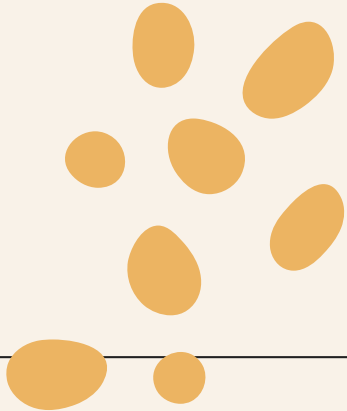
Age-adjusted rate of drug overdose deaths, by race and Hispanic origin: United States, 2021 and 2022



- Highest among American Indian and Alaska Native (AI/AN) people
- Greatest percent increase among AI/AN people
- Lowest among Asian people

# Overdose Disparities

- Overdose death rates increased:
  - 44% for Black people
  - 39% for AI/AN people
- Overdose deaths were:
  - **7X higher** for Black men than White men
  - **2X higher** for AI/AN women than White women
- Areas with **greater income inequality** have higher rates of overdose deaths
- Lower proportion of people from racial/ethnic minority groups receive treatment for substance use disorder



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# Opioid Overdose

# Signs and Symptoms of Opioid Intoxication



Pinpoint pupils



"Nodding out"



Slurred speech

# Signs and Symptoms of an Opioid Overdose



Blue fingernails and/or lips



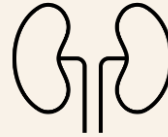
Cannot be awakened



Cold/clammy skin

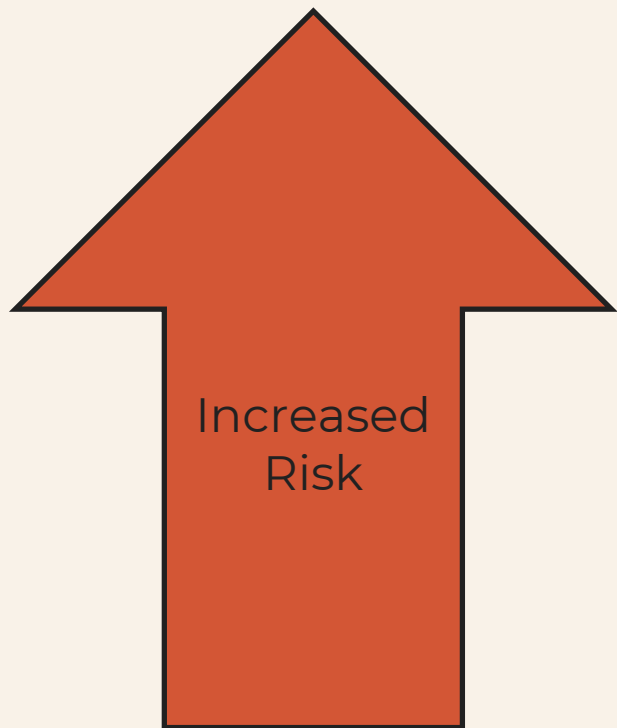


Limp body



Breathing and/or heart rate slows or stops

# Overdose Risk



- Taking amount > tolerance
- Underlying heart/lung condition
- Combining with other sedating substances (ex. alcohol, benzodiazepines)
- Using alone

# Overdose Risk



Decreased  
Risk

- Testing contents
- Obtaining from regulated source
- Using with others



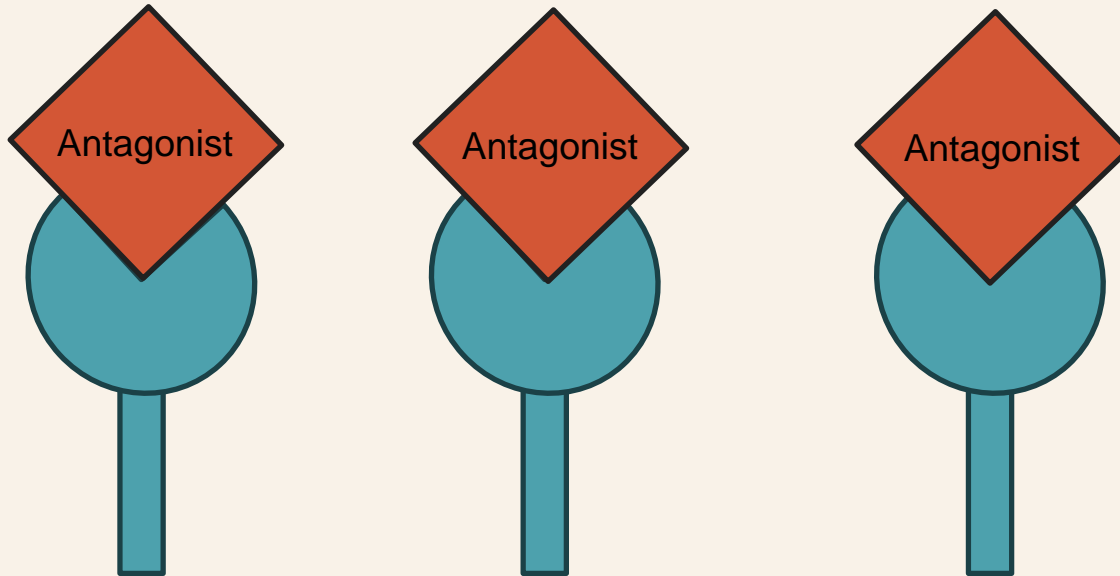
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# Reversal Agents



# Reversal Agent Mechanism of Action

- Pharmacological Class: Opioid antagonists



*Blocks opioid effects and restores breathing*

# Narcan® (naloxone)

- 4 mg nasal spray
- Pharmacokinetics:
  - Onset of Action: ~3 mins
  - Half-life: ~2 hours
  - Duration of Action: ~30-120 mins
- Adverse Effects: opioid withdrawal symptoms (body aches, sweating, piloerection, yawning, nervousness, restlessness or irritability, diarrhea, nausea or vomiting, abdominal cramps)

# Narcan® Administration

## 1. Identify Overdose and Check for Response

- Ask person if they are okay and/or shout their name
- Shake person's shoulders and firmly rub the middle of their chest
- Check for signs and symptoms of opioid overdose



# Narcan® Administration

## 2. Administer Narcan®

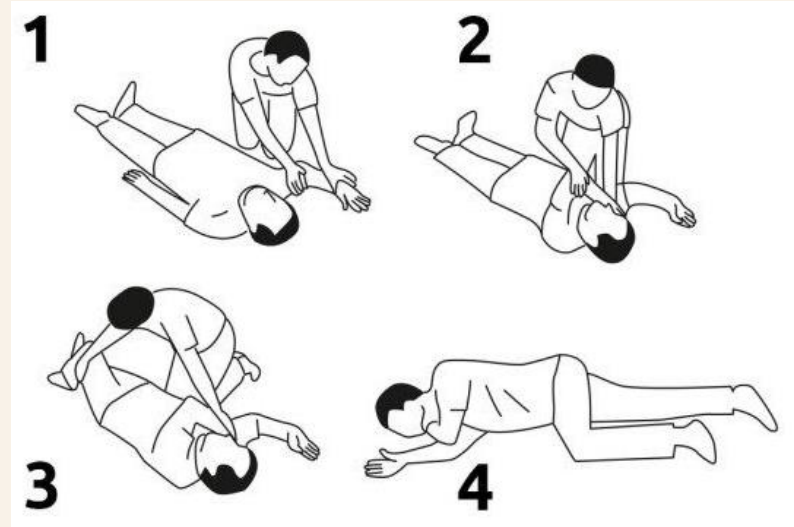
- Lay person on their back
- Hold Narcan® with thumb on the plunger
- Gently insert Narcan® into one nostril until your fingers are against the bottom of the person's nose
- Press nozzle firmly
- Remove Narcan® from the nostril



# Narcan® Administration

## 3. Call for emergency medical help

- Call 9-1-1 right away
- Move person onto their side into the recovery position
- Repeat Narcan® dose every 2-3 minutes if person does not wake up or breathe normally

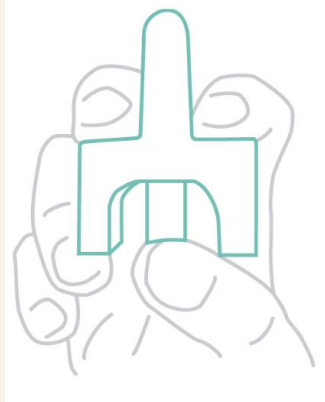


# Kloxxado® (naloxone)

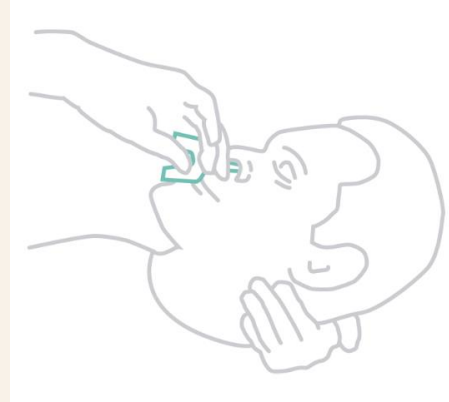
- **8 mg** nasal spray
- Pharmacokinetics:
  - Onset of Action: ~3 mins
  - Half-life: ~2 hours
  - Duration of Action: ~30-120 mins
- Adverse Effects: opioid withdrawal symptoms

*There is no evidence that a higher dose of naloxone is “better” for treating overdoses. Higher doses have been shown to worsen withdrawal symptoms.*

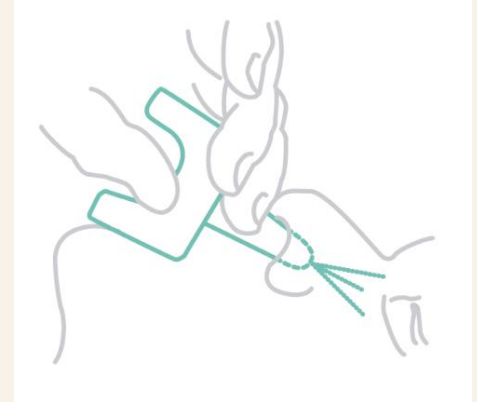
# Kloxxado® Administration



HOLD



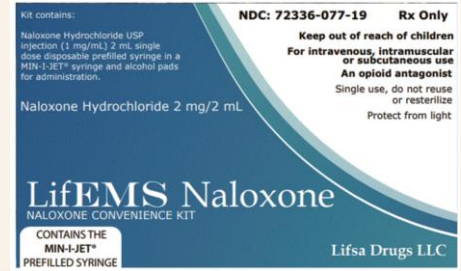
INSERT



PRESS

*Same process as Narcan®!*

# Naloxone Formulations



Available over-the-counter

Available by prescription

\*Drawing from vials for IV/IM administration may be appropriate in a healthcare setting



# Naloxone Formulations

- 10 mg intranasal formulation, Rezenopy, FDA-approved on April 19, 2024
- Launch date unannounced

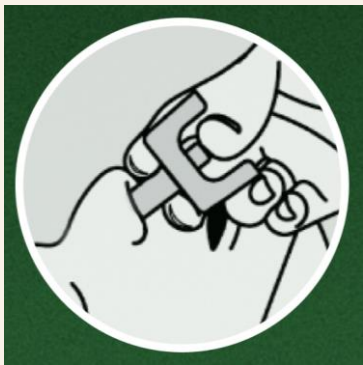
# Optimal Naloxone Dosing

- No consensus on optimal dosing
- Effects of precipitated withdrawal:
  - Common: agitation, nausea/vomiting, pain, anxiety
  - Rare, serious cases: cardiovascular instability, pulmonary edema
  - Disengagement with medical care
  - Negative attitudes toward naloxone
- Use lowest effective dose to minimize withdrawal while restoring breathing
  - Risk of overdose > risk of opioid withdrawal

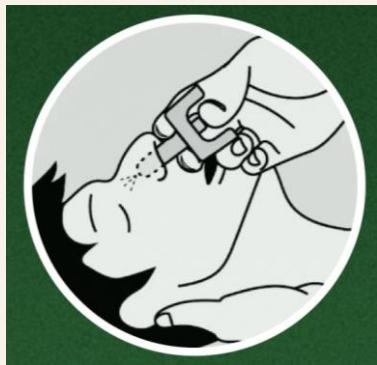
# Opvee® (nalmefene)

- 2.7 mg nasal spray
  - Pharmacokinetics:
    - Onset of Action: 2 to 5 mins
    - Half-life: ~11 hours
    - Duration of Action: ~8 hours
  - Adverse Effects: opioid withdrawal symptoms
- More rapid return to baseline minute ventilation following administration of an opioid agonist (5 mins with Opvee® vs. 20 mins with Narcan®)
  - Duration of action longer than full opioid agonists

# Opvee® Administration



PLACE



PRESS



PAUSE

*Same process as Narcan® and Kloxxado®!*

# Nalmefene Formulations



Available by prescription

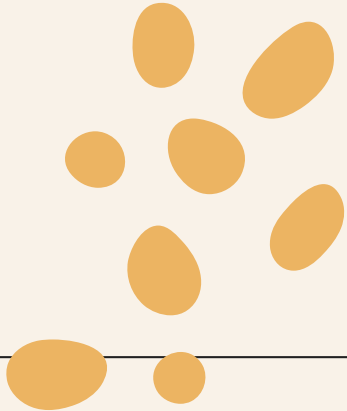
*\*Some agencies (Department of Health, Emergency Medical Services, community organizations) may be eligible to purchase without a prescription*

# Opioid Antagonist Comparison:

	<b>Narcan® (naloxone)</b>	<b>Kloxxado® (naloxone)</b>	<b>Opvee® (nalmefene)</b>
<b>Mechanism of Action</b>	Opioid Antagonist		
<b>Dose</b>	4 mg	8 mg	2.7 mg
<b>Route</b>	Intranasal		
<b>Onset of Action</b>	~3 mins	~3 mins	2 to 5 mins
<b>Duration of Action</b>	~30 to 120 mins	~30 to 120 mins	~8 hours
<b>Advantages</b>	Widespread availability	Some patients may prefer higher dose formulation	More rapid reversal of respiratory depression?
<b>Disadvantages</b>	May need repeat dosing to reverse overdose	Severity of withdrawal symptoms	Prolonged withdrawal symptoms

# What about oxygenation?

- Opioid antagonists may not be needed in every overdose
  - Suppression of respiratory drive may be improved through oxygenation alone
- Oxygen supply reduced naloxone use at overdose prevention site from 98% to 66%
- Pulse oximeter monitoring can guide need for oxygen and/or naloxone
- Reduce patient suffering (precipitated withdrawal)



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# Harm Reduction



# Principles of Harm Reduction:

- Practical strategies for **reducing negative consequences** associated with drug use
- National Harm Reduction Coalition Principles:
  - Accepts drug use and attempts to minimize harmful effects
  - Understands drug use is complex
  - Individual and community quality of life = success
  - People who use drugs (PWUD) are primary agents
  - Non-judgmental, non-coercive resources in communities
  - PWUD have a voice for services
  - Recognizes social inequities
  - Does not attempt to minimize harm associated with illicit drug use

# Examples of Harm Reduction



Needle Exchange Programs



Naloxone



Fentanyl Test Strips



Medications for Opioid Use Disorder (MOUD)



Supervised Consumption Sites

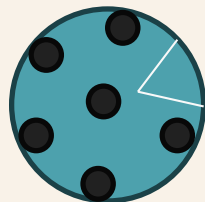
# Fentanyl Test Strips

- Can detect if drug supply contains fentanyl
- Many substances now contaminated with fentanyl
- If positive can:
  - Use smaller amount
  - Find different supply



# How to Use Fentanyl Test Strips

1. Put small amount of drug supply in clean, dry container
  - Either test entire supply or mix drugs thoroughly due to “chocolate chip cookie effect”



● = fentanyl

2. Add  $\frac{1}{2}$  tsp\* water and mix thoroughly
  - \*1 tsp for methamphetamine

# How to Use Fentanyl Test Strips

3. Place the wavy end of the test strip down in the water and let it absorb for about 15 seconds
4. Take the strip out of the water and place it on a flat surface for 2 to 5 minutes

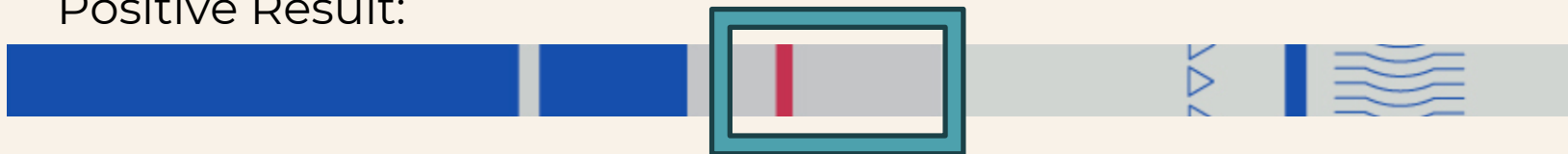


Image from: <https://www.shatterproof.org/learn/addiction-safety/how-to-use-fentanyl-test-strips>

# How to Use Fentanyl Test Strips

## 5. Read results

Positive Result:



Negative Result:





# Frequently Asked Questions

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# Frequently Asked Questions

1. How many doses of Narcan® can be administered? Are there any adverse consequences to administering multiple doses?

*As many doses of Narcan® can be administered as necessary to reverse an opioid overdose. Some patients may need higher doses based on the amount and type of opioid used. Patients using opioids will have opioid withdrawal symptoms when Narcan® is administered. Higher doses may worsen withdrawal symptoms, but there are no other adverse consequences to administering multiple doses and no consequences if Narcan® happens to be administered to someone not using opioids.*

# Frequently Asked Questions

2. How long does intranasal Narcan® last in someone's system?

*Intranasal Narcan® begins working in ~3 minutes, but only lasts 30 to 120 minutes. Because the duration of action of opioids can last longer than that of Narcan®, patients may overdose again, and it is important that they receive medical attention after Narcan® is administered.*

# Frequently Asked Questions

3. Who should carry Narcan®? Can Narcan® be self-administered?

*Everyone! Given the widespread opioid epidemic, it is recommended that everyone carry and be prepared to administer Narcan®. Narcan® cannot be self-administered, as patients who are overdosing on opioids will be unconscious.*

# Frequently Asked Questions

4. What is the difference between Narcan® and Kloxxado®? Is one better than the other?

*Kloxxado® and Narcan® are both intranasal naloxone formulations that are administered in the same fashion. Kloxxado® is an 8 mg dose that peaks ~5 minutes quicker, while Narcan® is a 4 mg dose. There is no evidence that a higher dose of naloxone is “better” for treating overdoses (no difference in overdose survival, amount of naloxone received). In fact, higher doses have been shown to worsen withdrawal symptoms and sour patient attitudes toward naloxone use.*

# Resources

- **SAMHSA Overdose Prevention and Response Toolkit** | [Link](#)
- **National Harm Reduction Coalition** | [Link](#)
- **CA Dept of Public Health Naloxone Resources** | [Link](#)
- **CA Bridge** (Resources on Harm Reduction, MAT, Health Equity) | [Link](#)
- **LA County Harm Reduction Resources** | [Link](#)
- **DanceSafe** (Harm Reduction Resources) | [Link](#)

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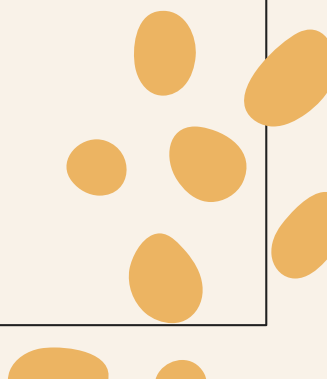

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# Thanks!

Do you have any questions?

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