Improving Overdose Response: Compassionate Care

August 14, 2025

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CSAM California Society of Addiction Medicine

CONFLICT OF INTEREST DISCLOSURE

I, Kelly S. Ramsey, have nothing to disclose, and I will be discussing “off label” use of medications or devices in this presentation.

- The information contained in this presentation does not constitute medical advice but rather is the provision of practical information to improve polysubstance overdose response.
- The information contained in this presentation is informed by the practical experience of harm reductionists and the staff at overdose prevention centers domestically and internationally. These strategies have not yet been vetted in randomized controlled trials or in other research settings.
- Having said that, too many people who use substances have already died and we can’t afford to wait for those studies to happen. People who use substances deserve more and deserve better strategies now.
- Thanks to Erin Russell and everyone who participated in the Compassionate Overdose Response Summit held in 3/2024; to my co-collaborators on a previous conceptual iteration of this training (which never came to light) in 2023, Mary Brewster, MSW, and Kailin See, then of OnPoint NYC; and to folks who have provided significant knowledge, experience, and some research on this topic: Philadelphia Department of Public Health, UPMC, University of Pennsylvania’s CAMP, Thomas Jefferson University, CFSRE, and Nab Dasgupta.

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EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Discuss the current unregulated drug supply, with a focus on sedative adulterants

2. Discuss appropriate opioid antagonist use and the concept of compassionate overdose response

3. Discuss an appropriate overdose response for the current (and any future) drug supply

4. Discuss how to augment your overdose response with additional tools to better assess and support airway and breathing

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HOW MIGHT A PATIENT PRESENT AFTER USING A BAG OF THIS MIXTURE?

This is a messy brew of 9 major substances:

- **benzocaine**
- **phenibut**
- **caffeine**
- **diphenhydramine**
- **lidocaine**
- **medetomidine**
- **procaine**
- **promethazine**
- **bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate**

And we also found traces of 4-ANPP + tianeptine + fentanyl. Trace substances in small quantities are usually harmless, but can sometimes cause health problems. Unexpected sensations may be due to these.

St. Ann's Corner of Harm Reduction (SACHR) drug checking, South Bronx, 4/2025

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SEDATIVES IN THE UNREGULATED DRUG SUPPLY: XYLAZINE (“TRANQ”)

- **Mechanism of action:** central alpha-2 agonist; KOR full agonist (enhanced sensitivity to withdrawal in females); nonopioid sedative used for its anesthetic, analgesic, and muscle relaxation properties in veterinary medicine; never approved for human use due to sedative effects
- **Typical presentation:** an adulterant with fentanyl or having supplanted fentanyl completely
- **Typical clinical effects:** hyperglycemia, hypotension and bradycardia, sedation, respiratory depression, skin ulcerations, physiological dependence
- **Metabolism:** highly lipophilic; primarily excreted in urine
- **Withdrawal management:** can complicate opioid withdrawal management; nascent withdrawal management protocols exist
- **Wound care management:** keep wounds clean, moist, and covered; chemical debridement; assess for superinfection; nascent wound care management protocols exist

Bedard, ML, et al. Addict Neurosci, 2024

Floresta, G, et al. Arch Pharm, 2025

Xylazine Withdrawal and Overdose – CAMP

Recommendations for Caring for Individuals with Xylazine-Associated Wounds

BUILDING MULTIDISCIPLINARY CONSENSUS ON INPATIENT XYLAZINE MANAGEMENT THROUGH CLINICAL PROTOCOLS

Table 1. Recommendations for Withdrawal Management with Co-exposure to Opioids and Xylazine.

When to consider additional xylazine withdrawal management
- Prior history of xylazine withdrawal
- Self-reported use and/or exposure to xylazine
- Prior or current confirmatory testing demonstrating xylazine
- Presence of xylazine-related harms, specifically xylazine wounds
- Continued symptoms of severe dysphoria and/or anxiety despite aggressive management of opioid withdrawal

Medications for xylazine withdrawal (prioritize treatment of alpha-2-agonist and escalate in stepwise fashion):
1. Clonidine* 0.1 mg PO every 6 hours scheduled (hold for BP < 100/60 or HR < 60)
   - Titrate by 0.1 mg up to clonidine 0.3 mg PO every 6 to 8 hours scheduled
   - If unable to tolerate clonidine due to vitals, skip to step 2
2. Tizanidine 4 mg PO every 8 hours scheduled (switch clonidine to as-needed dosing)
   - Can up titrate to tizanidine 8 mg PO every 8 hours scheduled
3. Dexmedetomidine drip if care needs to be escalated to intensive care unit level

*For patients who are more prone to hypotension such as pregnant individuals, consider scheduling tizanidine instead with clonidine as needed

Adjunct medications
- Olanzapine 5 mg PO at bedtime for ongoing irritability, dysphoria, insomnia, and/or anxiety (use 2.5 mg for elderly/frail) and can titrate up to 10 mg if needed
- Hydroxyzine pamoate 50 mg PO every 6 hours scheduled for anxiety

Use with caution and clear expectations about tapering prior to discharge
1. Gabapentin 300 to 600 mg PO TID scheduled for anxiety
2. Lorazepam or clonazepam PO as needed for anxiety (dosing per primary team and patient need)

Duration of xylazine withdrawal management
- Continue for up to 1 week, then make any scheduled medications as needed
- No need to taper agents but can consider discharging with clonidine, tizanidine, and/or hydroxyzine as needed for a 3 to 5 day prescription to assist with any ongoing withdrawal symptoms

Abbreviations: BP, blood pressure; HR, heart rate; PO, by mouth.

Shang, M, et al. Substance Use & Addiction Journal, 2025

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OVERLAPPING WITHDRAWAL SYNDROMES

TABLE 2. Overlapping Withdrawal Symptoms

XYLAZINE	OPIOID	BENZODIAZEPINE
Anxiety	Tachycardia	Tachycardia
Dysphoria	Diaphoresis	Hypertension
Restlessness	**Restlessness**	Diaphoresis
	Mydriasis	**Anxiety**
	Body aches	Tremor
	Rhinorrhea	Altered mental status
	GI symptoms	Seizures
	Tremor	**Dysphoria**
	Yawning	
	Piloerection	
	Anxiety	
	Dysphoria	

Reagan-Udall Foundation of the FDA, 2/2024

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SEDATIVES IN THE UNREGULATED DRUG SUPPLY: MEDETOMIDINE ("DOMITOR")

- **Mechanism of action:** Central alpha-2 agonist that is significantly stronger than xylazine; non-opioid veterinary sedative/anesthetic/analgesic/anxiolytic/muscle relaxant; not approved for human use
- **Typical presentation:** Found in the unregulated highly potent synthetic opioid supply, often along with xylazine and/or synthetic benzodiazepines
- **Typical clinical effects:** Hypotension, bradycardia, widely fluctuating blood pressure and heart rates, bradyarrhythmia, nausea/vomiting/other GI effects, profound sedation, hyperglycemia, hallucinations/delusions, dizziness, peripheral vasoconstriction, muscle twitching, hypothermia, reduced cardiac output, and respiratory depression
- **Metabolism**: Metabolized by the liver, and, when used alone, peak plasma levels occur within 10-30 minutes of administration; duration of sedation is 2-3 hours
- **Withdrawal management:** Not well described; nascent protocols emerging: recommendations similar to withdrawal management for xylazine

CFSPE, NPS Discovery, 5/2024

Philadelphia DPH, 5/2024

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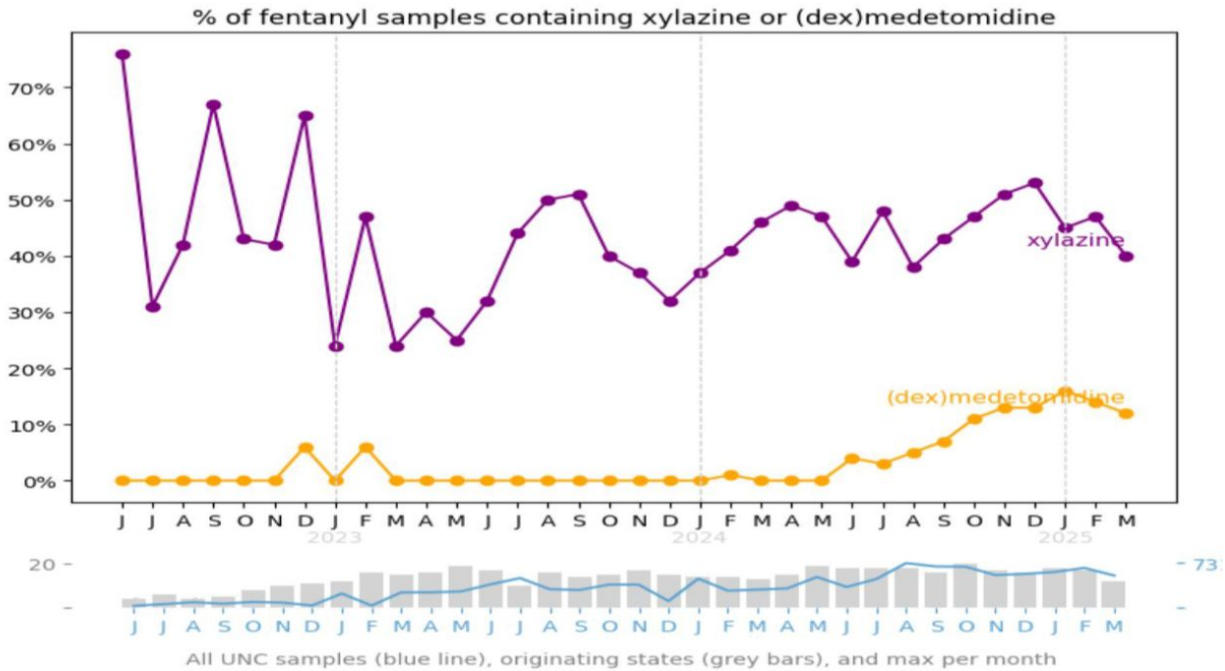
PERCENTAGE OF FENTANYL SAMPLES CONTAINING XYLAZINE AND/OR MEDETODOMIDINE



Nabarun Dasgupta, Opioid Data Lab, 2025

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XYLAZINE V. MEDETOMIDINE: SIMILARITIES AND DIFFERENCES

SIMILARITIES

- *Both are not opioids, so not responsive to naloxone*
- Both are veterinary medications
- Both are alpha-2-agonists
- Both have a rapid onset of action
- Both cause prolonged sedation
- Both are typically found mixed with fentanyl
- Both have been involved in fatal overdose (though not causative)
- Both are associated with acute withdrawal syndromes
- Both are not federally scheduled (yet)

DIFFERENCES

- **XYLAZINE**
  - Clear association with wounds
  - Scheduled in some states
- **MEDETOMIDINE**
  - Significantly more potent than xylazine
  - Associated with longer sedation
  - Associated with more pronounced effects on blood pressure and heart rate
  - Anecdotal reports of hallucinations and worse withdrawal symptoms

Megan Reed, Thomas Jefferson University, and Rose Laurano, Philadelphia Department of Public Health

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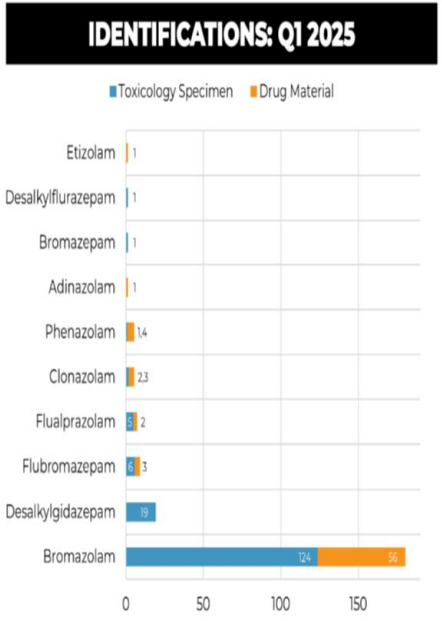
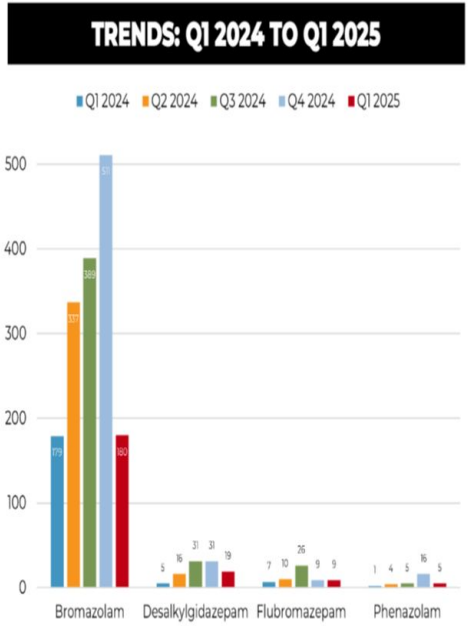
SEDATIVES IN THE UNREGULATED DRUG SUPPLY: RX BENZODIAZEPINES AND SYNTHETIC BENZODIAZEPINES

- Isolated overdoses involving oral BZDs rarely lead to respiratory failure; however, when combined with other sedatives, it may be encountered.
- **Synthetic BZDs are significantly more potent than prescription BZDs.**
- Between 2019 to April 2020: Synthetic BZDs were identified in **48%** and **83%** of postmortem and DUID cases reported to the UNODC.





DUID=driving under the influence of drugs

UNODC=United Nations Office on Drugs and Crime

Simone, CG and Bobrin, BD. Stat Pearls, 2025

Brunetti, P, et al. Pharmaceuticals, 2021

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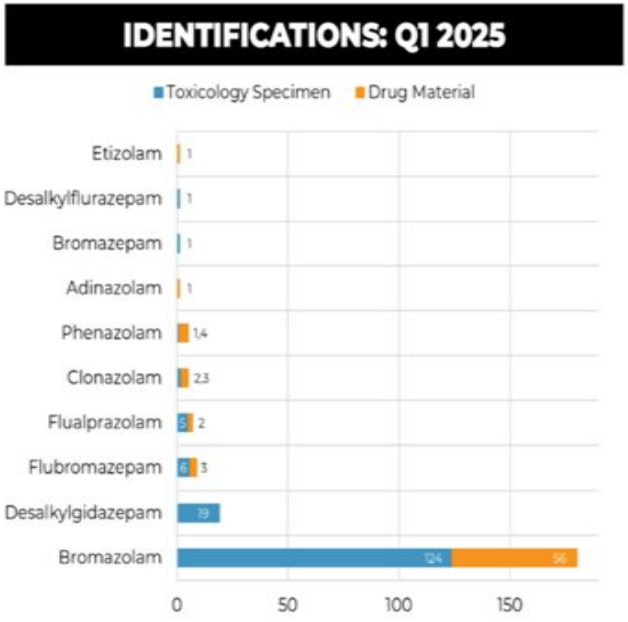

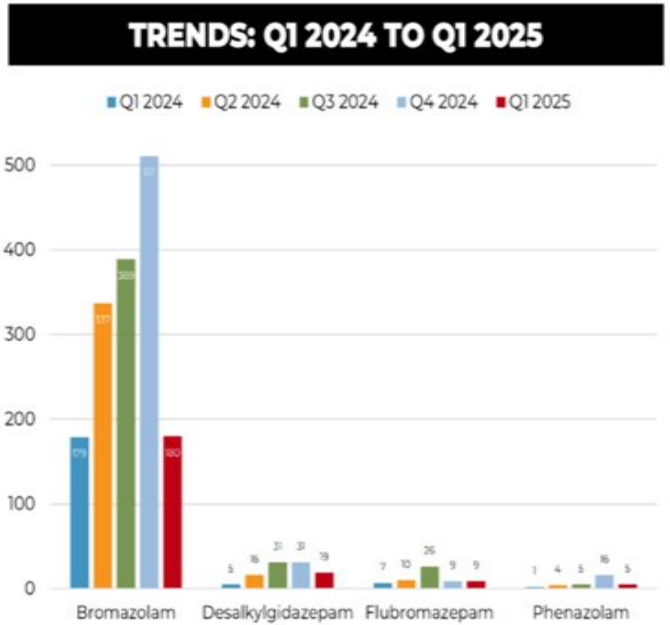

CFSRE, Q1 2025 NPS Discovery Report

OTHER ADULTERANTS IN THE UNREGULATED DRUG SUPPLY

- ***There will always be other and newer adulterants in the unregulated drug supply.***

- We should follow the same steps when responding to all overdoses.

- **Assume polysubstance overdose.** Don't perseverate on which substances someone may have taken but rather do an assessment and respond to the symptoms you are seeing.

- Assess airway, breathing, and circulation.

- Give naloxone *if indicated*. Give rescue breaths. Reassess breathing. Wait a minimum of 3 minutes before giving any additional naloxone.
- If no improvement in breathing, continue rescue breathing or administer oxygen or utilize other tools.

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OPIOID ANTAGONISTS IN THE US

- High dose and long-acting opioid antagonists were approved without testing for precipitated withdrawal and are often aggressively marketed.
- In 2021, the US FDA approved two high-dose naloxone products, an 8 mg IN spray and a 5 mg IM injectable. The only studies reported in the FDA package inserts for both products are pharmacokinetic studies in healthy volunteers.
- In April 2024, based on a pharmacokinetic study of 30 healthy adult subjects, the FDA approved a 10 mg IN naloxone.
- In 2023, the FDA approved a 2.7 mg IN formulation of nalmefene, a more potent and longer acting opioid antagonist than naloxone. The approval of nalmefene was also based on pharmacokinetic studies performed in healthy volunteers.

Russell, E, et al. International Journal of Drug Policy, 2024

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COMPARISON OF ADMINISTRATION OF 8-MILLIGRAM AND 4-MILLIGRAM INTRANASAL NALOXONE BY LAW ENFORCEMENT DURING RESPONSE TO SUSPECTED OPIOID OVERDOSE — NEW YORK, MARCH 2022–AUGUST 2023

TABLE. Reported outcomes and postnaloxone signs and symptoms among persons who received naloxone for suspected opioid overdose, by intranasal naloxone formulation as reported by New York State Police personnel (N = 354) — New York, March 2022–August 2023

Characteristic	Naloxone doses administered, no. (%) 8 mg (n = 101)	4 mg* (n = 253)	RR (95% CI)	p-value for RR
Reported outcome				
Survived	100 (99.0)	248 (99.2)	0.81 (0.07–8.99)	0.86
Perceived anger or combativeness	11 (10.9)	20 (7.9)	1.42 (0.66–3.09)	0.37
Refused transport to hospital	19 (19.0)	66 (26.6)	0.65 (0.36–1.15)	0.14
Postnaloxone sign or symptom				
Opioid withdrawal sign or symptom, including vomiting†	38 (37.6)	49 (19.4)	2.51 (1.51–4.18)	<0.001
Vomiting only	21 (20.8)	35 (13.8)	1.64 (0.90–2.98)	0.11
Disorientation	67 (66.3)	148 (58.5)	1.40 (0.86–2.27)	0.17
Lethargy	53 (52.5)	110 (43.5)	1.44 (0.90–2.28)	0.13

Abbreviation: RR = relative risk.

* Referent group.

† New York training materials for law enforcement naloxone administration include nausea, vomiting, and withdrawal (sick feeling) as the key components of opioid withdrawal signs and symptoms for which to monitor after naloxone administration.

Those who received the initial 8 mg dose had 2.5 times the risk of withdrawal.

Payne, ER, et al. MMWR, 2024

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TRENDS AND CHARACTERISTICS DURING 17 YEARS OF NALOXONE DISTRIBUTION AND ADMINISTRATION THROUGH A HARM REDUCTION PROGRAM IN PITTSBURGH, PENNSYLVANIA

- **Results:**
  - From July 2005 to January 2023 there were 16,904 service encounters by 7,582 unique participants, resulting in 70,234 naloxone doses dispensed, with 5,521 overdose response events (OREs), utilizing 8,756 naloxone doses.
  - ***On average, 1.63 (95% CI: 1.60, 1.65) naloxone doses were administered per ORE, which did not change substantially over 17 years ($\chi 2=0.28$, 3 df, p=0.60) during evolution from prescription opioids, to heroin, to illicitly manufactured fentanyl. In 98.0% of OREs the person who experienced overdose "was okay", i.e., survived.***
  - ***There were 106 more emesis events per 1,000 OREs with 4mg nasal spray compared to intramuscular injection; and 48 per 1,000 more reports of anger.*** Titration of intramuscular naloxone was associated with lower rates of adverse events.

- **Conclusions:** Long-term consistency of <2 doses per ORE, high survival rate, and robust utilization all lend confidence in prioritizing naloxone distribution directly to people who use drugs and their social networks.

Dasgupta, N, et al. medRxiv, 2024

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TRENDS AND CHARACTERISTICS DURING 17 YEARS OF NALOXONE DISTRIBUTION AND ADMINISTRATION THROUGH A HARM REDUCTION PROGRAM IN PITTSBURGH, PENNSYLVANIA

- Although deaths in Allegheny County involving fentanyl increased from 3% to 68% to 95%, the reports of naloxone doses during the same time period did not change.

Doses Administered per ORE	
Arithmetic mean (SD)	1.63 doses (0.99)
Median (IQR)	1 dose (1, 2)
Missing	133 (2.4%)
Range	0.25 to 10 doses

RESPONSE BEHAVIORS & SERVICE UTILIZATION			
Rescue Breathing			
No		2,768	50.1%
Yes		2,419	43.8%
Missing		334	6.0%
		0	0%
	Total Reversals	5,521	100%
Chest Compressions*			
No		2,092	69.60%
Yes		711	23.70%
Missing		201	6.70%
	Total Reversals	3,004	
Called 911			
No		4,530	82.0%
Yes		903	16.4%
Missing		88	1.6%
	Total Reversals	5,521	100%
Ambulance Arrived After Calling 911			
No		456	50.5%
Yes		444	49.2%
Missing		3	0.33%
	Total 911 Calls	903	100%
Hospital Transport			
No		5,209	94.3%
Yes		274	4.96%
Missing		38	0.69%
	Total Reversals	5,521	100%

*Collected November 2015 to December 2020

Dasgupta, N, et al. medRxiv, 2024

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COMPASSIONATE OVERDOSE RESPONSE: DOES OVER-ANTAGONISM MATTER?

- Iatrogenic harm with extraneous naloxone *matters* to the person who experiences severe precipitated opioid withdrawal syndrome (OWS) and we should care about causing the least harm possible
- ***Negative reactions are commonly reported after naloxone administration; negative reactions are not benign as they often result in self-medical discharge, self-medication with additional opioids, risk of additional overdose, reluctance to carry naloxone and reluctance to have naloxone administered again***
- Titration of the naloxone dose and good communication with the person who overdosed result in better experiences for the person who overdosed
- People are less likely to be angry, despite precipitated OWS, if the person resuscitating them communicated with them in a positive manner
- The Michigan Drug Users Health Alliance (MIDUHA) distributed a survey in 2023 asking PWUD about their overdose experiences and opioid antagonist product preferences. More than 90 percent of the respondents said they had experienced an overdose, and 87 percent reported experiencing withdrawal after an overdose reversal. ***Most of the respondents (90%) said longer-acting antagonists (i.e., eight to 12 hours) and stronger dose alternatives than the standard 0.4 mg intramuscular and <4 mg intranasal were unnecessary.***

Neale, J and Strang, J. Addiction, 2015
Farrugia, A, et al. Addiction Research & Theory, 2019
Parkin, S. et al. Int J Drug Policy, 2020
Neale, J, et al. J Subst Abuse Treat, 2020
Michigan Drug Users Health Alliance (MIDUHA) - Overdose Survey
Jo Neale, Compassionate Overdose Response Summit, 3/2024

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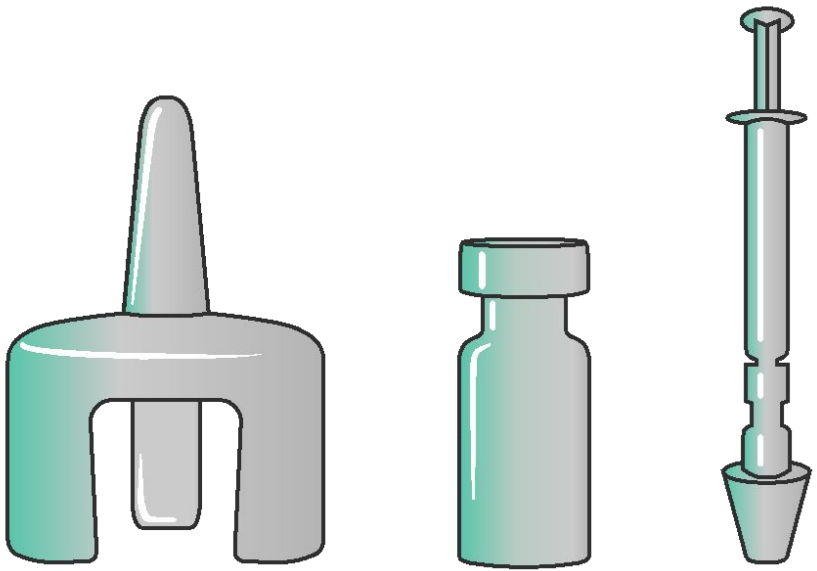
RECOMMENDED OPIOID ANTAGONISTS

- 0.4 mg/mL generic naloxone for intramuscular (IM) use
- 3.0 mg/mL naloxone for intranasal (IN) use
- 4.0 mg/mL IN naloxone
- 1 mg/mL and 2 mg/2 mL nasal atomizer device (intended for clinical training only; not approved by the FDA)



Practi-Intranasal Naloxone Pack for Clinical Training | Medline

Washington State Department of Health: Issue Brief: The Risks High-Dose Naloxone Products and Nalmefene for Community Opioid Overdose Response, November 2024

Informed by Megan Reed, Thomas Jefferson University, and Rose Laurano, Philadelphia Department of Public Health

ACMT & AACT Joint Position Statement: Nalmefene Should Not Replace Naloxone as the Primary Opioid Antidote at This Time, September 28, 2023

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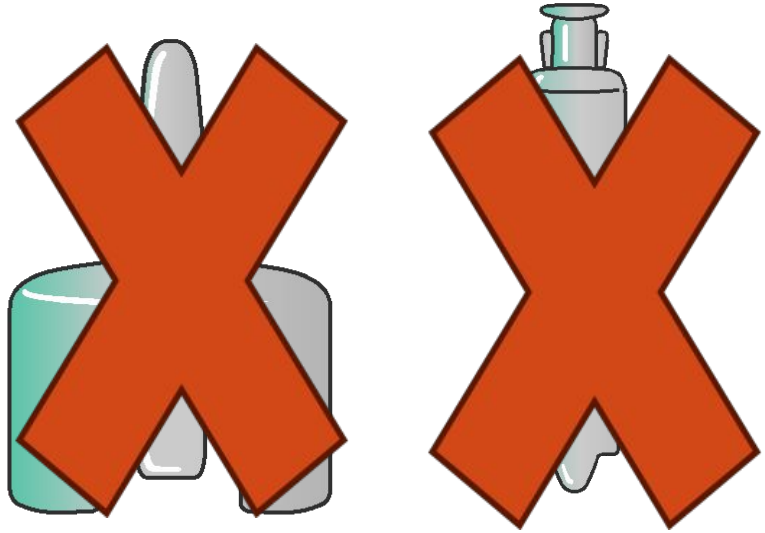
OPIOID ANTAGONISTS NOT RECOMMENDED

- 5 mg/0.5 mL naloxone prefilled syringe
- 8 mg/0.1 mL IN naloxone
- 10 mg/0.11 mL IN naloxone
- 2.7 mg/0.1 mL IN nalmefene
- 1.5 mg/0.5 mL nalmefene autoinjector



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PATHOLOGY AND TREATMENT OF OPIOID OVERDOSE

- Opioids cause reduced breathing and reduced consciousness that progress to cardiac arrest
- **The time from drug use to cardiac arrest** differs with the type of opioid, dose taken, tolerance in the person using, and other substances used
- The main treatment is *stimulation, assisted breathing, and oxygen*
- Naloxone will reverse the effect of opioids
- In cardiac arrest, opioid antagonism has little or no effect; the individual needs CPR

HOW NALOXONE IS DOSED IN OVERDOSE

- Traditional dose 0.4-2.0 mg intravenous (IV) or intramuscular (IM)
- *It is very well documented that 0.8 mg IM is very effective in opioid overdoses.*
- Ideally, naloxone should always be titrated - that is - given in smaller doses with repetition until the patient starts breathing
- Early intranasal naloxone 2 mg/mL (actual dose 0.4 mg) worked effectively, even 0.4 mg/mL (actual dose 0.1 mg) was as effective

1: Skulberg AK, et al. Comparison of intranasal and intramuscular naloxone in...Addiction. 2022;117(6):1658-67
2: Thompson J, et al. Safety, Efficacy, and Cost of 0.4-mg Versus 2-mg Intranasal Naloxone ... Ann Pharmacother. 2022;56(3):285-9.
3: Carpenter J, et al. Naloxone Dosing After Opioid Overdose in the Era of Illicitly Manufactured Fentanyl. J Med Toxicol. 2020;16(1):41-8.
4: Bell A, et al. Amount of naloxone used to reverse opioid overdoses outside of medical practice in a... Subst Abus. 2019;40(1):52-5.

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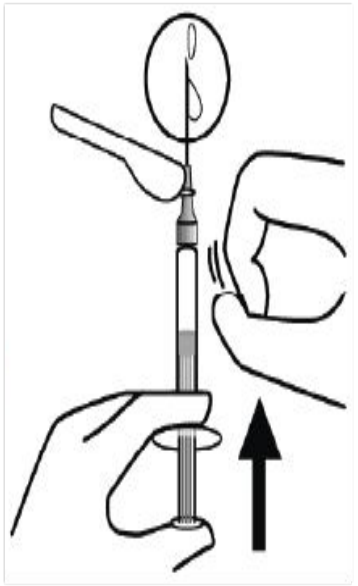
WHAT ABOUT IM NALOXONE?

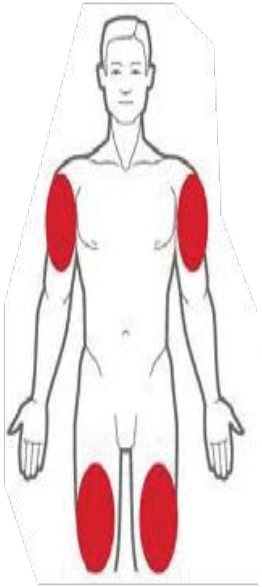
- **Low doses of IM naloxone are preferable**. The widely available 4 mg IN naloxone is an unnecessarily high dose *in most cases*.

- The 0.4 mg/mL IM naloxone, given in one or two doses with a *full 3 minutes* between doses, is often enough to enable a person to breathe on their own and raise their oxygen to an acceptable level.

- To administer, load one 0.4mg/mL vial of naloxone into a 23-gauge x 1-inch, 3 cc syringe. Insert syringe at 90-degree angle into either lateral bicep or anterior thigh.

  - *Can inject through one layer of clothing if needed.*
  - *Can titrate the dose, if comfortable doing so, or push in the entire dose and remove the syringe.*
  - *Immediately after removing the syringe, do rescue breaths and/or begin using a bag valve mask (BVM) and/or administer oxygen.*





Jamaal Shaban, DO, Savage Sisters Harm Reduction
DYK? Naloxone Administration - HealthDirect

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WHAT ARE THE IMPLICATIONS OF HIGHLY POTENT SYNTHETIC OPIOIDS AND OTHER ADULTERANTS ON OVERDOSE RESPONSE?

- Fentanyl, fentanyl analogues, nitazenes, etc.: No evidence that additional naloxone is needed
- There is not a linear relationship between the potency of the opioid and the naloxone requirement
- Sedatives added to the unregulated drug supply and other adulterants are not affected by naloxone
- ***Therefore, if first aid, including rescue breathing and/or oxygen administration are not included in the response to an overdose, then it appears that more naloxone is needed though the naloxone has already played its role in reversing the opioid portion of the overdose***
- What is most important is the time to first aid/rescue breathing starting and naloxone administration or the dose/route of administration of naloxone

OXYGEN MONITORING AND ADMINISTRATION: EXPERIENCE FROM OVERDOSE PREVENTION CENTERS (OPC)

- At an unsanctioned OPC in San Francisco: staff would assess people in early stages of an overdose to determine the best course of action, particularly whether the person needed rescue breaths or administered oxygen. If the person remained unresponsive, staff would either titrate IM naloxone, or onsite medical staff or EMTs would administer IN naloxone.
  - ***Over 46 weeks, the OPC responded to 333 overdoses, and all were reversed successfully, either with rescue breathing, naloxone, oxygen only, or a combination of oxygen and naloxone.***

- At the OPCs operated by OnPoint NYC:
  - ***Key points are to return to the fundamentals of assessing breathing and oxygenation, monitoring the person's symptoms, and using agitation to confirm responsiveness.***
  - ***In its first year of operation, trained staff responded to over 600 potential overdoses and 83% of those were resolved without the need for naloxone through oxygenation, agitation, and close monitoring (100% survived).***

Russell, E and Lovitz, N, Compassionate Overdose Response Summit: highlights and Key Takeaways, 2024
Cleo Jenkins, HealthRIGHT360
Kailin See, OnPoint NYC

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OVERVIEW OF OVERDOSE SEVERITY ASSESSMENTS

	Mild	Moderate	Severe
Appearance	Alert or drowsy	Nodding, eyes closing	Unresponsive OR blue/gray/ashen lips & fingertips
LOC	Alert but drowsy; can hold a conversation	Responds to verbal & physical stimuli	Responds *only* to physical pain OR unresponsive
RR	Over 10 breaths/min	Less than 10/min	No spontaneous breaths OR gasping/gurgling
SpO2	Over 90%	81-90%	Less than 80%
Call 911?	No	Only if no response to naloxone OR condition worsens within 5 min	YES, Immediately!

Vancouver Coastal Health (adapted by SACHR)

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MILD OVERDOSE RESPONSE

1. **Stimulate verbally** by talking/calling their name. Encourage them to take breaths, do a sternal rub.
Try to get them up and moving or bicycle their legs to get the blood flowing.

2. **Observe and monitor** RR, SpO2, and LOC

3. **Proceed to Moderate OD interventions** if RR or SpO2 are abnormal

Vancouver Coastal Health (adapted by SACHR)
Informed by Kailin See

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MODERATE OVERDOSE RESPONSE

1. **Stimulate** verbally by talking. Encourage them to take breaths, do a sternal rub, bicycle their legs to get the blood flowing. *If no improvement within 1 min, go to step 2.*
2. **Apply O2 at 6 L/min via a simple face mask.** *If no improvement within 1 min, increase oxygen up to 10 L/min. If no improvement within 1 min, use a non-rebreather mask to give 15 L/min. If breathing worsens, proceed to step 3.*
3. **Administer/titrate naloxone 0.4 mg IM.** If no improvement within 5 min, CALL 911 and repeat the dose of naloxone in 3-5 min with goal RR at least 10/min, SpO2 over 90%.
4. **Constantly monitor** respiratory status and heart rate until SpO2 above 92%.
5. **Observe for 3 hours** or transfer to a hospital for observation.
6. **Proceed to Severe OD interventions** if SpO2 decreases below 80%, RR decreases to less than 10, or person appears cyanotic (blue/gray color), proceed to "Severe OD" interventions.

Consider how long it takes EMS to arrive on-site.

Vancouver Coastal Health (adapted by SACHR)
Informed by Kailin See

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SEVERE OVERDOSE RESPONSE

1. **Immediately call 911** and assist the person to the floor (if not already on the floor)
2. **Start rescue breaths** give 1 breath every 5 seconds
3. **Give oxygen** at 15 L/min via non-rebreather mask (preferred). Watch for the chest to rise, re-adjust head position, and/or insert an airway if needed.
4. **Give naloxone 0.4mg IM (titrate if possible)** and wait at least 3 minutes for the naloxone to take effect
    a. If SpO2 and RR increase within 3 minutes → monitor RR, SpO2, and HR for 5 minutes & repeat dose if condition worsens
    b. If SpO2 and RR do NOT increase within 3 min → administer a second dose and monitor for improvement (improvement/normalization of SpO2 and RR, not responsiveness)
    c. If the person loses their pulse, begin CPR (as trained)/utilize an AED (if available), continue rescue breaths or oxygenation via BVM or oxygen administration (if breathing), and give naloxone IM immediately
5. **Once SpO2 is > 90% and RR is over 10/min:**
    a. Continue to monitor until EMS arrives
    b. If vomiting occurs, place them in the rescue/recovery position and clear their mouth

Vancouver Coastal Health (adapted by SACHR)

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POLYSUBSTANCE OVERDOSE RESPONSE

- ***FIRST:*** assess responsiveness (agitate), airway, breathing (look, listen, and feel; set a timer: count respirations), and circulation (check pulse, bicycle legs)
- ***SECOND:*** administer naloxone *if indicated by RR and SpO2*
- ***THIRD:*** call 911 *if indicated*
- ***FOURTH:*** support airway and breathing *if indicated*; rescue breathing or additional tools according to your skill set/training and access; with O2 administration, start low (2L for a nasal cannula) and titrate up to achieve a SpO2 >90%
- ***FOCUS on airway/breathing, not responsiveness:*** people don't need to wake up or respond to you but they do need to be breathing/oxygenating adequately

Informed by Kailin See

Open Resources for Nurses, 2021

Oxygen Administration – Vitali

Starr, LM. AAOHN J, 1994

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POLYSUBSTANCE OVERDOSE RESPONSE

- ***For O2 administration:*** standing orders for nursing and medical personnel, can specify oxygen administration for when a physician is not onsite. In emergency situations, oxygen administration can be done by nurses without a standing order.
- ***For other personnel:*** medical volunteers, first responders, other designated staff, etc., they can obtain an Oxygen Administration certification, that is OSHA-compliant.
- ***The FDA distinguishes between medical and emergency oxygen.*** Oxygen standing orders for non-medical personnel typically involve pre-approved protocols that allow individuals, often first responders or workplace safety personnel or other designated staff, to administer oxygen without a direct physician order in specific, emergency situations. These orders often specify the conditions under which oxygen should be given and the equipment to be used, ensuring a quick and appropriate response in cases of respiratory distress.

Informed by Kailin See

Open Resources for Nurses, 2021

Oxygen Administration – Vitali

Starr, LM. AAOHN J, 1994

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RESCUE BREATHING

- Ensure the person is on their back
- Do a head tilt/chin lift to open the airway; make sure the tongue isn't blocking the airway
- Pinch the nose closed
- Form a seal over the person's mouth with your mouth; you can use a one-way mask or a t-shirt or any breathable material if a mask isn't available
- Begin with TWO quick breaths
- The person's chest should rise—if not, re-tilt the head, check the position of the tongue, and give two more quick breaths
- Continue with ONE breath every FIVE seconds
- If you are CPR trained, follow your training

NIDA

Rescue Breathing Stock Illustrations – 766 Rescue Breathing Stock Illustrations, Vectors & Clipart - Dreamstime

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RESCUE BREATHS V. CHEST COMPRESSIONS v. CPR: DO WHAT YOU ARE TRAINED TO DO

- There isn't enough evidence to recommend one strategy over another
- Because overdoses are often primarily (at least initially) a respiratory issue, rescue breaths and supporting airway and breathing make the most sense
- If an overdose has progressed, then the cardiovascular system will be affected and chest compressions or, more likely, full CPR will be needed
- *Most importantly, do what you have been trained to do*

Desfulian, C, et al. Circulation, 2021
The Ontario HIV Treatment Network
New York State Department of Health, AIDS Institute. Technical Working Group on Resuscitation Training in Naloxone Provision Programs, 2016
SAMHSA, Opioid Overdose Toolkit: Five Essential Steps for First Responders, 2013

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WHAT ARE YOUR AVAILABLE TOOLS AND WHAT TRAINING HAVE YOU RECEIVED?

- Adding tools to the basic toolbox/kit of naloxone/one-way mask/rescue breathing

- Consider training staff* and adding tools depending on your setting (in the street v. in a building v. in a clinic setting v. an OPC setting v. a harm reduction setting):
  - pulse oximeter
  - bag valve mask (BVM)
  - oral and/or nasal airways
  - oxygen tanks/canisters

**Your facility/organization should determine what works for your staff and patients; at many harm reduction programs and at the OPCs, ALL staff are trained in providing a more comprehensive, nuanced overdose response, including titration of IM naloxone, rescue breathing, and administration of oxygen*

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USING A PULSE OXIMETER

ADVANTAGES

- A relatively cheap and easy to use tool that can provide important data (HR and SpO2) in a potential overdose situation
- Provides additional information on respiratory status (besides counting the number of respirations)
- Can inform responders regarding changes in HR and SpO2 during an overdose
- Normal heart rate range: 60-100 beats per minute (bpm)
- Normal oxygenation (SpO2) range: 90-100%

CAVEATS

- Non-medical pulse oximeters, which are available cheaply online and in pharmacies, are less accurate, especially with non-White persons
- Nail changes (nail polish, artificial nails, thickened nails), skin changes (calluses), and cold/wet/dirty skin may give no reading or inaccurate readings (try a toe or ear instead)
- If a person is moving or agitated, the reading may not be accurate

Lipnick, MS, et al. JAMA, 2025
Gerke, S and Shachar, C. JAMA Intern Med, 2025
www.amazon.com

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USING A BAG VALVE MASK (BVM)

WHAT IS A BVM?

- BVMS are hand-held devices that can provide manual ventilation to a person who is not breathing or not breathing adequately.
- A one-way valve between the bag and the person allows oxygen to flow into the person's lungs but prevents exhaled air from entering the bag.
- With requisite training and expertise, a BVM may be used to respond to an overdose.
- BVMs are relatively expensive (~$11-$18 each)
- BVM use can be done with one or two persons

HOW TO USE A BVM

- Ensure the airway is clear of secretions and the tongue is not blocking the airway.
- Do a head tilt/chin lift. Place something under the neck or shoulders to maintain the position.
- Ensure the bag is sealed and connected properly.
- Place the mask tightly over the nose and mouth. There must be a seal over the nose and mouth.
- Begin ventilating the person. Squeeze the bag firmly to make the chest rise. Squeeze once every 2-3 seconds for a child, every 5-6 seconds for an adult. If the chest is not rising, adjust the position and try again.

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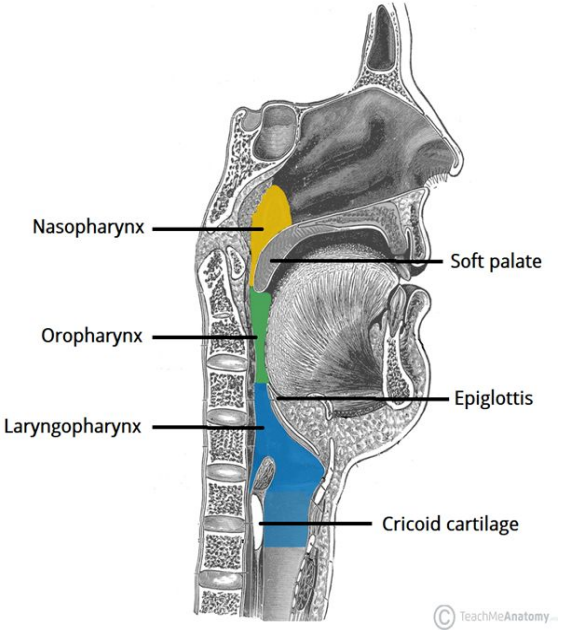
BC Centre for Disease Control Position Statement, Bag Valve Masks for Overdose Response, 2018
ems1.com

USING ORAL AND NASAL AIRWAYS

- Oropharyngeal (OPA) or nasopharyngeal airways (NPA) are tools that can be used to obtain/maintain an open airway.
- Either device can be used depending on the indications for use and patient circumstances.
- The oropharynx is the primary site of upper airway obstruction in unconscious individuals.



Thanks to Synn Stern, RN, MPH for sharing nursing protocols for overdoses at OnPoint NYC

The Pharynx - Subdivisions - Blood Supply – TeachMeAnatomy

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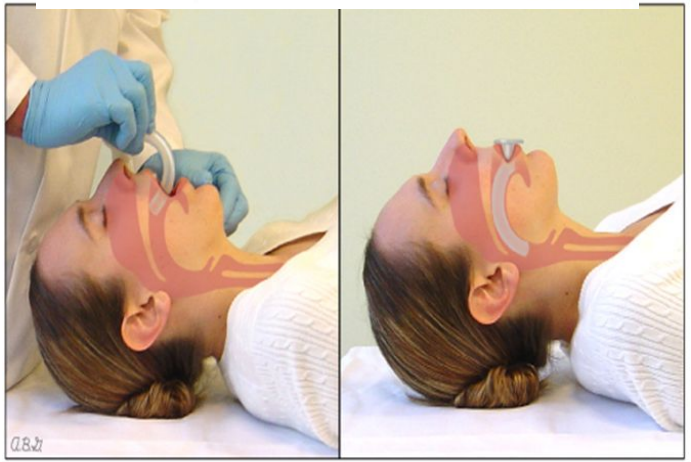
USING ORAL AIRWAYS

- ***The main indication for the use of an oropharyngeal airway (OPA) is if an individual is at risk of airway obstruction, due to the relaxed upper airway muscles or blockage of the airway by the tongue.***
- An OPA is helpful in relieving these potential obstructions as it moves the tongue and the bottom part of the throat forward, clearing the block in the airway.
- If you perform a head tilt/chin lift or jaw thrust on a person to open their airway and are not able to ventilate the person successfully, placement of an OPA is indicated.
- ***An OPA can only be used in the unconscious person to prevent gagging and vomiting of gastric contents.***



Thanks to Synn Stern, RN, MPH for sharing nursing protocols for overdoses at OnPoint NYC
www.amazon.com
Merck Manual

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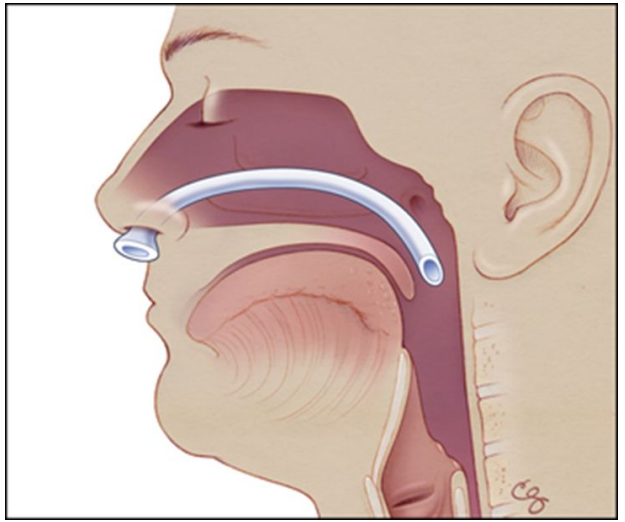
USING NASAL AIRWAYS

- Nasal airways (NPA) are hollow plastic or soft rubber tubes that ***can be utilized to assist with oxygenation and ventilation in individuals who are difficult to oxygenate or ventilate via BVM ventilation.***
- ***NPAs can be used to keep the airway open and utilized with persons who are conscious or semi-conscious.***
- NPAs are passed into the nose and through to the posterior pharynx.
- NPAs do not cause persons to gag and are the best airway tool in an awake person and a better choice in a semiconscious person that may not tolerate an OPA due to the gag reflex.



Thanks to Synn Stern, RN, MPH for sharing nursing protocols for overdoses at OnPoint NYC
Atanelov, Z, et al. StatPearls, 2025

cylinder wrench

USING AN OXYGEN TANK

Types of oxygen delivery devices:

- nasal cannula (max 6L/min)
- simple face mask (max 10L/min)
- non-rebreather mask (max 15L/min)

anatomy of an oxygen tank

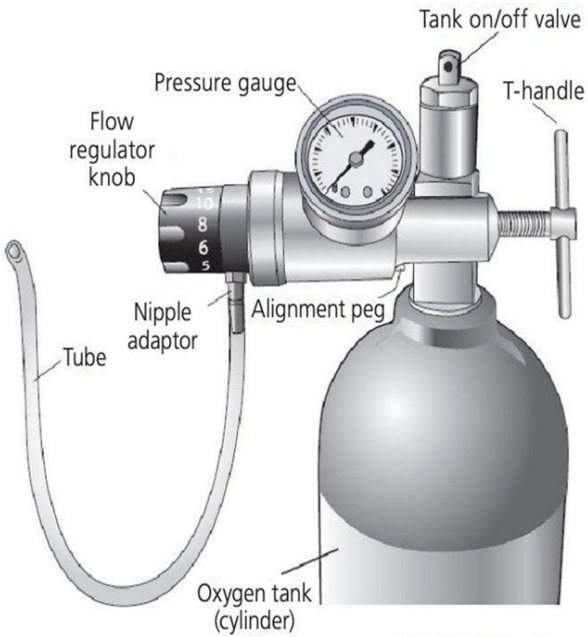


Illustration 2

nasal cannula

simple face mask

non-rebreather mask

SACHR

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RECREATIONAL OXYGEN CANS/CANISTERS

ADVANTAGES

- Uses beyond opioid overdose response
- More accessible and affordable than oxygen tanks; can be purchased online without a prescription
- Less bulky than oxygen tanks
- Good complement to rescue breathing and airway management

CAVEATS

- Supplemental oxygen only
- Bulky for unhoused people
- Should not be used near an open flame
- Moderately expensive for widespread distribution ($10-$20)
- Vary significantly in oxygen concentration (anywhere from 40%-99.5%)

Informed by Megan Reed, Thomas Jefferson University, and Rose Laurano, Philadelphia Department of Public Health

The Rise of Oxygen Bars (WebMD)

Does Oxygen in a Can Deliver on Its Altitude and Energy Claims? (University of Colorado Anschutz Medical Campus, 2023)

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POST-OVERDOSE RESPONSE WITH PROLONGED SEDATION

- Continue to monitor the individual for as long as they are sedated (if unable to do so, they should be transported somewhere they can be monitored)
- Ensure their airway is not compromised
- Place in the rescue/recovery position
- Move/massage the person's limbs periodically to avoid medical complications (DVT, compartment syndrome, rhabdomyolysis)
- Safeguard the person and their belongings (they are vulnerable to physical assault, sexual assault, and theft)

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SUMMARY/TAKEAWAYS

1. Adulterants in the unregulated drug supply are ubiquitous. Currently, they are dominated by sedative adulterants.
2. Opioid antagonism should be done thoughtfully given the impact on the person experiencing it.
3. Overdose response should include a thorough assessment of airway, breathing, and circulation. Supporting airway and breathing, in addition to use of opioid antagonists, is necessary given the presence of sedative adulterants in the drug supply.
4. Tools (pulse oximeters, BVMs, oral/nasal airways, oxygen) are available to make overdose response and support of airway/breathing more effective.

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REFERENCES

References for each slide are listed on the slide and/or in the notes of the slides themselves. Also, see next slide.

Appendix

I have included an appendix of slides that were not able to be included in the delivery of this presentation.

NITAZENES (2-benzylbenzimidazoles)

- **Mechanism of action:** a novel class of highly potent synthetic opioids initially developed in the 1950s as an analgesic; never approved by the FDA for human or veterinary use; highly selective for MOR over KOR and DOR; more potent than fentanyl; in the 1960s, only etonitazene and clonitazene were scheduled in the US; the DEA initially placed isotonitazene in the schedule I category in 2020 and later added seven more nitazenes including butonitazene, etodesnitazene (etazene), flunitazene, metodesnitazene, metonitazene, etonitazepyne (pyrrolidino etonitazene) and protonitazene, in 2021
- **Typical presentation:** powder, tablet, solution; typically found alongside fentanyl and sedatives in the unregulated drug supply; in testing of nitazene samples from US Crime Laboratories, 2.6% of cases (55 exhibits) contained 19 or more substances besides the principal component, usually fentanyl
- **Typical clinical effects:** analgesia, euphoria, sedation, respiratory depression, physiological dependence, bradycardia, overdose
- **Metabolism:** CYP2D6, CYP2B6 and CYP2C8 are the primary CYPs responsible for the metabolism of nitazenes; nitazenes are rapidly metabolized in human liver microsomes and the human liver; the rapid metabolism of nitazenes in hepatic matrices may also have implications for the detection of the unchanged compounds in the urine and other body matrices.
- **Withdrawal management:** acute opioid withdrawal management with methadone and adjunctive medications

Chiron, 7/2023

CFSRE, Colombo Plan Health Alert, 1/2025

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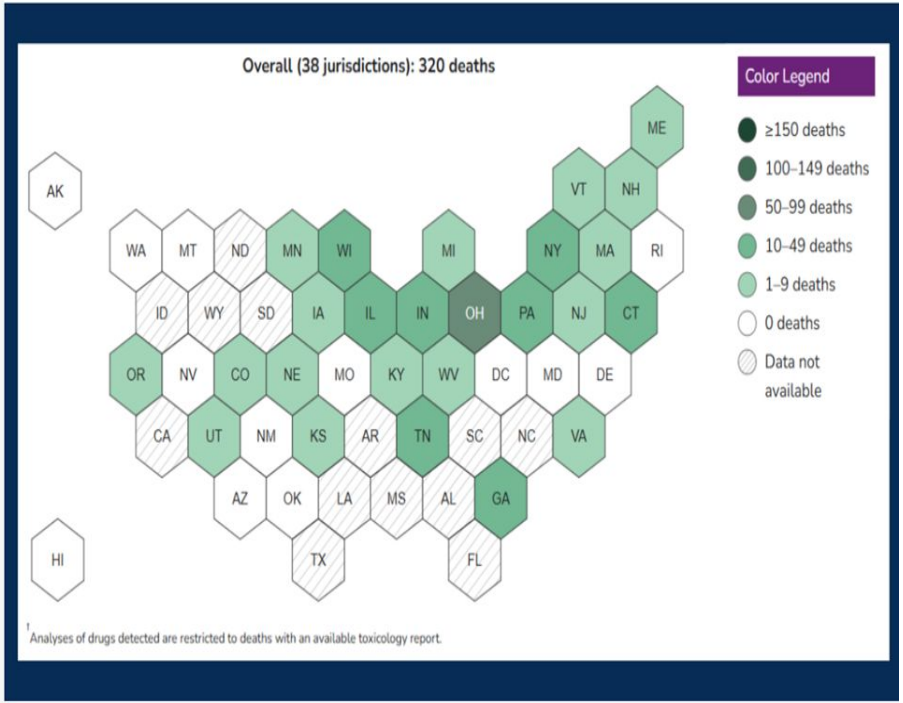
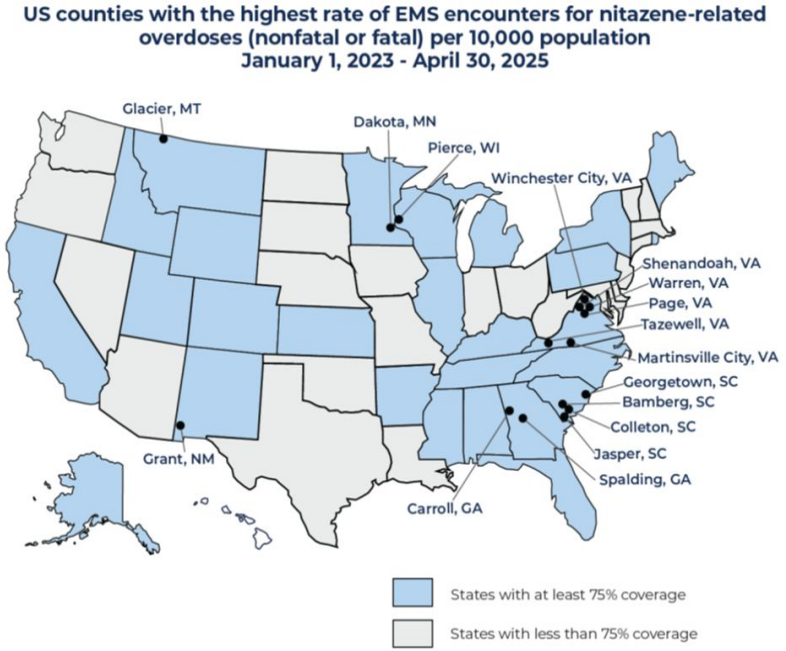
NITAZENE-LINKED DEATHS AND EMS ENCOUNTERS FOR NITAZENE-RELATED OVERDOSES





NDEWS-2025-nitazene-overdoses

Centers for Disease Control and Prevention. State Unintentional Drug Overdose Reporting System (SUDORS).

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XYLAZINE-ASSOCIATED WOUND CARE

TABLE 1. The Prevention Point Philadelphia Wound Care Clinic's Approach to Care for Xylazine-associated Wounds

Stepwise Dressing Change	Dressing Products Used	Notes
Step 1: Premedicate if possible		In settings where available, advocate for adequate pain/withdrawal management before dressing change
Step 2: Remove soiled dressing		Soak soiled dressing with water/saline to decrease pain with removal. Offer patient option to remove their own dressing.
Step 3: Clean	Normal saline, generic wound washes For wounds with heavy burden of nonviable tissue: • Vashe, Dakins 0.125%	Test cleansers on small area of wound to assess tolerance.
Step 4: Debride	Enzymatic debridement • Santyl: Requires prescription; costly Autolytic: • Medihoney: Consider outdoor exposure and potential insect attraction • Hydrogel silver • Silver gel/Silver sulfadiazine • PHMB topical	Topicals may be applied to the primary dressing (step 6) to avoid directly touching sensitive wounds. Alert patient to the likelihood of increased drainage with use of topical debriding agents. Cross-hatching of eschar, if tolerated, promotes deeper penetration of topical debriding agents and may be appropriate in some settings.
Step 5: Apply other topicals	Skin protectant to periwound tissue (eg no-sting skin prep, A&D ointment, Coloplast Triad) Topical antibiotic if indicated and compatible (eg, Mupirocin)	Preservation of intact periwound tissue is priority, especially with necrotic and heavily exudative wounds. Systemic antibiotics do not penetrate above the wound bed, and a topical may be required to reduce the overall bioburden.
Step 6: Apply primary dressing	Based on assessment of wound drainage: • Wet/normal wound: Oil-emulsion (e.g. Adaptic) • Dry wound: Petroleum-based (e.g. Xeroform)	Cut to shape of wound to avoid coverage of periwound area, which can promote breakdown. Check compatibility of Xeroform and any topicals used.
Step 7: Apply secondary of dressing	Super absorbent dressing, layers of woven gauze, abdominal pads, or nonstick gauze	
Step 8: Secure	Gauze wrap secured with Tubigrip, IV netting, self-adherent wrap, or ACE bandage	Self-adherent or ACE bandages should be applied just tight enough to secure underlying dressings, not for compression. Self-adherent wrap may contribute to skin breakdown if not changed daily.

Harm reduction and trauma-informed care considerations

- Assess the patient's history of wound care—what dressing supplies or strategies have and have not worked?
- Ask if patient would like to remove dressing themselves, to support engagement and autonomy and minimize pain.
- Recognize the distress and stigma often associated with wound odor—offer air freshener, aromatherapy inhalers, and change trash frequently.
- Dispense oral antibiotics or other oral medications in lanyard-attached container (eg, clear plastic badge holder) to prevent theft or loss (for unhoused individuals)
- Establish a wound dressing change schedule that is feasible for patient – provide dressing change supplies to accommodate several dressing changes when possible.
- Build relationships with local emergency medicine, internal medicine, infection disease and addiction medicine departments to facilitate warm handoffs of patients to and from hospitals

McFadden, R, et al. J Addict Med, 2024

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METODOMIDINE-ASSOCIATED OPIOID OVERDOSES IN CHICAGO, IL: A REPORT OF 3 CASES

- **Case Summary:** We present 3 cases of opioid overdoses involving medetomidine at the same emergency department, which are part of a larger series of at least 12 confirmed, 26 probable, and 140 suspected cases in Chicago between May 11 and May 17, 2024.
- Each presented with sinus bradycardia, hypertension, and prolonged sedation, which persisted after naloxone administration.
- Laboratory results confirmed medetomidine, fentanyl, and other substances in their systems.
- Management involved symptomatic treatment, including cardiorespiratory support and antihypertensive therapy.

TABLE 1. Results of Drug Enforcement Administration's Toxicology Testing Program (DEA TOX) for 3 Cases

	Case 1	Case 2	Case 2	Case 3
Sample source	Serum	Serum	Drug	Serum
4-anilino-N-phenethylpiperidine (4-ANPP)	*	2.4	12	0.3
6-Acetylmorphine	*	*	38	*
Benzoylecgonine	36.5	300	*	214
Beta hydroxy fentanyl	*	2.4	*	*
Bromazolam	*	0.3	*	*
Cocaine	*	*	86	1.2
Despropionyl para-fluorofentanyl	*	*	2	*
Diphenhydramine	120	187	104	38.5
Fentanyl	1.1	20.6	209	3.3
Heroin	*	30	*	*
Ketamine	229	*	*	*
Medetomidine	4.9	4.1	4.96	20.5
Morphine	15.6	*	*	*
Norfentanyl	2.7	19.7	*	3.5
Para-fluorofentanyl	*	*	8	*
Quinine	8.7	12.8	171	*
Xylazine	*	0.4	144	4.9

Values reported in ng/mL. 4-ANPP, 4-anilino-N-phenethylpiperidine, is a direct precursor to fentanyl.
*Indicates not detected.

Navani, Z, et al. J Addict Med, 2025

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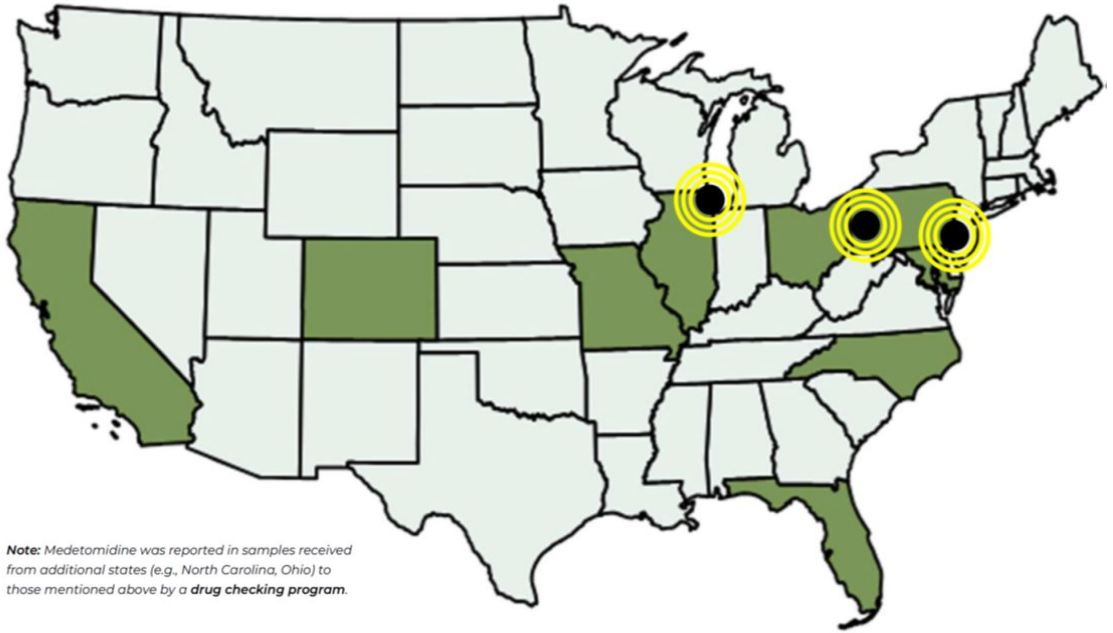
MEDETOMIDINE RAPIDLY PROLIFERATING ACROSS USA — IMPLICATED IN RECREATIONAL OPIOID DRUG SUPPLY & CAUSING OVERDOSE OUTBREAKS, 5/2024

Medetomidine has been identified across several states in the U.S. and Canada, and is recently being observed in severe overdose outbreaks in major metropolitan areas (as marked).



Note: *Medetomidine was reported in samples received from additional states (e.g., North Carolina, Ohio) to those mentioned above by a* ***drug checking program****.*

Krotulski, AJ, et al. CFSRE, 2024

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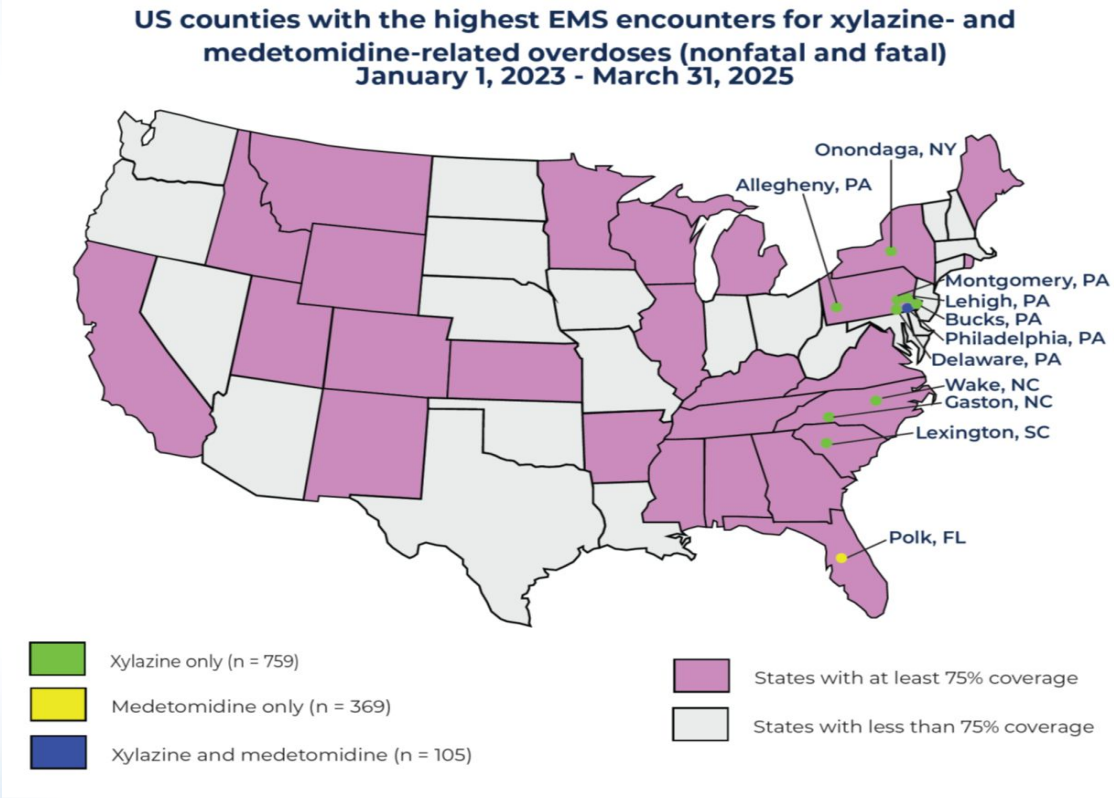
NDEWS WEEKLY BRIEFING, 4/11/25



NDEWS Weekly Briefing Issue 226

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LOCAL ANESTHETICS (‘CAINES) IN THE DRUG SUPPLY

Recommendations for Clinicians

- Adulteration of street drugs contributes to the uncontrolled intake of significant amounts of LAs.
- The use of drugs mixed with LA compounds can lead to toxicity.
- Because cocaine is the drug most frequently adulterated with LA compounds, patients using large amounts of cocaine have the highest potential for being over-exposed to LAs from illicit drug sources.
- Pay attention for signs and symptoms of cardiotoxicity or methemoglobinemia from LA in users of cocaine and to a lesser extent, users of heroin/fentanyl.

Indicators of Cardiotoxicity

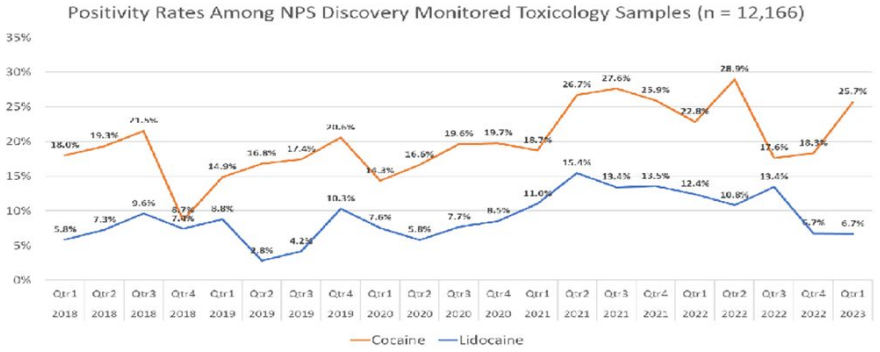
- Bradycardia or tachycardia
- Abnormal heart rhythms
- Low blood pressure
- Altered mental status (depressed level of consciousness)

Indicators of Methemoglobinemia

- Cyanosis (blue skin color)
- Low blood oxygen
- Distressed breathing
- Headache
- Dizziness
- Delirium
- Seizures

Recommendations for forensic practitioners

- Assess laboratory scope and capabilities for analyzing lidocaine, procaine and benzocaine in post-mortem, forensic, and clinical toxicological cases.
- Consider reporting on the frequency and co-occurrence with drugs with stakeholders in the jurisdiction.
- In post-mortem investigations, look for elevated levels of lidocaine in conjunction with positive cocaine or fentanyl.



CFSRE, NPS Discovery Alert, June 2023

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LOCAL ANESTHETICS (LA) TOXICITY

POSSIBLE COMPLICATIONS OF LA TOXICITY

The complications that can manifest with lidocaine toxicity are as follows:

- Seizure
- Coma
- Hypotension
- Atrioventricular heart block
- Idioventricular rhythms
- Ventricular tachycardia and fibrillation
- Cardiovascular collapse and death

MANAGEMENT OF LA TOXICITY

- Call 911 as the individual will need emergency department level of care for lipid emulsion therapy via infusion.
- While awaiting EMS, consider:
- Seizure suppression: raise the seizure threshold by administering benzodiazepines
- Airway management: ventilate with 100% oxygen
- Utilization of BLS/ACLS strategies and an AED to manage cardiac abnormalities while awaiting EMS

Torp, KD, et al. StatPearls, 2022

Stringer, CM, et al. StatPearls, 2023

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ROLE OF DRUG CHECKING

- Drug checking is a powerful tool to utilize with PWUD.
- Test strips give a qualitative assessment (yes, present or no, not present) of a substance's presence in a sample; however, often have cross sensitivity with other substances and their sensitivity often picks up any amount of a substance (which may not be clinically relevant).
- Drug checking that is quantitative and detects all substances in a sample is far more useful in informing PWUD and empowers them regarding their own substance use.
- At SACHR, in the South Bronx, we use an FTIR machine to test samples and inform participants what is in their sample.

CONTENTS OF “DOPE” BAGS IN THE SOUTH BRONX DETERMINED BY FTIR DRUG CHECKING

John Doe	Heroin Fentanyl Xylazine	Renegade	Medetomidine Fentanyl Caffeine Xylazine
Hummer	Fentanyl Xylazine	Tap Out	Medetomidine Fentanyl Caffeine Xylazine
Facebook	Heroin Mannitol	Prada	Fentanyl Xylazine Benzo Caffeine
Monster High	Heroin Fentanyl Xylazine Benzo Carfentanil	Black Bag	Benzocaine Phenibut Caffeine Diphenhydramine Lidocaine Medetomidine Procaine Promethazine Bis sebacate
Pink Bag	Mannitol (Major)| Fentanyl HCl (Major)| Caffeine (Major)	Luxury	Mannitol (Major)| Fentanyl HCL (Major)| Heroin HCL (Major)
NINJA	Procaine Fentanyl Caffeine Phenacetin Mannitol	END GAME	Caffeine Mannitol Procaine Fentanyl Xylazine

Bugatti	BTMPS Heroin Fentanyl Mannitol Bis sebacate Procaine Xylazine	Blue Bag	Heroin Carfentanil
Drop Dead	Procaine Caffeine Fentanyl	You Tube	Mannitol Fentanyl Benzo
Green Bag	Fentanyl Mannitol Xylazine Procaine	Pedigree	Mannitol BTMPS Bis sebacate Procaine
Purple Bag	Heroin Xylazine Fentanyl Benzo	Grey (sticky) dope	Xylazine Bromazolam Benzocaine Fentanyl
Plain White Bag 14th	Fentanyl Xylazine Benzo	Yukon	Heroin Fentanyl Xylazine
100%	Heroin	Passion	Fentanyl Xylazine Benzo
World Wide	Heroin Fentanyl Xylazine Benzo	Voto Perdido	Fentanyl Xylazine Benzo
Sabrosura	Mannitol Heroin Lidocaine	Toxic	Procaine Fentanyl Caffeine

SACHR drug checking, South Bronx, NY, 4/2025

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OPIOID ANTAGONISTS IN THE US

- High dose and long-acting opioid antagonists were approved without testing for precipitated withdrawal and are often aggressively marketed despite decades of evidence from naloxone distribution programs worldwide that the ideal dose of naloxone is one that restores breathing without inducing withdrawal.
- In 2021, due to the widespread availability of high-potency synthetic opioids like fentanyl, the US FDA approved two high-dose naloxone products, an 8 mg IN spray and a 5 mg IM injectable. The only studies reported in the FDA package inserts for both products are pharmacokinetic studies in healthy volunteers, which demonstrated substantially higher naloxone plasma levels than standard doses of naloxone (0.4 mg IM vs. 8 mg IN and 2 mg IM vs. 5 mg IM, respectively).
- In April 2024, based on a pharmacokinetic study of 30 healthy adult subjects, the FDA approved a 10 mg IN naloxone. None of these approval trials was conducted among opioid overdose patients at risk for precipitated withdrawal.
- In 2023, the FDA approved a 2.7 mg IN formulation of nalmefene, a more potent and longer acting opioid antagonist than naloxone. The approval of nalmefene was also based on pharmacokinetic studies performed in healthy volunteers that showed higher plasma levels than standard naloxone doses and one pharmacodynamic study among opioid-experienced, but “non-dependent” participants which showed successful reversal of respiratory depression induced by laboratory administered remifentanil.

Russell, E, et al. International Journal of Drug Policy, 2024

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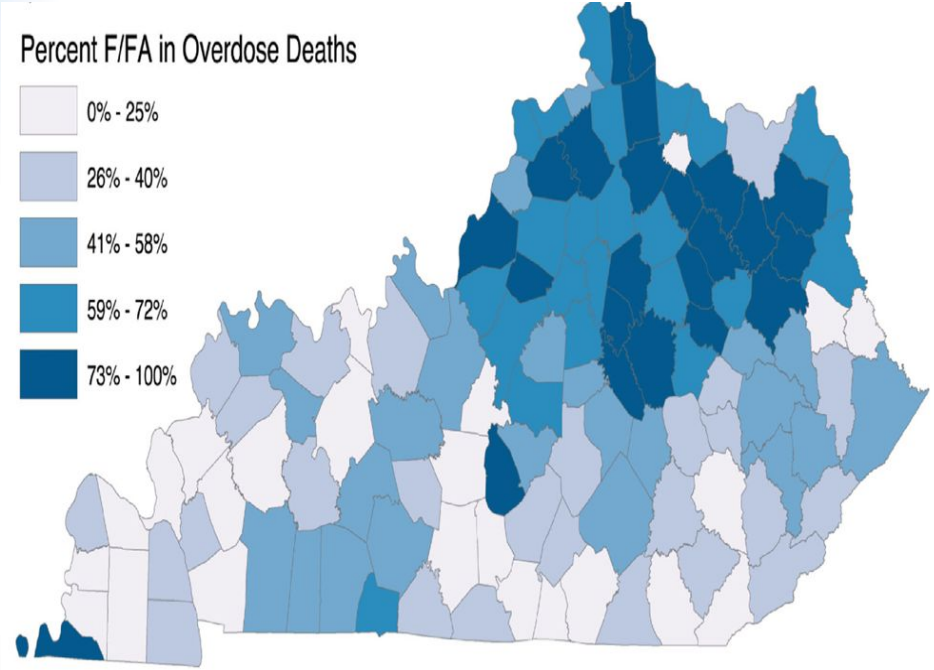
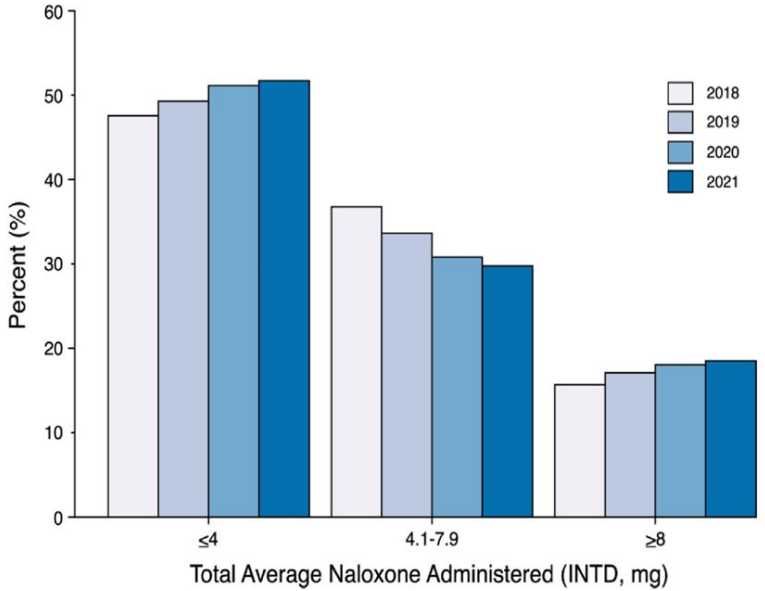
EXAMINATION OF NALOXONE DOSING PATTERNS FOR OPIOID OVERDOSE BY EMERGENCY MEDICAL SERVICES IN KENTUCKY DURING INCREASED FENTANYL USE FROM 2018 TO 2021



Geographical map with percentage of drug overdose deaths that involved F/FA, by county of death, 2018–2021 combined.



Description of the administered intranasal equivalent total dose (administered by EMS personnel and/or bystanders), by year.

After analyzing data from more than 30,000 suspected overdose encounters, they were unable to identify a relationship between fentanyl availability and the dose of naloxone administered by EMS and bystanders together.

Rock, P, et al. Drug Alcohol Depend, 2024

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MISSOURI'S OVERDOSE FIELD REPORT: DESCRIPTIVE ANALYSIS, SURVIVAL TRENDS, AND NALOXONE DOSING PATTERNS FROM A COMMUNITY-BASED SURVEY TOOL, 2018-2022

- ***Results:***
  - Between 2018 and 2022, 12,225 overdoses (67% male; 78% White) were reported through the ODFR, with a 96% (n = 11,225) survival rate.
  - ***Intramuscular naloxone in particular was associated with a significantly higher odds of survival compared to nasal naloxone (OR = 2.11). An average of 1.6 doses of naloxone per incident were administered. Additional doses were associated (ps < .02) with being older (OR = .45), female (OR = .90), nasal naloxone (versus intravenous) (OR = .65), and the belief fentanyl was present (OR = 1.49).***
- ***Conclusion:*** Our reporting form provides a comprehensive picture of the events surrounding reported overdoses, including factors associated with survival, how much naloxone was used, and the effects of respondents believing fentanyl was involved. Missouri's report can provide support for current naloxone dosing.
- ***Nearly 90% of overdoses were reversed with one or two doses of naloxone. The findings do not support a need for higher dose naloxone.***

Budesa, Z, et al. Am J Drug Alcohol [Ab]use, 2024

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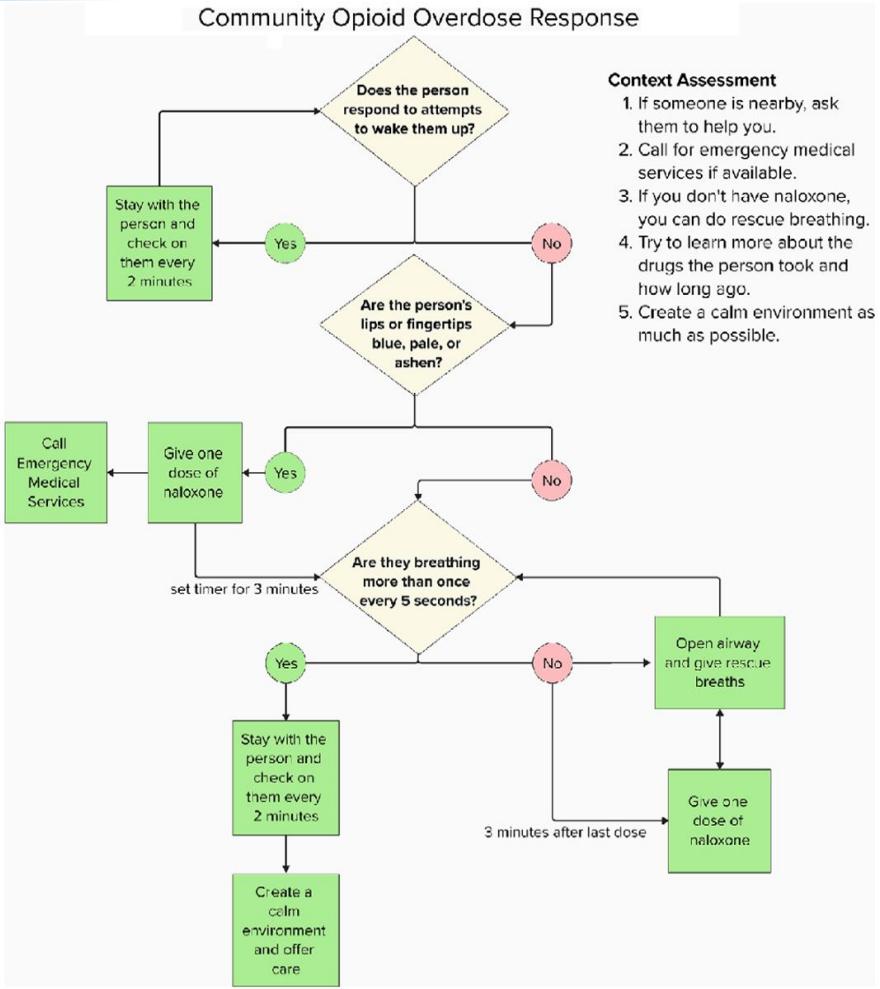
COMPASSIONATE OVERDOSE RESPONSE



Russell, E, et al. International Journal of Drug Policy, 2024

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COMPASSIONATE OVERDOSE RESPONSE

At the March 18–19, 2024, *Compassionate Overdose Response Summit & Naloxone Dosing Meeting,* a panel of harm reduction experts issued the following call to action:

1) people who use drugs should be directly involved in decisions regarding the research, development, selection, and distribution of opioid overdose reversal products;

2) regulatory agencies and pharmaceutical manufacturers should carefully consider and communicate the risk and duration of withdrawal associated with higher dose and longer-acting opioid antagonists;

3) take-home naloxone kits should include at least two doses of an intramuscular (IM) product containing 0.4 mg or an intranasal (IN) product containing ≤4 mg;

4) at this time, high dose and long-acting opioid antagonists have no use in acute opioid overdose response; and,

5) overdose response educational materials, instructions on overdose response, and training should emphasize the restoration of breathing, avoiding withdrawal, and compassionate post-overdose support and care.

Russell, E, et al. International Journal of Drug Policy, 2024

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WHY A 3 MG DOSE OF IN NALOXONE?

- Harm Reduction Therapeutics uses a 3.0 mg formulation of naloxone to reverse opioid overdoses, including fentanyl overdoses. The 3.0 mg dose is based on the scientific literature supporting the efficacy of both 2.0 mg and 4.0 mg intranasal (IN) naloxone formulations. Extensive input from harm reduction experts, the long history of reversing opioid overdoses using 0.4 mg of intramuscular naloxone, and the desire to administer enough naloxone to restore spontaneous breathing without inducing precipitated opioid withdrawal, all supported their decision to formulate a 3.0 mg naloxone formulation.

- Even 2.0 mg of intranasal naloxone given in various concentrations reverses opioid overdose in 74-82% of patients. Opioid-related overdose deaths are increasingly being driven by exposure to highly potent fentanyl and fentanyl analogs. A subset of opioid overdoses requires multiple administrations of 2.0 mg IN naloxone to successfully reverse. However, in a study of over 2166 people who received naloxone in the field followed by paramedic support, 91% experienced complete resolution and reversal of symptoms after a single (mostly 2.0 mg; 51%) dose of IN naloxone and required no further advanced life support intervention. Only 9% required two or more doses of naloxone, and only 2.4% required a third dose. Even in the context of illicitly manufactured fentanyl, studies have found no increases in the average number of naloxone doses used to reverse an overdose.

STATEMENTS AGAINST HIGH DOSE NALOXONE AND/OR NALMEFENE PRODUCTS

- ACMT & AACT Joint Position Statement: Nalmefene Should Not Replace Naloxone as the Primary Opioid Antidote at This Time, September 28, 2023
- AF Infante, et al: Stronger, longer, better opioid antagonists? Nalmefene is NOT a naloxone replacement, February 2024
- TN Harm Reduction Coalition, University of TN, Harm Reduction Innovation Lab, Brown University: High-Dose Naloxone Formulations Are Not as Essential as We Thought, May 13, 2024
- California Syringe Exchange Programs Coalition (CASEP): Statement Regarding High Dose Naloxone and Long Acting Nalmefene Opioid Overdose Reversal Formulations, July 29, 2024
- Washington State Department of Health: Issue Brief: The Risks High-Dose Naloxone Products and Nalmefene for Community Opioid Overdose Response, November 2024
- Expert Statement Regarding High-Dose Naloxone and Long-Acting Opioid Overdose Reversal Formulations in North Carolina, November 27, 2024
- HMA/JHU: Opioid Overdose Reversal Products FAQ
- NACCHO Naloxone Dosing Considerations Statement, February 2025

Lemen, PM, et al. Harm Reduct J, 2024

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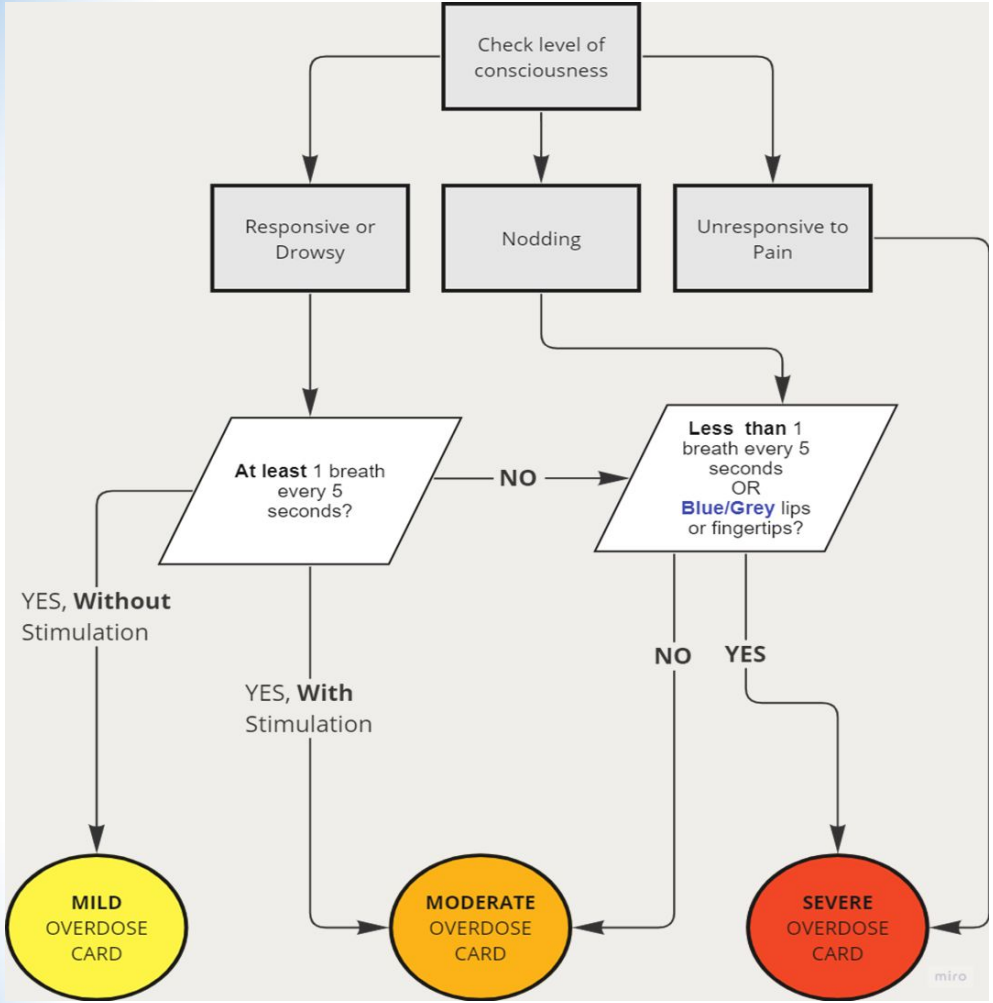

ASSESSING OVERDOSE SEVERITY ALGORITHM

Vancouver Coastal Health (adapted by SACHR)

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BVM CAVEATS

- Although BVMs are appropriate for trained persons, effective BVM ventilation is an advanced skill, requiring training and hands-on practice.
- If performed incorrectly, BVM ventilation can accelerate hypoxia and exacerbate the airway obstruction that naturally occurs during profoundly depressed levels of consciousness.
- BVM ventilation increases the risk of air entering and inflating the stomach, reducing oxygen delivery to the lungs.
- BVM ventilation increases the risk of aspiration of stomach contents into airways and lungs.
- BVMs are relatively expensive (~$11-$18 each)
- BVM use can be done with one or two persons

BC Centre for Disease Control Position Statement, Bag Valve Masks for Overdose Response, 2018
ems1.com

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