

INNOVATIONS IN POLYSUBSTANCE OVERDOSE RESPONSE: RESPONDING MORE EFFECTIVELY AND COMPASSIONATELY

Presentation for NYSACHO, 8/27/26

“Overdose is a medical emergency with differences in its presentation and appropriate response.”
– Kailin See, 3/2024

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DISCLOSURES, CAVEATS, AND ACKNOWLEDGEMENTS

- Kelly S. Ramsey MD, MPH, MA, FACP, DFASAM has no significant financial disclosures.
- 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.



LEARNING OBJECTIVES/AGENDA

- Discuss the current unregulated drug supply, with a focus on sedative adulterants
- Discuss appropriate opioid antagonist use and the concept of compassionate overdose response
- Discuss an appropriate overdose response for the current (and any future) drug supply
- Discuss how to augment your overdose response with additional tools to better assess and support airway and breathing
- Discuss briefly overamping due to stimulants and appropriate response
- Discuss briefly synthetic cannabinoid “overdose” and appropriate response
- Discuss how to support patients after an overdose and support staff after responding to an overdose



THE CURRENT UNREGULATED DRUG SUPPLY WITH A FOCUS ON SEDATIVE ADULTERANTS



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

NITAZENE-INVOLVED DEATHS IN THE US, 2024

Where were select drugs of interest detected¹² in drug overdose deaths in 2024, Overall (43 jurisdictions)?[†]

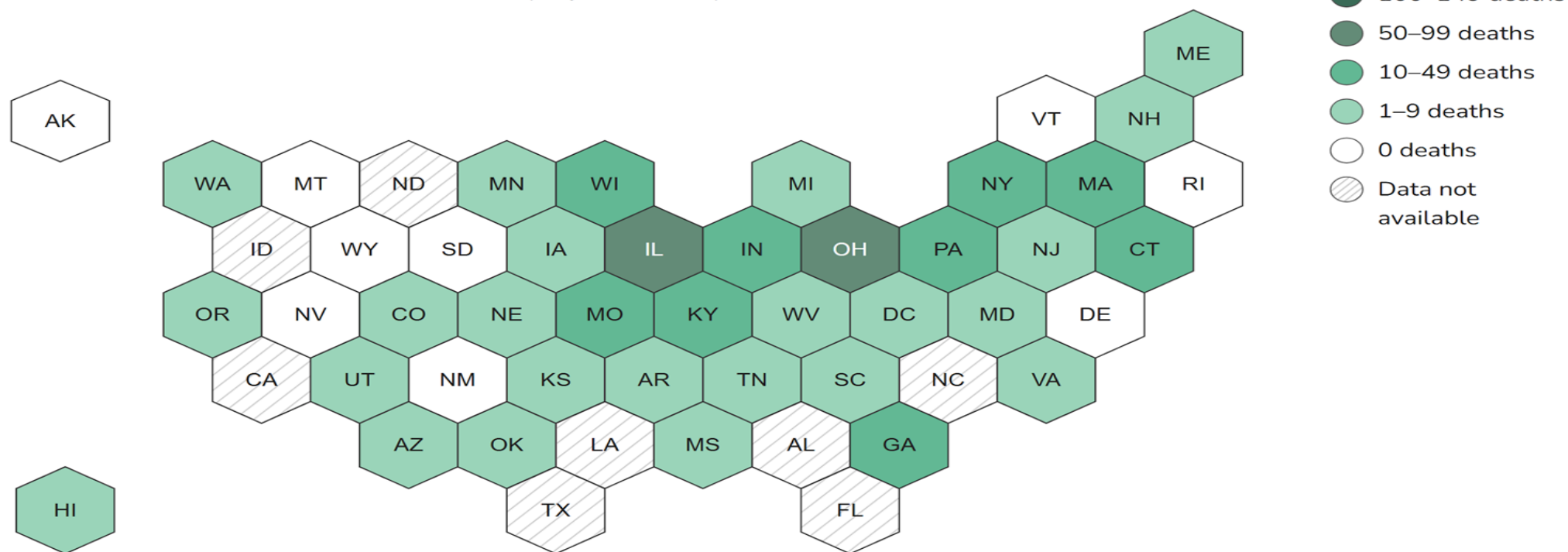
2024 ▾

Nitazene analogs¹⁴

Metric: ☒ Count ☐ Percent

Overall (43 jurisdictions): 409 deaths

Color Legend



[†] Analyses of drugs detected are restricted to deaths with an available toxicology report.

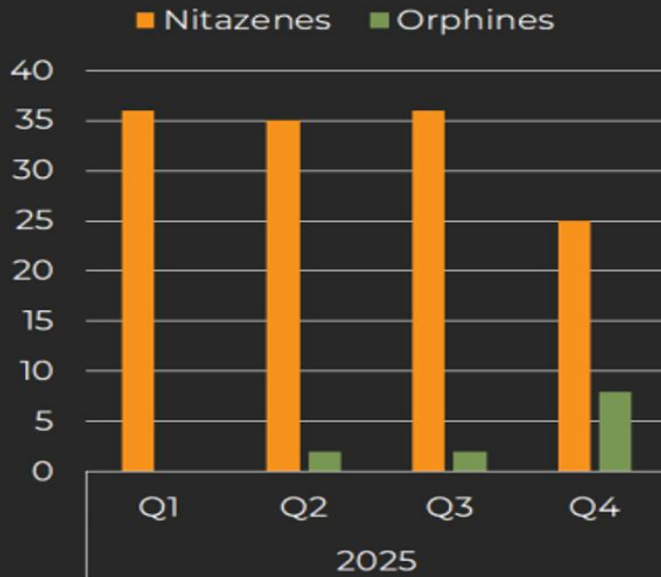
ORPHINES (benzimidazol-2-ones)

- Following the recent core structure scheduling by China of the nitazenes (benzimidazoles), markets have seen a decline in these potent opioids in late 2025, and their replacement by a new class of synthetic opioids, the benzimidazol-2-ones, also known as the “orphines.”
- Following initial alerts, brorphine was rapidly scheduled or emergency-controlled in multiple jurisdictions (e.g., EU, UK, US, Canada). This regulatory response appears to have accelerated structural diversification, with multiple halogenated and cyclized analogs appearing about four years after brorphine controls were put in place.
- •As analytical reference standards have become more widely available, orphine analogs detected now include Chlorphine, N-Propionitrile Chlorphine (Cychlorphine), 5,6-Dichloro Desmethylchlorphine (SR-17018), Spirochlorphine (R-6890), Spirobrorphine and 5,6-Dicholoro Brorphine (SR-14968), various members of which have been reported in the UK, Europe, US, and Canada.
- **N-propionitrile chlorphine** was detected on 2/4/2026 by SACHR in the South Bronx.
- Overdose response and treatment for OUD due to orphines would be the same as for other high potency synthetic opioids.

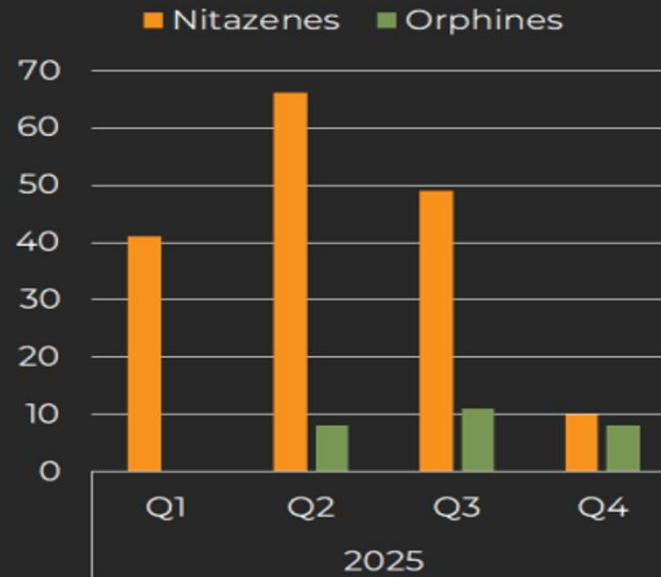
EARLY ORPHINE ANALOGUE TRENDS

EARLY ORPHINE ANALOGUE TRENDS

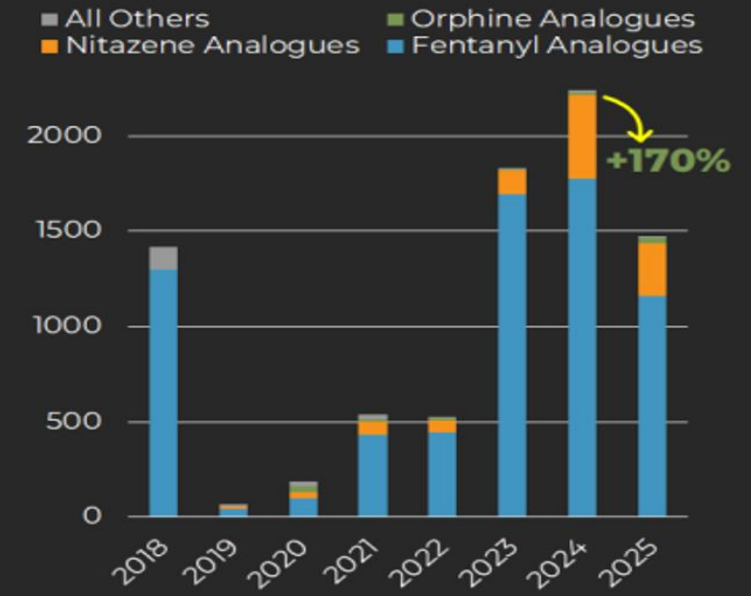
TOXICOLOGY SPECIMENS



DRUG MATERIALS

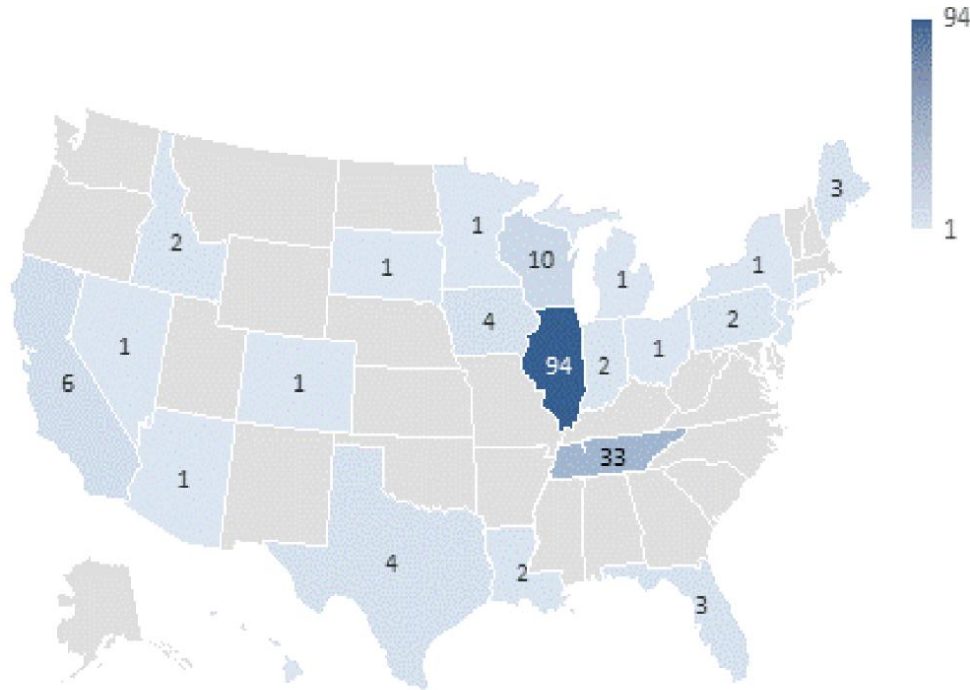


TOTAL DETECTIONS



GEOGRAPHIC SPREAD OF ORPHINES AND THE MAIN NOVEL PSYCHOACTIVE SUBSTANCE (NPS) OPIOID SUBCLASSES

- The geographic spread of the presumptive positive cases is shown below:



MAIN NPS OPIOID SUBCLASSES

FENTANYLS 2013 - PRESENT

Fentanyl
3-Methylfentanyl
Carfentanil
Butyrylfentanyl
Cyclopropylfentanyl
Isobutyrylfentanyl
Fluoro-Isobutyrylfentanyl
Methoxyacetylfentanyl
O-methyl fentanyl
P-Fluorofentanyl
Others (~65) ...

All controlled either by name or through core structure scheduling.

NITAZENES 2019 TO PRESENT

Isotonitazene
Metonitazene
Butonitazene
Protonitazene
Flunitazene
Etodesnitazene
N-Pyrrolidino protonitazene
N-Pyrrolidino metonitazene
N-Pyrrolidino etonitazene
N-desethyl isotonitazene
Others (~4)...

Most currently controlled in the US permanently or temporarily, by name

ORPHINES 2025 - PRESENT

Brorphine
Chlorphine
N-Propionitrile Chlorphine
5,6-Dicholoro
Desmethylchlorphine
Spirochlorphine
Spirobrorphine
5,6-dicholoro Brorphine
(others evolving rapidly)

Only Brorphine currently scheduled in the US
Others are not scheduled



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

- **Mechanism of action:** central alpha-2 agonist; KOR full agonist (enhanced sensitivity to withdrawal in females); serotonin (5HT₇R) receptor agonist; 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 (when combined with fentanyl), sedation, respiratory depression (due to muscle relaxation of the tongue thus blocking the airway), skin ulcerations, physiological dependence
- **Metabolism:** highly lipophilic; primarily excreted in urine
- **Withdrawal management:** can complicate opioid withdrawal management; treat with clonidine, tizanidine, dexmedetomidine, benzodiazepines, ketamine, gabapentin; limited data to case studies, no best practices clearly defined
- **Wound care management:** keep wounds clean, moist, and covered; chemical debridement; assess for superinfection

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

XYLAZINE-INVOLVED DEATHS IN THE US, 2024

Where were select drugs of interest detected¹² in drug overdose deaths in 2024, Overall (43 jurisdictions)?[†]

2024 ▾

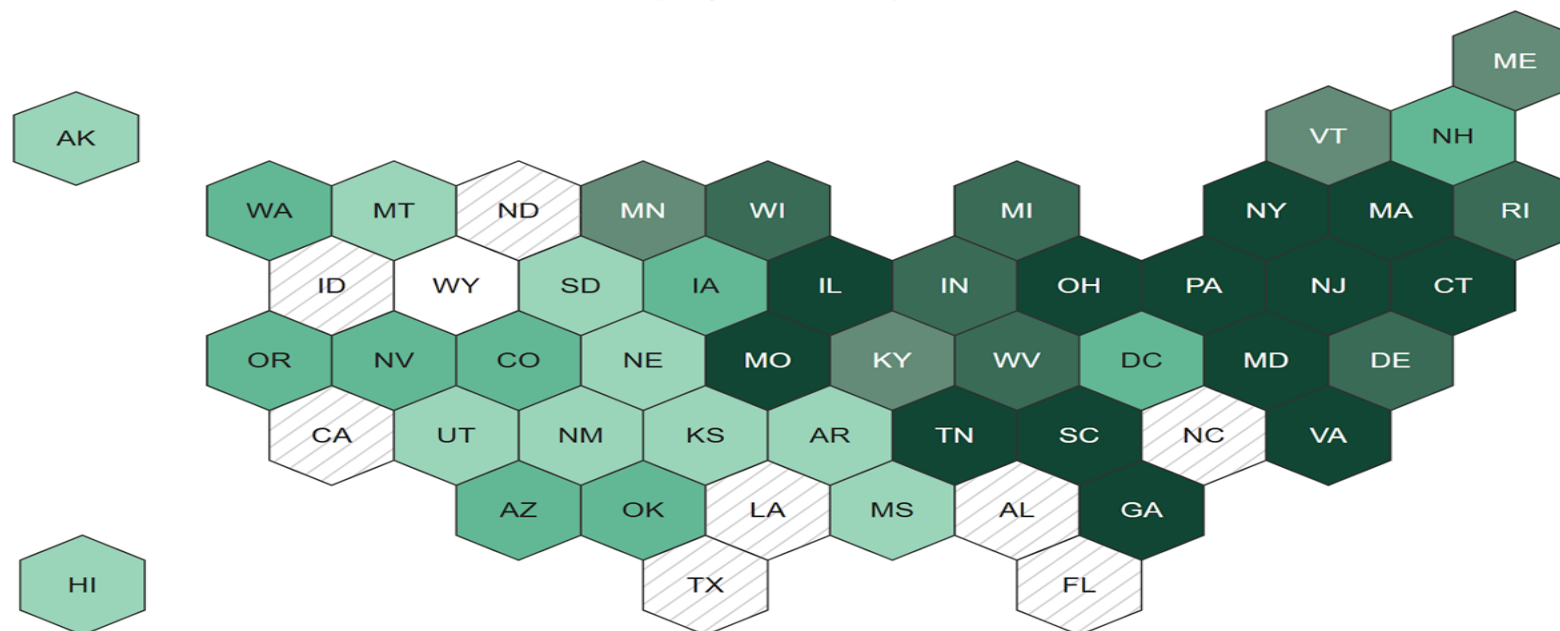
Xylazine ▾

Metric: ☒ Count ☐ Percent

Overall (43 jurisdictions): 6,088 deaths

Color Legend

- ≥150 deaths
- 100–149 deaths
- 50–99 deaths
- 10–49 deaths
- 1–9 deaths
- 0 deaths
- ▨ Data not available



[†] Analyses of drugs detected are restricted to deaths with an available toxicology report.

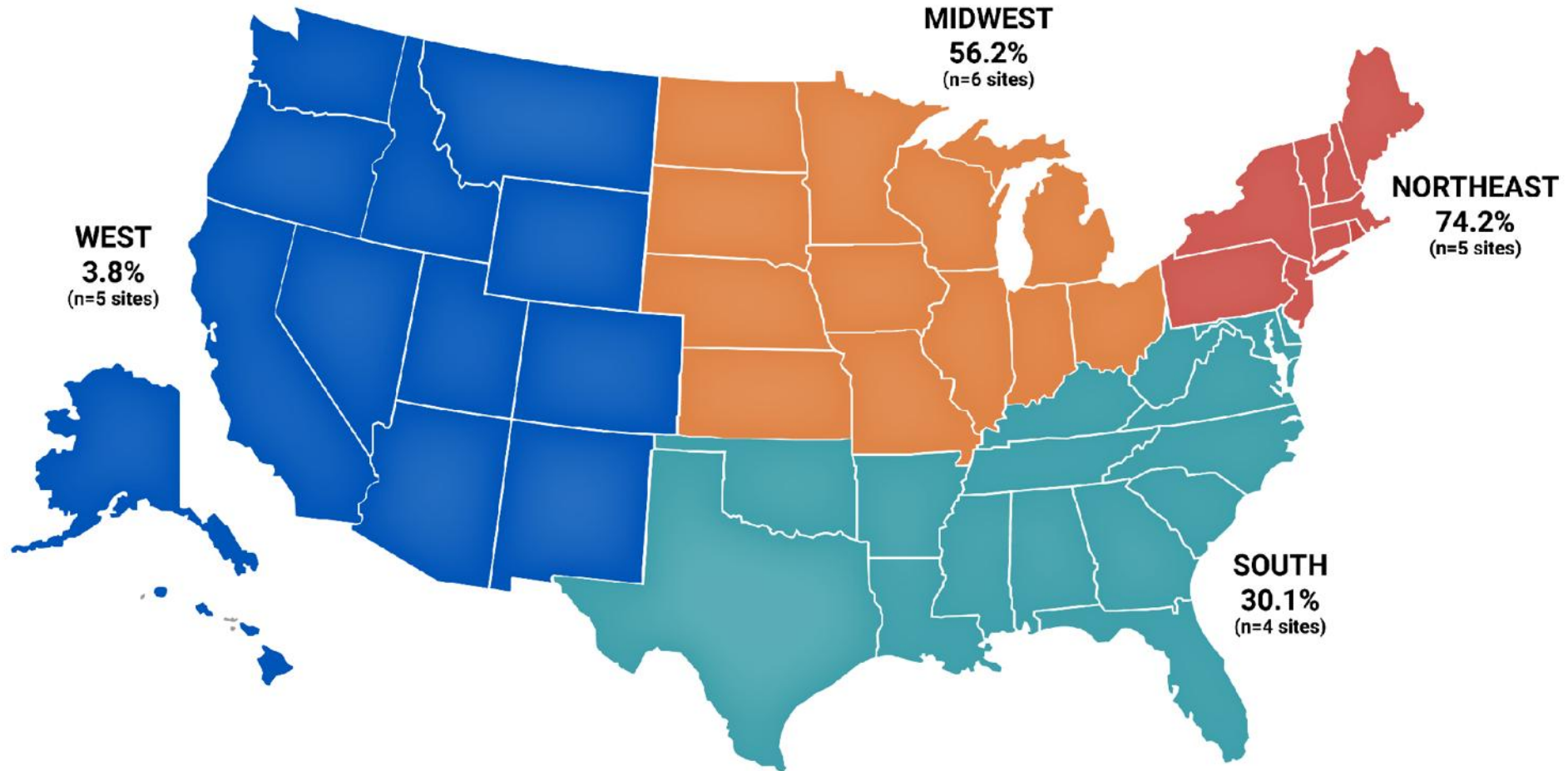
OVERLAPPING WITHDRAWAL SYNDROMES

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

SEDATIVES IN THE UNREGULATED DRUG SUPPLY: MEDETOMIDINE (“DOMITOR”)

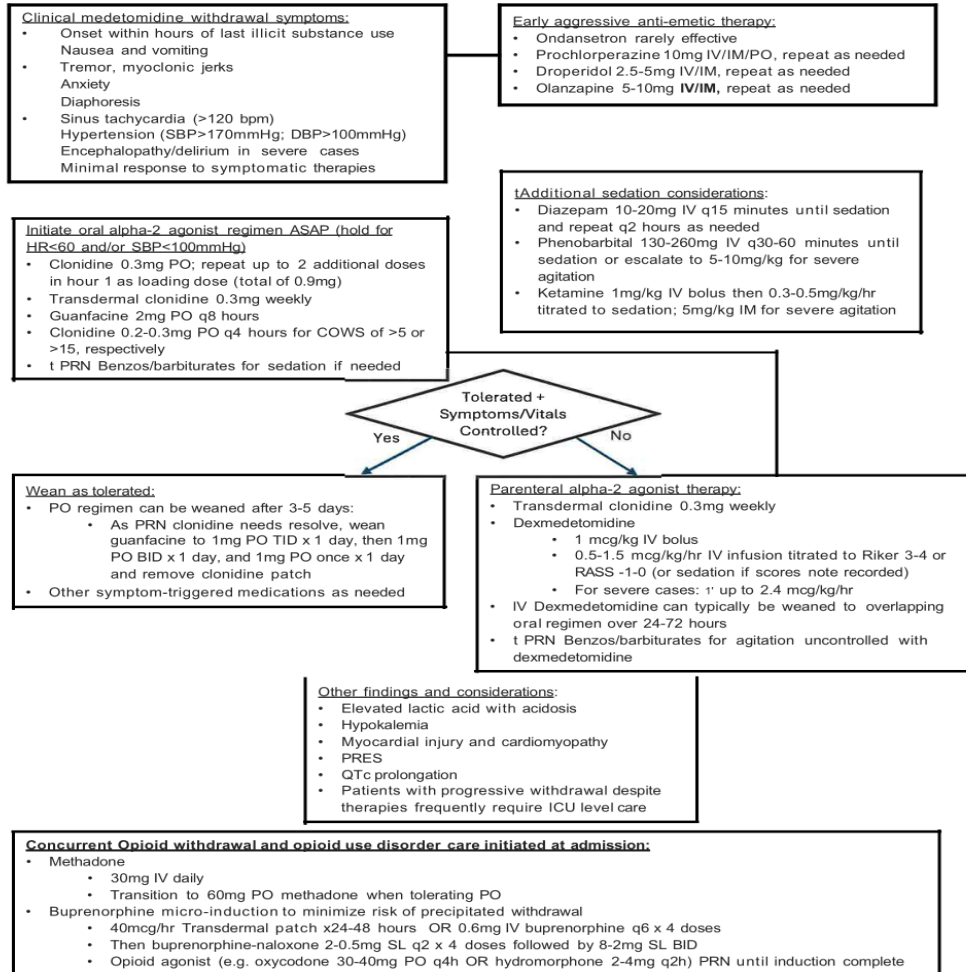
- **Mechanism of action:** a central alpha-2 agonist that is significantly stronger than xylazine; non-opioid veterinary sedative/anesthetic/analgesic/anxiolytic/muscle relaxant; not approved for human use
- **Typical presentation:** found in the unregulated highly potent synthetic opioid supply, often 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 (which may impact wounds and wound healing), muscle twitching, hypothermia, reduced cardiac output, and respiratory depression
- **Withdrawal management:** protocols have emerged for different settings; recommendations for management are more complicated than for xylazine: often requires multiple medications to manage; may require ICU admission if not caught early

MEDETOMIDINE DETECTION, 2025



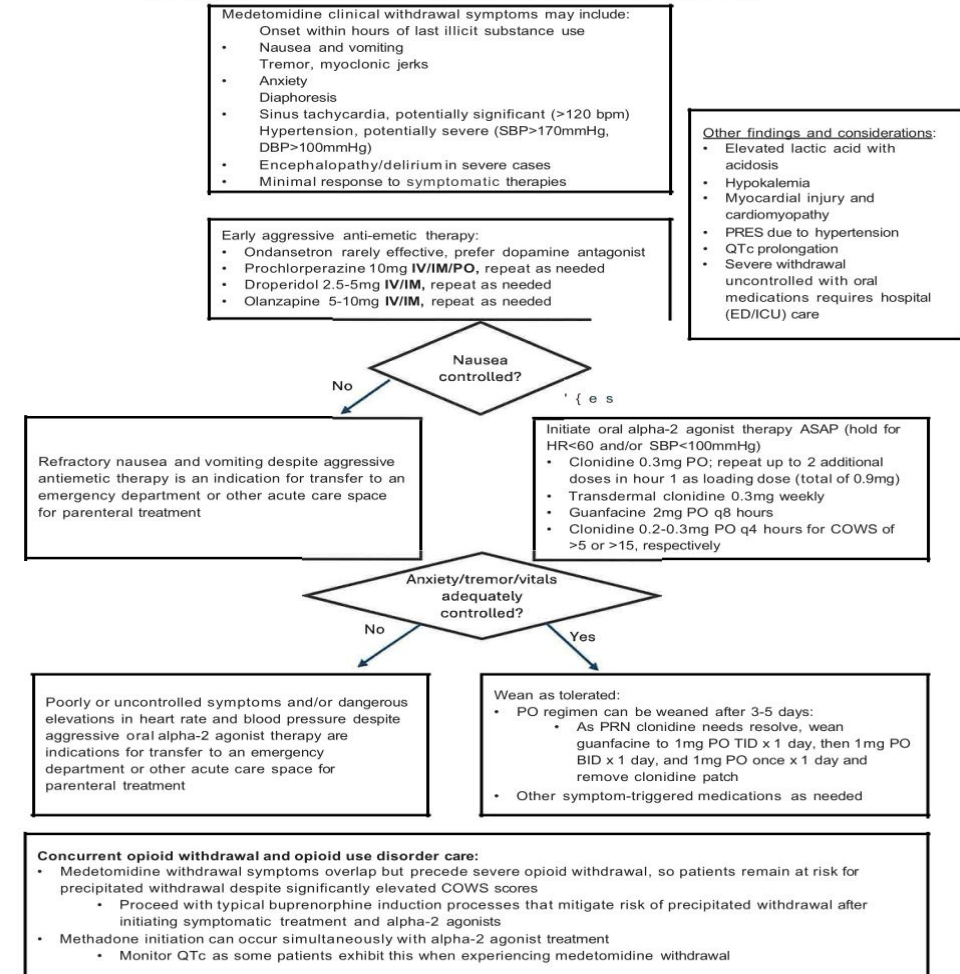
MEDETOMIDINE WITHDRAWAL PROTOCOLS

Medetomidine Withdrawal Treatment Guideline



*Recommendations based on current clinical experience and limited published evidence as of 9/8/2025.

Outpatient Medetomidine Withdrawal Treatment Guideline



*Recommendations based on current clinical experience and limited published evidence as of 9/8/2025.

XYLAZINE V. MEDETOMIDINE: SIMILARITIES AND DIFFERENCES

SIMILARITIES

- Both are veterinary medications
- Both are alpha-2-agonists
- Both are not opioids, so not responsive to naloxone
- 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 (yet) federally scheduled

DIFFERENCES

- **XYLAZINE**
Has a clear association with wounds
Is scheduled in some states
- **MEDETOMIDINE**
Is significantly more potent than xylazine
Is associated with longer sedation
Is associated with more pronounced effects on blood pressure and heart rate
Has multiple reports of association with hallucinations and significantly worse withdrawal symptoms

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

- Clinically, the patient may appear to have slurred speech, ataxia, and depressed mentation, especially if co-ingested with another form of sedative. Isolated overdoses involving oral benzodiazepines rarely lead to respiratory failure; however, when combined with other sedatives, it may be encountered.
- Synthetic benzodiazepines are significantly more potent than prescription benzodiazepines.
- Between 2019 and April 2020, synthetic benzodiazepines were identified in 48% and 83% of postmortem and DUID cases reported to the UNODC.

LOCAL ANESTHETICS ('CAINES) IN THE DRUG SUPPLY

RECOMMENDATIONS FOR CLINICIANS

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

INDICATORS OF CARDIOTOXICITY

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

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

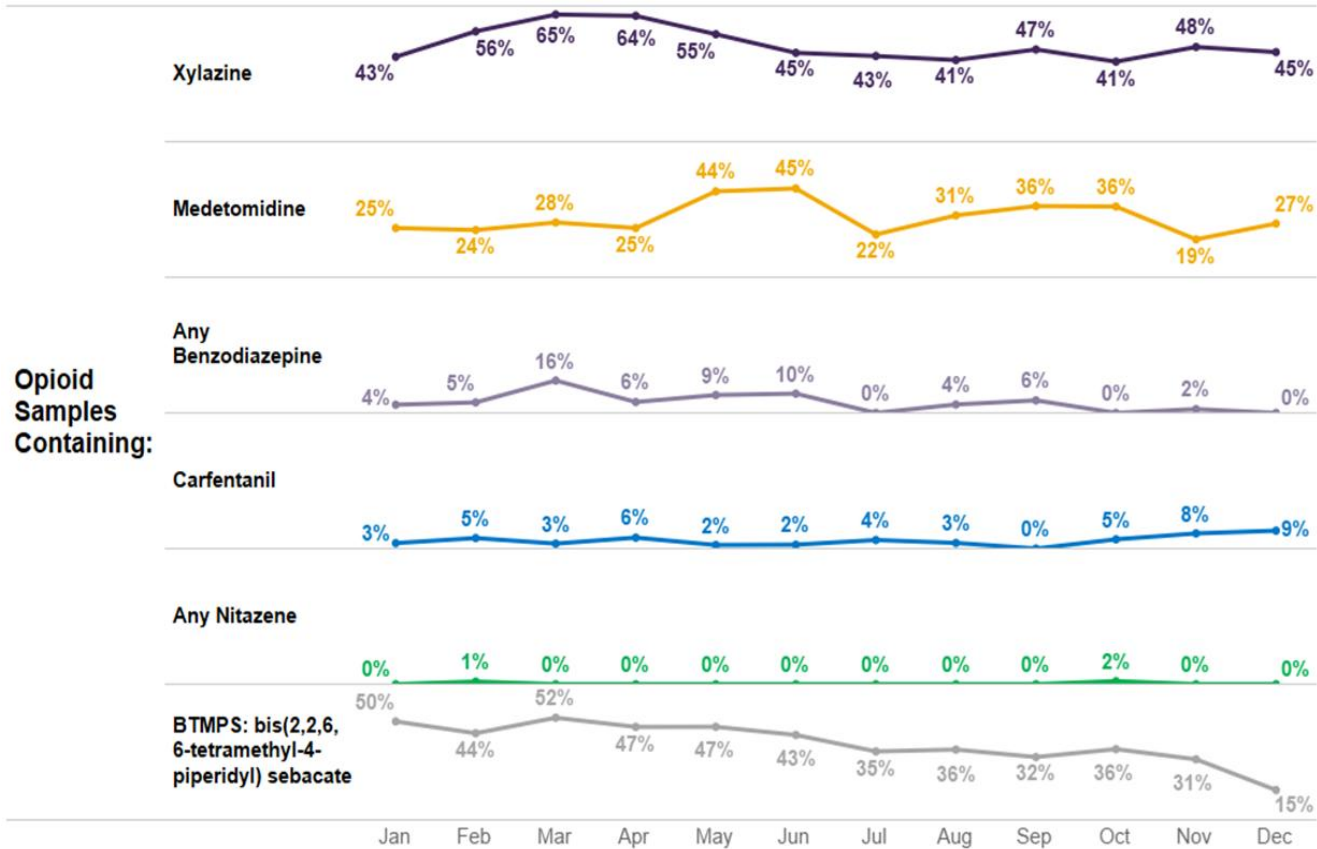
ROLE OF DRUG CHECKING

- 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.
- Drug checking allows for monitoring of local trends in the drug supply. There is substantial variation in the drug supply across regions.

EPIDEMIOLOGY OF THE CURRENT NYC UNREGULATED DRUG SUPPLY

- NYC DOHMH drug checking data as of 8/31/25 from 6 low threshold sites in the Bronx, Manhattan, and Brooklyn; a total of 3,533 samples from 590 unique individuals
- Of the 1,602 opioid samples tested, 95.9% produced a positive FTS result
- Just 1.7% of 1,370 non-opioid samples produced a positive FTS result; none of these results indicated fentanyl contamination in non-opioids
- Of 1,342 opioid samples with secondary testing, 44.3% contained xylazine; xylazine is found almost exclusively in fentanyl samples
- Medetomidine has been detected in 156 samples; medetomidine is found almost exclusively in fentanyl samples

NYS DOH DRUG CHECKING PROGRAM, 2025



Source: NYS Drug Checking Programs, 2026. Notes. Data limited to samples received between July 1, 2025, and December 31, 2025, with at least one opioid detected by confirmatory lab testing.; More recent data are provisional, and findings may change as additional lab results become available.

In 2025:

- **Xylazine** detection in opioid samples remained steady **between 41% and 48%** of samples in the last six months of 2025, after reaching 65% of samples in March 2025.
- **Medetomidine** detection in opioid samples fluctuated **between 19% and 45%** of samples in 2025.
- **Benzodiazepines** was detected in **between 0% and 6%** of opioid samples in the last six months, down from 16% in March 2025.
- **Carfentanil** detection in opioid samples reached a **peak at 9%** of samples in December 2025.
- **Nitazenes** were found in **2% or less** of monthly opioid samples in 2025.
- **BTMPS** detection in opioid samples declined from 52% in March to less than **15%** of samples in December 2025.

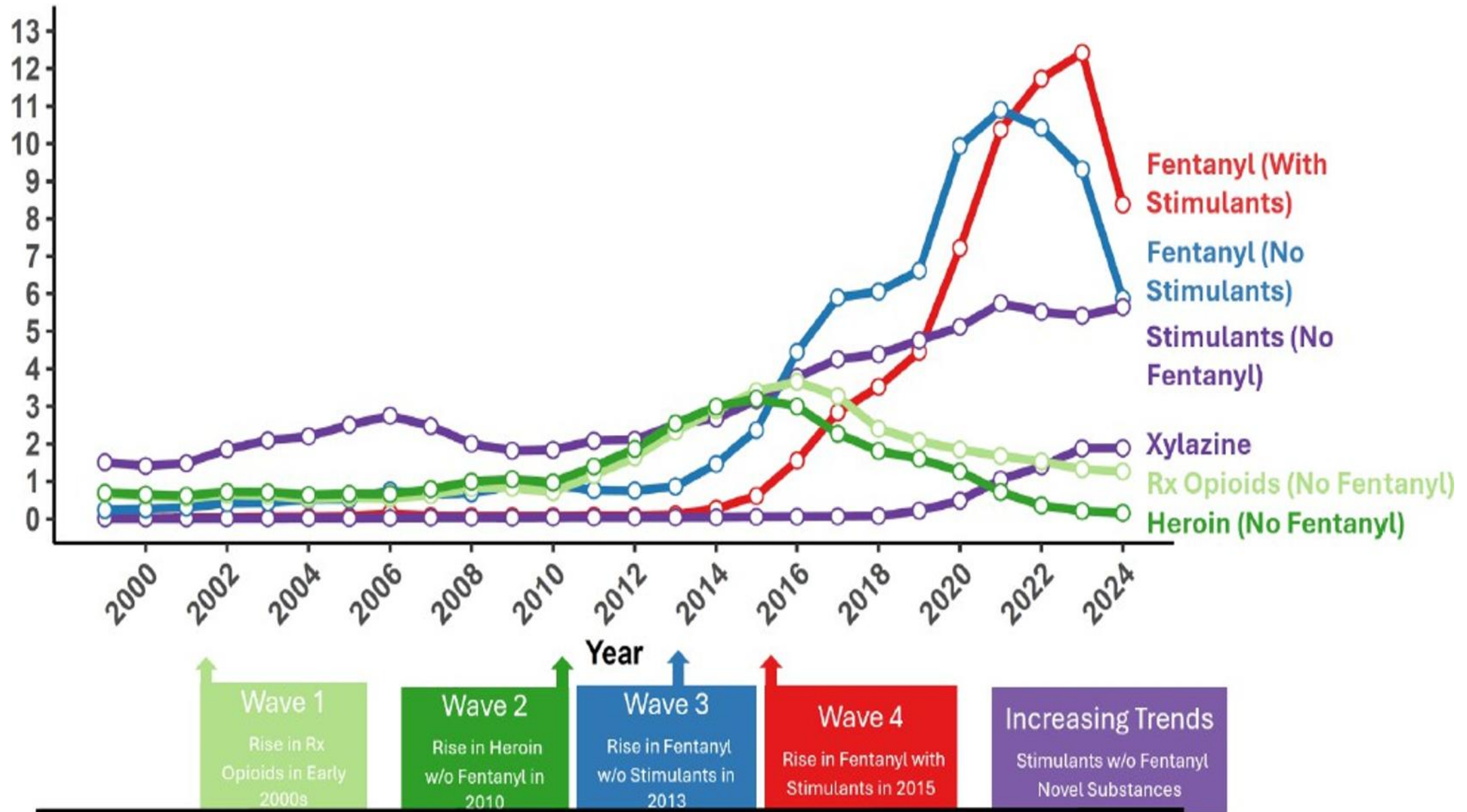
OTHER ADULTERANTS IN THE UNREGULATED DRUG SUPPLY

- ******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. 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 (in forthcoming slides).

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APPROPRIATE OPIOID ANTAGONIST USE AND THE CONCEPT OF COMPASSIONATE OVERDOSE RESPONSE

The Four Waves of the Overdose Crisis



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, 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.
- 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 opioid withdrawal.

OPIOID ANTAGONISTS IN THE US

- 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 and one pharmacodynamic study among opioid-experienced, but “non-dependent” participants which showed successful reversal of respiratory depression induced by laboratory administered remifentanyl.
- In September 2025, NYS Attorney General Letitia James’ office announced a settlement with the pharmaceutical company Indivior, the manufacturer of the above mentioned nalmefene product, to stop “misleading marketing of their unauthorized [in NYS] opioid overdose drug.” Indivior, in a separate letter to their stakeholders, announced cessation of all marketing for their nalmefene product.

Attorney General James Stops Misleading Marketing of Unauthorized Opioid Overdose Drug
Indivior Halts Marketing of Controversial Overdose Drug Opvee Following New York Settlement

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

EVIDENCE REGARDING OPIOID OVERDOSE AND OPIOID ANTAGONISTS

- Despite the dominance of high potency synthetic opioids in the unregulated drug supply, there is no evidence to support the use of high dose naloxone (> 4 mg/mL IN, >0.4 mg/mL IM), multiple doses of naloxone (> two standard doses of naloxone) or any nalmefene products in opioid overdose reversal.
- In a study done in NYS by the NYS DOH in conjunction with the NYS police, survival rates were the same whether troopers used the 4 mg IN or the 8 mg IN naloxone product; however, those who received the 8 mg IN dose had 2.5 times the risk of experiencing precipitated opioid withdrawal, including vomiting.
- In a study done using 17.6 years of overdose response data from a low threshold program in Pittsburgh, PA, they found that despite the changes in the unregulated drug supply over time (a transition from heroin to fentanyl; with fentanyl involved in 95% of overdose deaths), the number of standard doses (4 mg/mL IN) needed to reverse an opioid overdose did not change, with an average of 1.63 doses (< 2 doses) being given and survival rates remaining the same.

EVIDENCE REGARDING OPIOID OVERDOSE AND OPIOID ANTAGONISTS

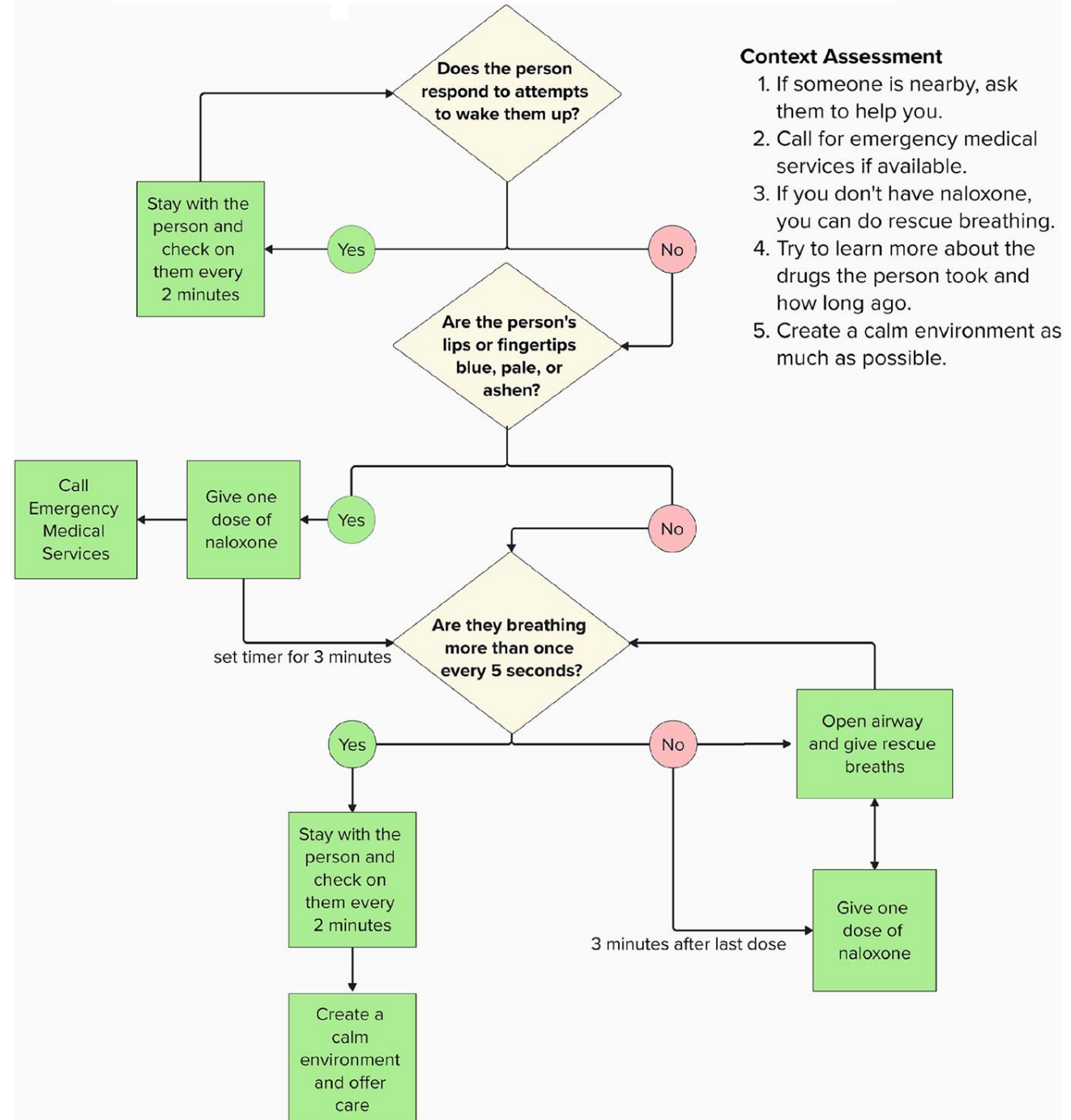
- In a study examining naloxone dosing patterns for opioid overdose response by emergency medical services in Kentucky during a period of transition (2018-2021) from heroin to increased fentanyl presence in the unregulated drug supply, after analyzing data from more than 30,000 suspected overdose encounters, they were unable to identify a relationship between fentanyl availability and the dose of naloxone administered by EMS and bystanders together. In other words, the dosing of naloxone did not change despite the dominance of fentanyl.
- In a study from Missouri, they looked at the circumstances in overdose responses between 2018-2022 (12,225 overdoses in total). Nearly 90% of all overdoses were reversed with 1 or 2 standard doses (4 mg/mL IN or 0.4 mg/mL IM) of naloxone (on average, 1.6 doses). The findings do not support a need for higher doses of naloxone.

COMPASSIONATE OVERDOSE RESPONSE

- At the March 18–19, 2024, *Compassionate Overdose Response Summit & Naloxone Dosing Meeting*, a panel of 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.

COMPASSIONATE OVERDOSE RESPONSE

Community Opioid Overdose Response



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 and published the data on the MIDUHA website in early 2024. 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

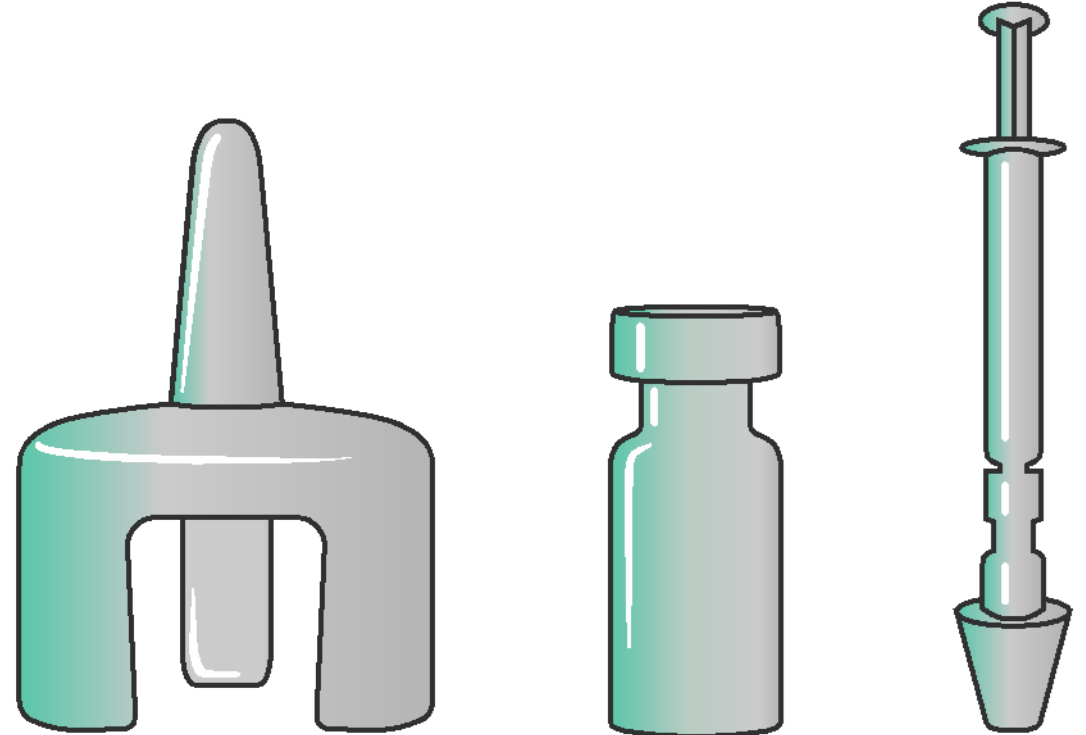
Jo Neale, Compassionate Overdose Response Summit, 3/2024

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
- 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
- (NYS) Attorney General James Stops Misleading Marketing of Unauthorized Opioid Overdose Drug (September 2025)

RECOMMENDED OPIOID ANTAGONISTS

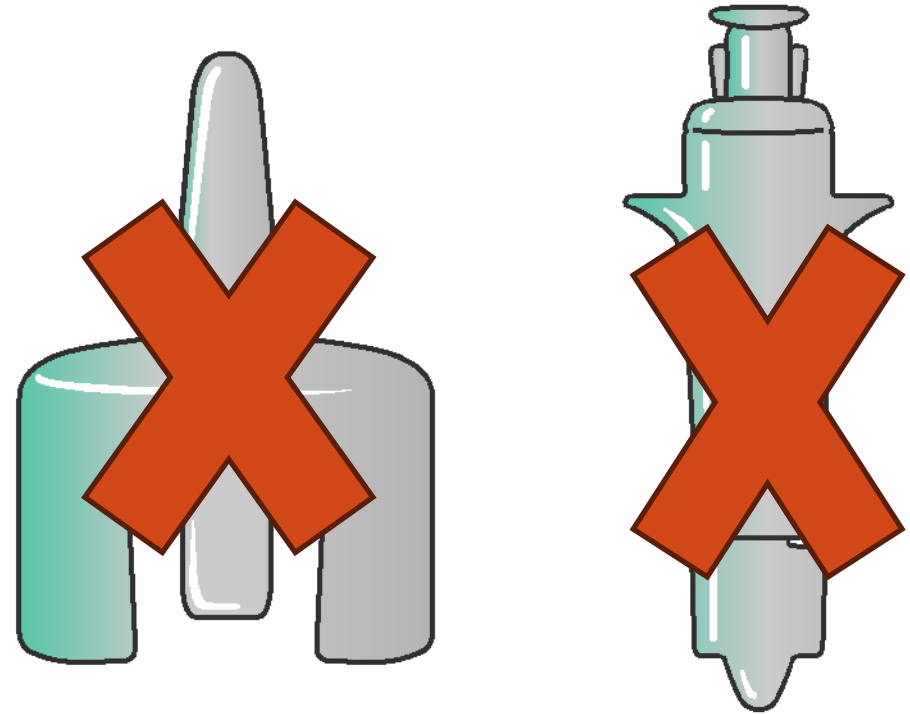
- 0.4 mg/mL generic naloxone for intramuscular (IM) use
- 3.0 mg/mL naloxone for intranasal (IN) use*
- 4.0 mg/mL IN naloxone



*Currently, the NYS DOH only distributes 4 mg IN naloxone and 0.4 mg IM naloxone to its OOPPs

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



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
- While naloxone is an established treatment of opioid-induced respiratory arrest, it has not been a standard treatment for opioid-induced cardiac arrest. As a consequence, naloxone treatment may indicate that emergency medical services (EMS) thought a clinically undifferentiated patient was potentially in respiratory arrest, even if empiric cardiopulmonary resuscitation (CPR) was provided for possibility of cardiac arrest.
- However, in a recently published retrospective cohort study, among patients with suspected opioid-associated out-of-hospital cardiac arrest (OA-OHCA), EMS-administered naloxone was associated with improved survival and neurologic status and sustained return of spontaneous circulation (ROSC). These findings support the need for a randomized trial to assess the effects of naloxone in opioid-associated cardiac arrest.
- These findings support the need for a randomized trial to assess the effects of naloxone in opioid-associated cardiac arrest.

HOW NALOXONE IS DOSED IN OVERDOSE

- Traditional dose 0.4- 2.0 mg intravenous 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 2mg/ml (actual dose 0.4 mg) worked effectively, even 0.4 mg/ml (actual dose 0.1 mg) was as effective
- Several studies have found no increase in naloxone is necessary even with the dominance of fentanyl in the unregulated drug supply.

1: Skulberg AK, et al. Comparison of intranasal and intramuscular naloxone in...Addiction. 2022;117(6):1658-67

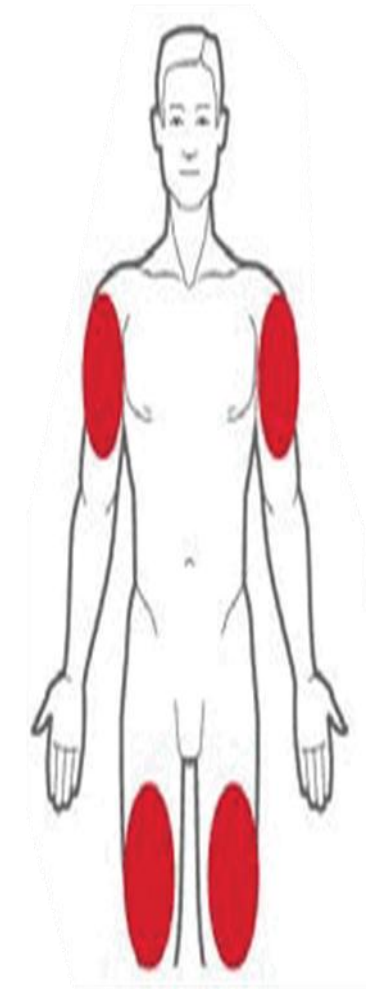
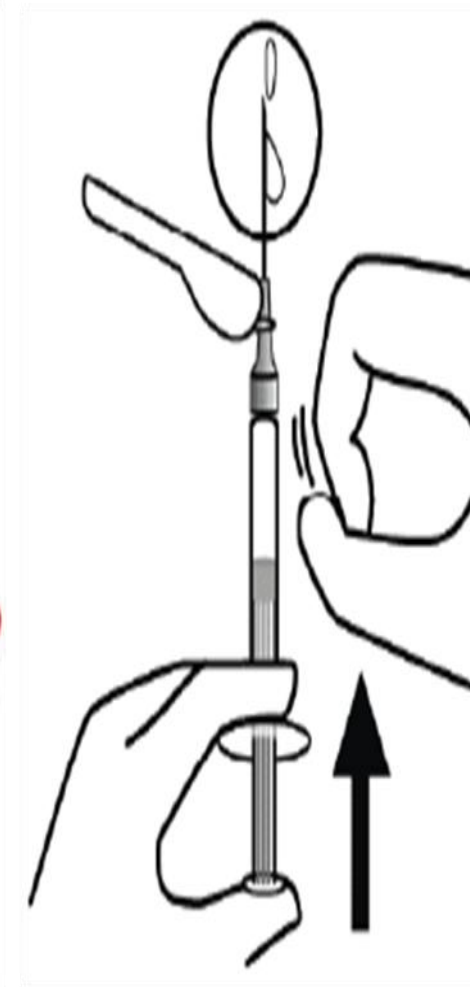
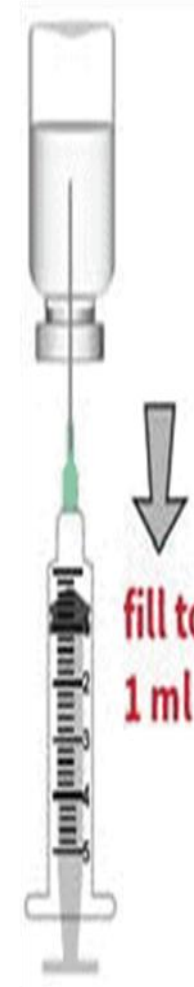
2: Thompson J, et al. Safety, Efficacy, and Cost of 0.4-mg Versus 2-mg Intranasal Naloxone ...Ann Pharmacother. 2022;56(3):285-9.

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.

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.



WHAT ARE THE IMPLICATIONS OF HIGH POTENCY SYNTHETIC OPIOIDS AND OTHER ADULTERANTS ON OVERDOSE RESPONSE?

- Fentanyl, fentanyl analogues, nitazenes, orphines, etc.: No evidence that additional naloxone is needed
 - There is not a linear relationship between the potency of the opioid and the naloxone requirement; it is about the affinity of the substance for the mu opioid receptor (MOR)
- 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



APPROPRIATE OVERDOSE RESPONSE FOR THE CURRENT (AND ANY FUTURE) DRUG SUPPLY

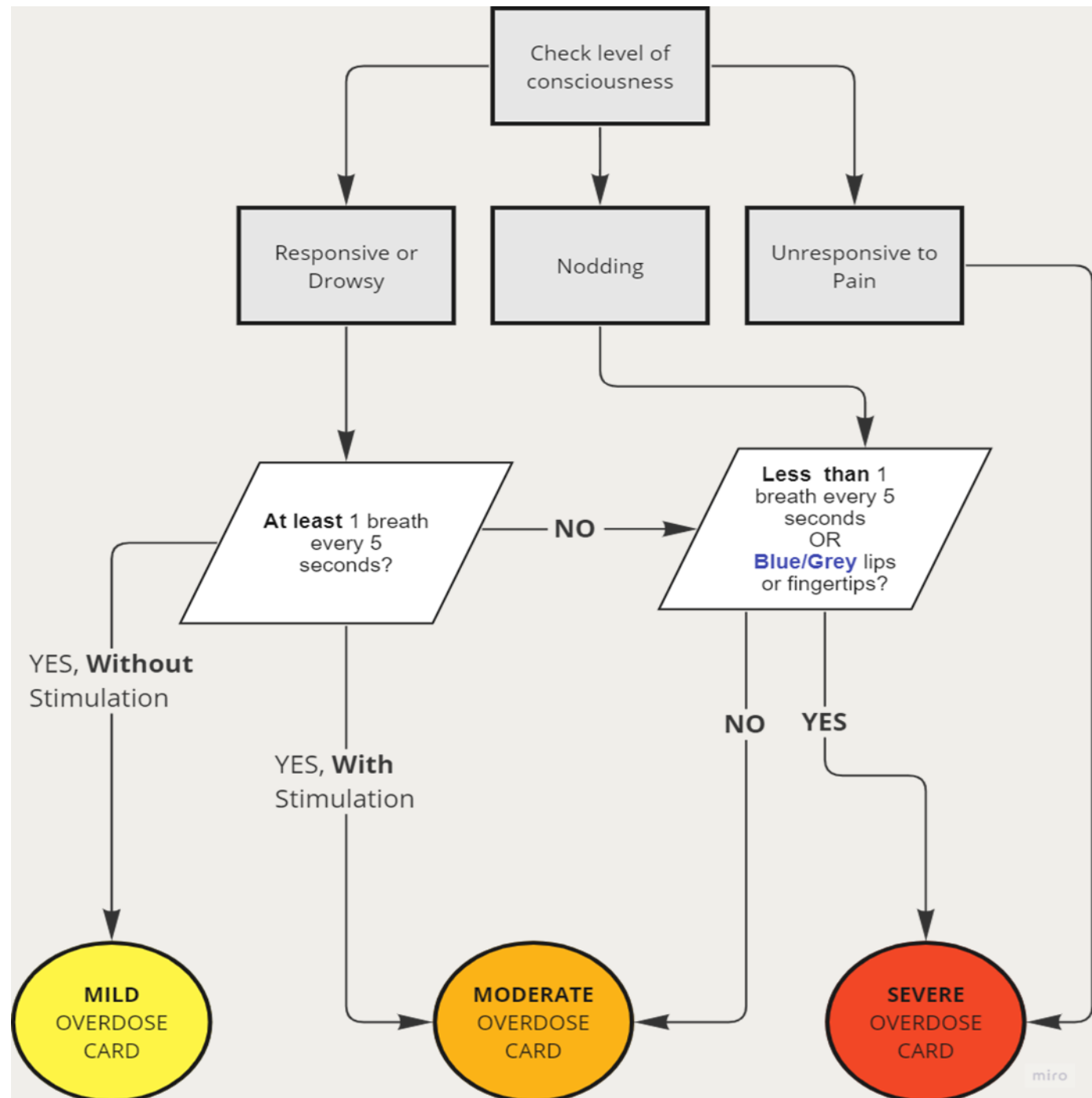
OVERDOSE SEVERITY ASSESSMENT AND TAILORED RESPONSES

- The overdose response guidance presented in this training is not intended for opioid overdose/naloxone administration training to laypersons (the general public), The guidance presented here is distinct from that given to laypersons (the general public).
- The presented overdose response protocols are appropriate in different settings depending on your location, your staff, your training, and your access to additional tools to support individuals experiencing an overdose.
 - e.g., street outreach may not be an appropriate location for these response protocols.
 - e.g., staff on your team may not have any clinical personnel (nurses, medical providers), so there are no standing orders for oxygen administration, etc.
 - e.g., your staff may not be trained and has not been assessed for competency in these response protocols.
 - e.g., your organization does not have the financial ability to buy the tools needed to do the overdose response recommended here (e.g., oxygen tanks, pulse oximeters)

OVERDOSE SEVERITY ASSESSMENT AND TAILORED RESPONSES

- There is no specific background (e.g., education level, degree, certification) required of staff to learn how to do compassionate overdose response. Any staff member who is willing and able to learn the necessary skills, demonstrate competency in these skills over time (I recommend reassessment on competency a minimum of every 6 months), and is able to use these skills effectively in a real overdose response situation should be able to do so.
- Not everyone on your staff will feel comfortable not giving naloxone (“I don’t want someone dying on my watch” is something I’ve heard), even when naloxone isn’t indicated based on the assessment. Not everyone will feel comfortable titrating IM naloxone.
- To compassionately respond to polysubstance overdose, additional tools are necessary. Those tools should include a pulse oximeter and a means to administer oxygen (oxygen tank or oxygen canister). Other tools can be helpful but are not necessary in most overdose responses.

ASSESSING OVERDOSE SEVERITY ALGORITHM



OVERVIEW OF OVERDOSE SEVERITY ASSESSMENTS

	MILD	MODERATE	SEVERE
APPEARANCE	Alert or drowsy	Nodding, eyes closing	Unresponsive or blue/gray/ashen lips and fingertips
LOC (level of consciousness)	Alert but drowsy; can hold a conversation	Responds to verbal and physical stimuli	Responds only to physical pain or unresponsive
RR (respiratory rate=number of respirations per minute)	>=12 breaths/minute	Less than 12/minute	No spontaneous breaths or gasping/gurgling
SpO2 (oxygen saturation in the blood)	Over 90%	81-90%	Less than 80%
Call 911?	No, in most cases	Only if no response to naloxone or condition worsens within 5 minutes	YES, immediately

MILD OVERDOSE RESPONSE

1. **Try to stimulate verbally** by talking/calling their name (recognizing that individuals under the influence of sedatives or even synthetic cannabinoids may be and remain completely unresponsive). If responsive, encourage them to take breaths; if they respond to a sternal rub, you may need to do several times. Try to get them up and moving (if safe to do so) or bicycle their legs to get the blood flowing.
2. **Observe and monitor** RR, SpO2, and LOC
3. **Proceed to MODERATE OD response interventions** if RR or SpO2 are abnormal

MODERATE OVERDOSE RESPONSE

1. **Try to stimulate** verbally by talking. If they are responsive with agitation or a sternal rub, encourage them to take breaths, bicycle their legs to get the blood flowing.
➡ If no improvement within 1 min, RR < 12/min and/or SpO₂ < 90%, go to step 2
2. **Apply O₂ at 2 L/min via nasal cannula**
➡ If no improvement within 1 min, increase oxygen up by 1-2 L/min at a time
➡ If no improvement within 1 min, continue to increase O₂ up to a max of 15 L/min (after 6 L/min, switch to a simple face mask; after 10 L/min, switch to a non-rebreather mask)
➡ If breathing/RR/SpO₂ worsen, proceed to step 3
3. **Administer naloxone if RR remains <12, ideally titrate 0.4 mg/mL IM or give 4 mg/mL IN**
➡ If no improvement within 5 min, CALL 911 and repeat the dose of naloxone in 3 min with goal RR at least 12/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 ED for observation.
6. **Proceed to SEVERE OD interventions** if SpO₂ decreases below 80%, RR decreases to <10, or person appears cyanotic (blue/gray color)

SEVERE OVERDOSE RESPONSE

1. **Immediately call 911** and assist the person to the floor (if not already on the floor)
1. **Start rescue breaths:** give 1 breath every 5 seconds
1. **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
2. **Give naloxone 0.4mg/mL IM (titrate if possible) or 4 mg/mL IN** and wait at least 3 minutes for naloxone to take effect
 - ➡ If SpO₂ and RR increase within 3 minutes → monitor RR, SpO₂, and HR for 5 minutes & repeat dose *if condition worsens*
 - ➡ If SpO₂ and RR do NOT increase within 3 min → administer a second dose and monitor for improvement (improvement/normalization of SpO₂ and RR)
 - ➡ *If the person loses their pulse, begin CPR (as trained)/utilize an AED (if available), continue rescue breaths or oxygenation via bag valve mask or oxygen administration*
3. Once SpO₂ is > 90% and RR is over 12/min:
 - ➡ Continue to monitor until EMS arrives
 - ➡ If vomiting occurs, place them in the rescue/recovery position and clear their mouth

RESPONDING TO SEDATIVE-INVOLVED OVERDOSES

- Overdose assessment
- Overdose response based on assessment
 - Naloxone administration only if indicated (both RR<12 and SpO2 <90% with inadequate response to stimulation and oxygen administration)
 - Ideally, titration of IM naloxone
 - No indication for high dose naloxone or nalmeffene products ever
 - >1 dose of naloxone given only if both RR<12 and SpO2<90% despite administering oxygen and giving a single naloxone dose and at least 3 minutes have passed since giving the prior dose of naloxone
 - Oxygen administration is indicated in any situation in which the SpO2 is <90%, even if the RR is adequate; staff would need to be trained and assessed for competency in oxygen administration; programs should have a standing order for oxygen administration by non-clinical personnel in emergency situations
- Execute a tailored overdose response based on your setting (onsite vs street outreach/in community) and staff skills/roles (outreach staff vs clinician vs onsite staff)
 - What is your program's capacity to monitor individuals, potentially, for hours? Do you have the space? Do you have the staff? Will you be open for as long as the person may need monitoring?

POLYSUBSTANCE OVERDOSE RESPONSE

- **FIRST:** assess responsiveness (try to agitate), recognizing that people may be and remain completely unresponsive; assess airway, breathing (look, listen, and feel; set a timer to count respirations for one full minute), and circulation (check pulse; bicycle legs)
- **SECOND:** administer naloxone only if indicated (RR <12 AND SpO2 <90%) and no change with actions in step 1
- **THIRD:** call 911 if indicated (your program should have protocols)
- **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%

POLYSUBSTANCE OVERDOSE RESPONSE

- **FOCUS on airway/breathing not responsiveness** (people don't need to wake up or respond to you but they do need to be oxygenating adequately)
- **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, 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, 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.

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AUGMENTING YOUR OVERDOSE RESPONSE WITH ADDITIONAL TOOLS TO BETTER SUPPORT AIRWAY AND BREATHING

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



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

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. another setting):
 - pulse oximeter
 - bag valve mask
 - oral and/or nasal airways
 - oxygen tanks or recreational oxygen canisters

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

USING A PULSE OXIMETER

ADVANTAGES

- A relatively cheap and easy to use tool that can provide important data (heart rate and oxygenation) 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



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.

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.

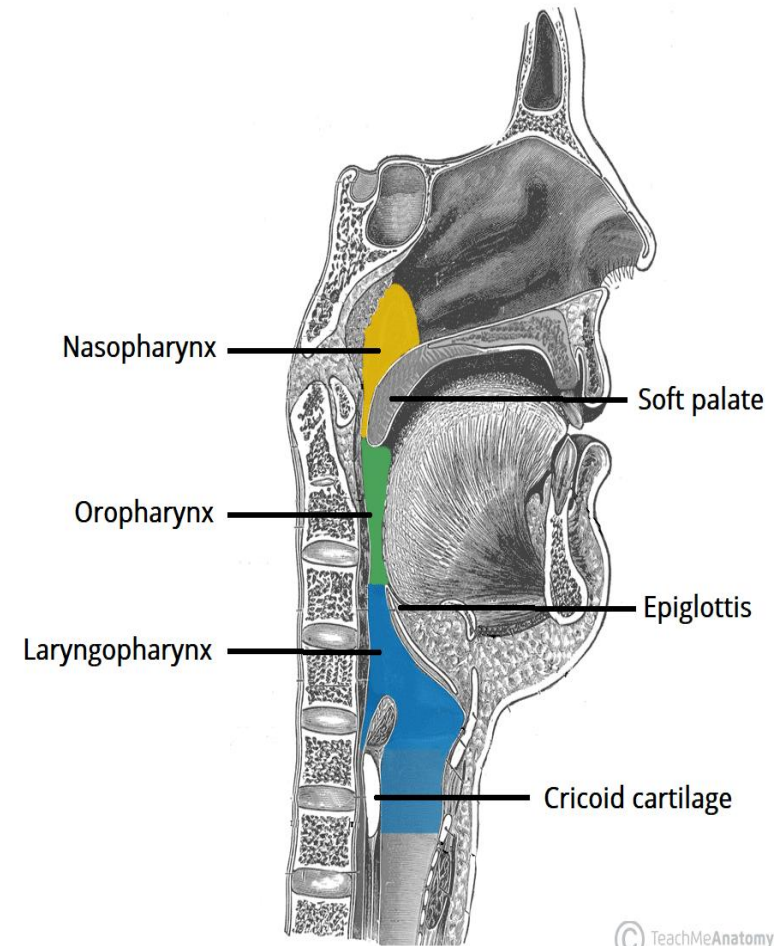
BVM CAVEATS

- 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 (~\$11.00-\$18.00 each)
- BVM use can be done with one or two persons



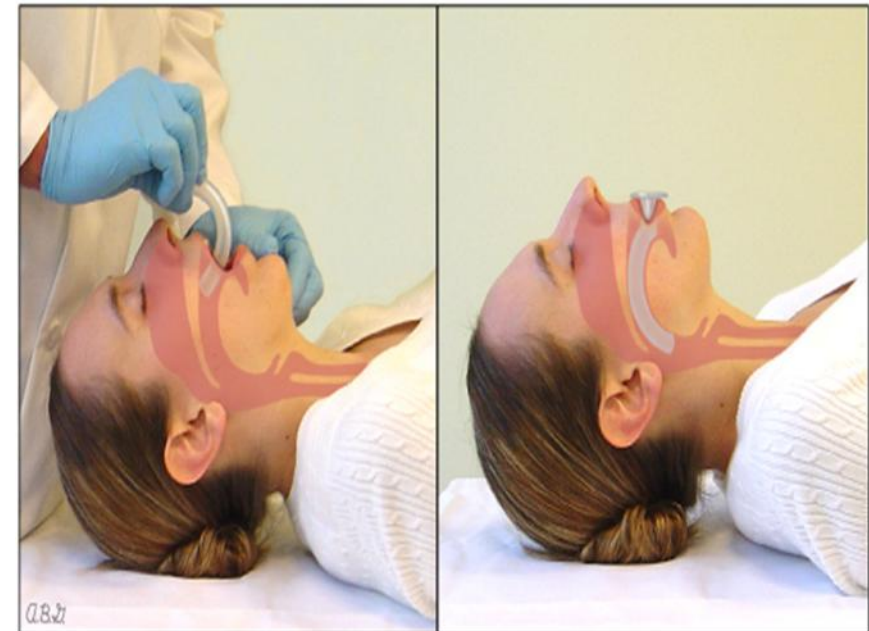
USING ORAL AND NASAL AIRWAYS

- 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.



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.



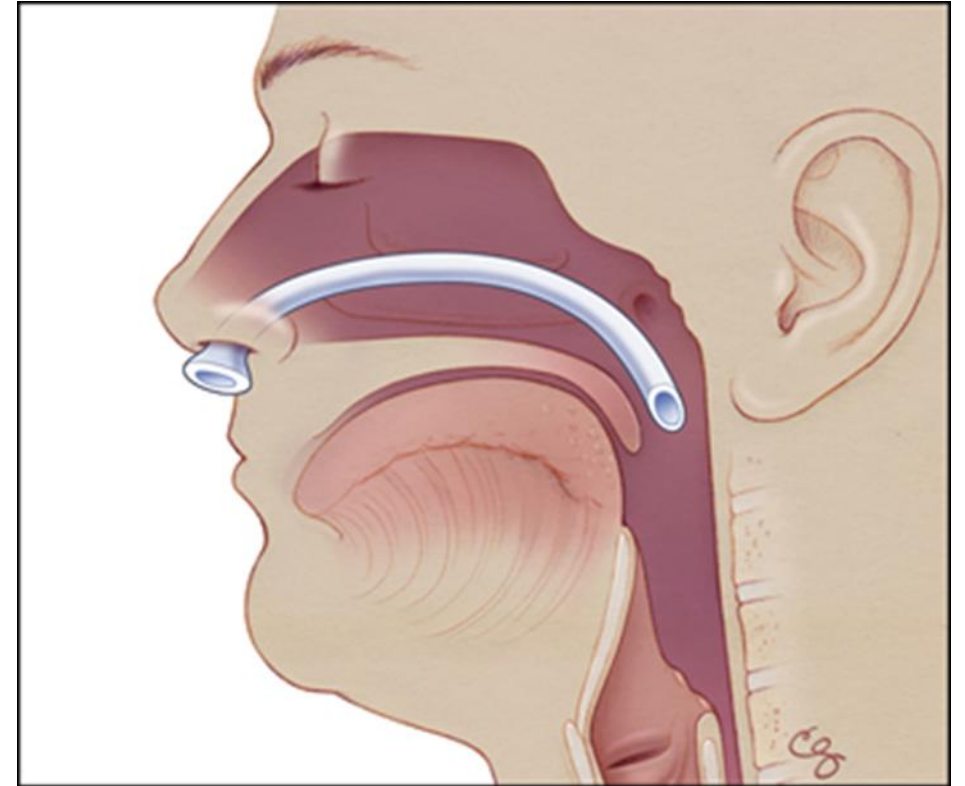
Thanks to Synn Stern, RN, MPH for sharing nursing protocols for overdoses at OnPoint NYC

www.amazon.com

Merck Manual

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 bag valve mask 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.



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)



nasal cannula



simple face mask



non-rebreather mask

SACHR

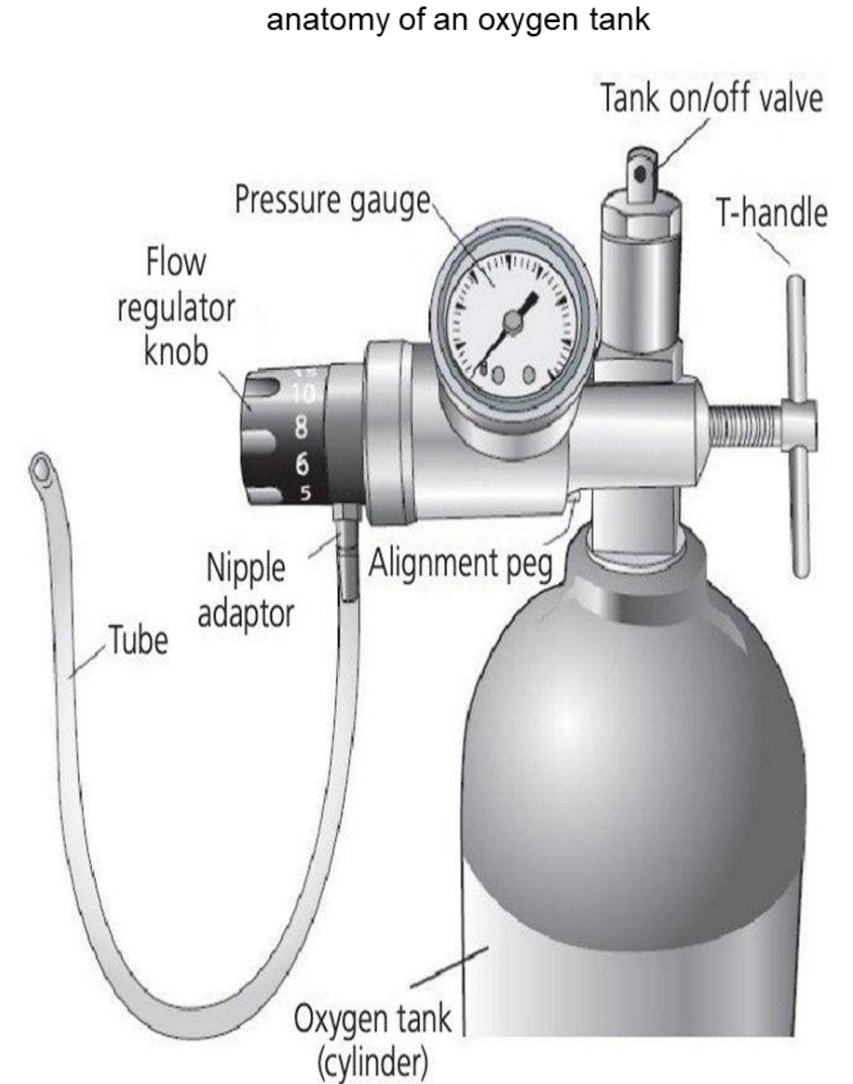
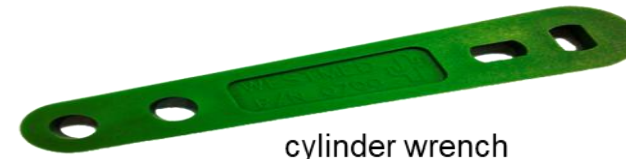


Illustration 2



cylinder wrench

BASIC OXYGEN SAFETY

- A site-specific Oxygen Safety Checklist should be completed every shift
- Check the pressure gauge on the oxygen tank before starting each shift and after every use
 - At 1000 PSI or less → switch out with a new O2 tank
- To prep, make sure the hose on the mask or nasal cannula is connected to the tank
 - Place the mask in the bag and hang from the tank so it's ready to use
- Keep open flames and AEDs away from the oxygen tanks at all times



USING AN OXYGEN TANK

How to Turn On an Oxygen Tank:

- Use the cylinder wrench to turn the valve at least one half-turn counterclockwise.
- Check the pressure gauge to verify that there is enough oxygen. Full is about 2,000 psi.
- Adjust the liter flow using the knob.

How to Use an Oxygen Tank:

- Attach the tubing to the oxygen tank. Make sure the tubing is not bent, blocked, or broken.
- Set the flow rate using the knob.
- Check the flow by holding the mask or cannula up to your ear and listening for the "hiss."
- Put the nasal cannula or mask on the person, ensuring it fits comfortably.
 - If using a non-rebreather mask, let the bag inflate about a third of the way full before placing on the person.

How to Turn Off an Oxygen Tank:

- Use the cylinder wrench to turn the valve clockwise until it is completely off or closed.
- Turn the knob to zero.
- Let out any remaining oxygen until the pressure gauge reads zero.

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 open flame
- Moderately expensive for widespread distribution (\$10-\$20)
- Vary significantly in oxygen concentration (anywhere from 40%-99.5%)
- Recreational oxygen canisters typically have a shelf life of 2 to 5 years from the date of manufacture or filling, depending on the manufacturer.

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)

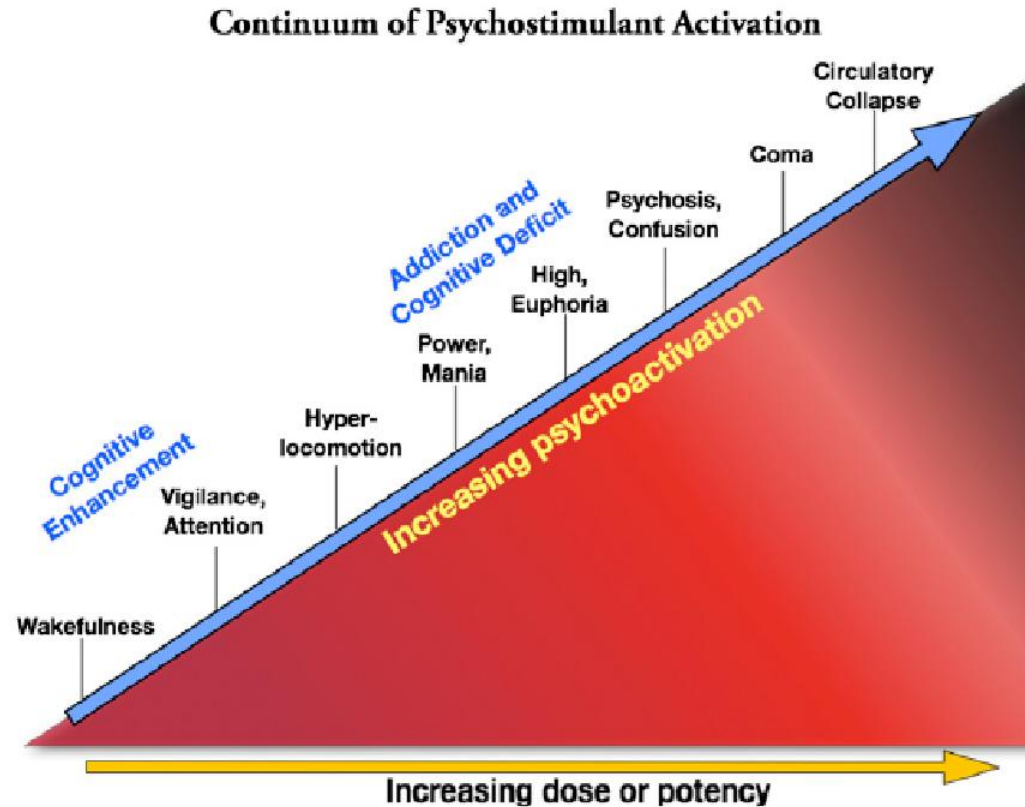
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RECOGNIZING AND RESPONDING APPROPRIATELY TO A STIMULANT OVERDOSE (OVERAMPING)

OVERAMPING: STIMULANT “OVERDOSE”

- Overamping is the term used to describe what one might consider an “overdose” on stimulants (methamphetamine, cocaine, etc.).
- There may be an array of physical and/or psychological symptoms.
- Occurs when someone is experiencing effects of stimulants so severe that their health or safety may be at risk.
- The effects of stimulants on the body can vary greatly based on multiple factors.
- Time of symptom onset is quickest when people use substances by smoking, sniffing, or injecting them, compared to when substances are taken orally.

DEFINING OVERAMPING



Overamping tends to begin after someone has experienced euphoria for an extended period of time or has used a dose that exceeds the level of euphoria desired.

Fig. 10. Continuum of psychostimulant activation. Increasing cognitive activation as stimulant dose increases initially produces increased wakefulness and cognitive enhancement. These are the desired therapeutic effects. As dose increases, a sense of power and euphoria can ensue; these are the effects addicts seek and are accompanied by cognitive deficits. Higher doses can result in overdose, psychosis, coma, and eventual circulatory collapse.

THE FIVE “D’s” OF OVERAMPING

- **Drug:** The type of stimulant someone takes as well as its purity greatly impacts the response someone may have. Some stimulants have direct effects on dopamine increasing the likelihood of an overamping situation.
- **Dose:** The amount of the substance that someone uses has a direct effect on the response that they will experience.
- **Delivery:** How the substance is delivered (route of administration) also contributes to the availability of the substance in the body.
- **Duration:** How long someone has been using for is another indicator for the risk of overamping. Using for several days in a row without a break increases the risk for a serious event.
- **Disorders/Diseases:** Underlying health conditions, including mental health conditions, may affect someone’s likelihood of experiencing overamping even in the setting of using small amounts or for a limited amount of time.

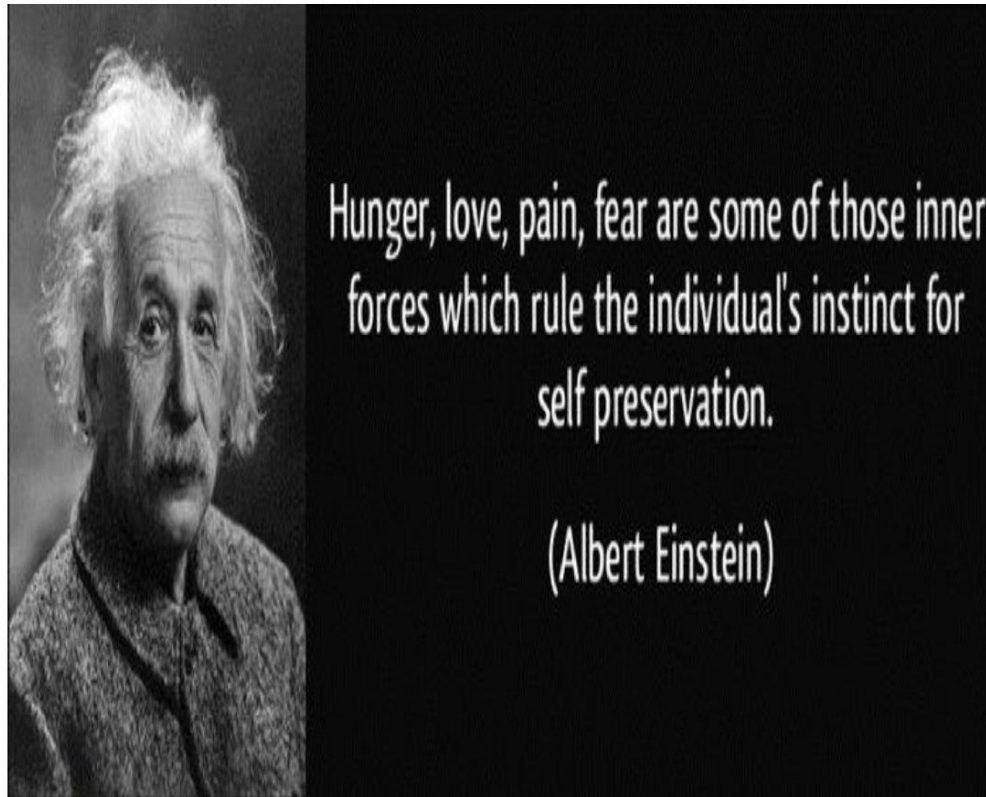
WHAT ARE THE POTENTIAL PHYSICAL SIGNS AND SYMPTOMS OF OVERAMPING?

- Jerking movements
- An inability to stay still
- Chest pain/angina
- Irregular breathing
- High body temperature
- Passing out (but still breathing)
- Uncontrollable teeth grinding
- Racing heartbeats
- Severe headache
- Nausea or vomiting
- Muscle stiffness or paralysis
- Fainting, but not unconscious
- Seizure
- Hyperthermia
- Hypertension
- Acidosis
- Rhabdomyolysis
- Neutropenia
- QRS widening
- Insomnia
- Xerostomia/dry mouth

WHAT ARE THE POTENTIAL PSYCHOLOGICAL SIGNS AND SYMPTOMS OF OVERAMPING?

- Confusion
- Restlessness
- Hypervigilance
- Intense panic
- Hallucinations: auditory, visual, tactile
- Protective behaviors (see next slide)
- Delusions
- Trauma response
- Extreme paranoia
- Extreme agitation
- Increased aggressiveness
- Suicidal ideation
- Enhanced sensory awareness
- Altered perception of reality
- Persecutory perceptions of the world

WHAT ARE PROTECTIVE BEHAVIORS?

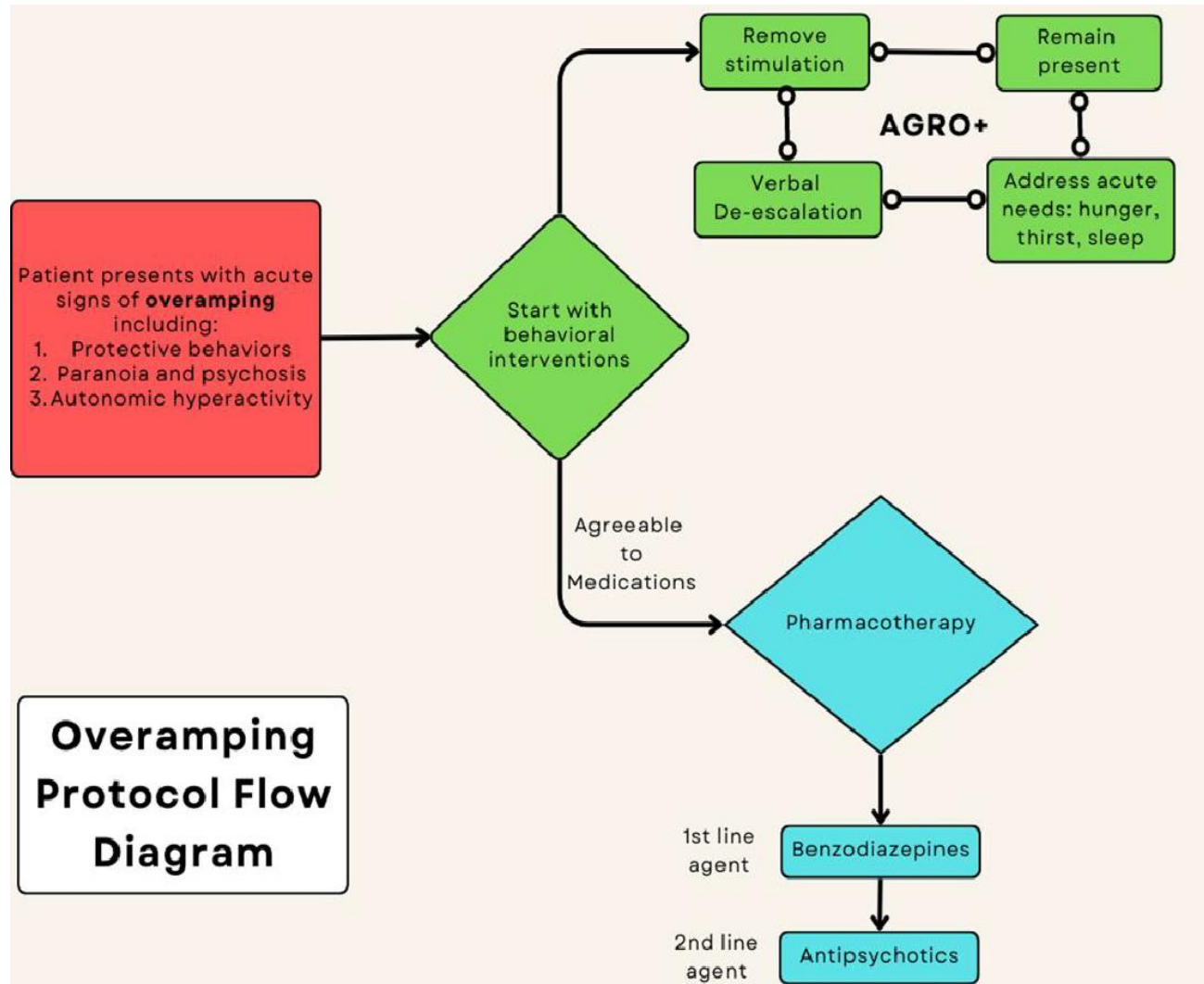


- Protective behaviors are ways in which people act instinctually for self-preservation.
- Protective behaviors include hypervigilance, panic, anxiety, fear, agitation, defensive posturing, and increased sensory awareness.
- Altered persecutory perceptions of reality force patients to go into survival mode.
- Acts of aggression, violence, or hypervigilance often occur in the setting of patients fearing for their lives.

WHAT CAN YOU DO WHEN SOMEONE IS OVERAMPING AND IT ISN'T AN EMERGENCY?

- **Cool them down.** Place ice packs or a cool, wet towel under their armpits and knees, crack a window, or sit in front of a fan or in the shade.
- **Hydrate and nourish them.** Have them drink some water or a sports drink like Gatorade and eat a nutrient-dense snack. Avoid drinks with caffeine, which can increase the intensity of their experience. If Gatorade isn't available, a salty snack or a small amount of salt mixed into water will help their body systems stay balanced and replenish nutrients.
- **Rest.** Encourage them to take a nap, close their eyes, or lay or sit down somewhere comfortable. They can practice breathing or meditation exercises, or listen to some calming music.
- **Shower.** A cool or warm shower can help bring mental and physical relief.
- **Change up their environment.** Encourage them to take a walk, get some fresh air, or move to a more comfortable place.
- **Physical contact.** Massaging themselves or having someone else massage them can help ground them in their body.
- **Have them talk to themselves or someone else about what is happening.** It can be very powerful to name their feelings and remind them that what they are experiencing is temporary.
- **Avoid using more, different substances, including alcohol.** It can be tempting to use benzodiazepines or other sedatives to help move out of overamping. Taking benzodiazepines, especially in combination with heroin or alcohol can raise the risk for more serious complications like respiratory depression. A safer choice would be to drink some herbal tea, like chamomile.

AMBULATORY MANAGEMENT OF OVERAMPING

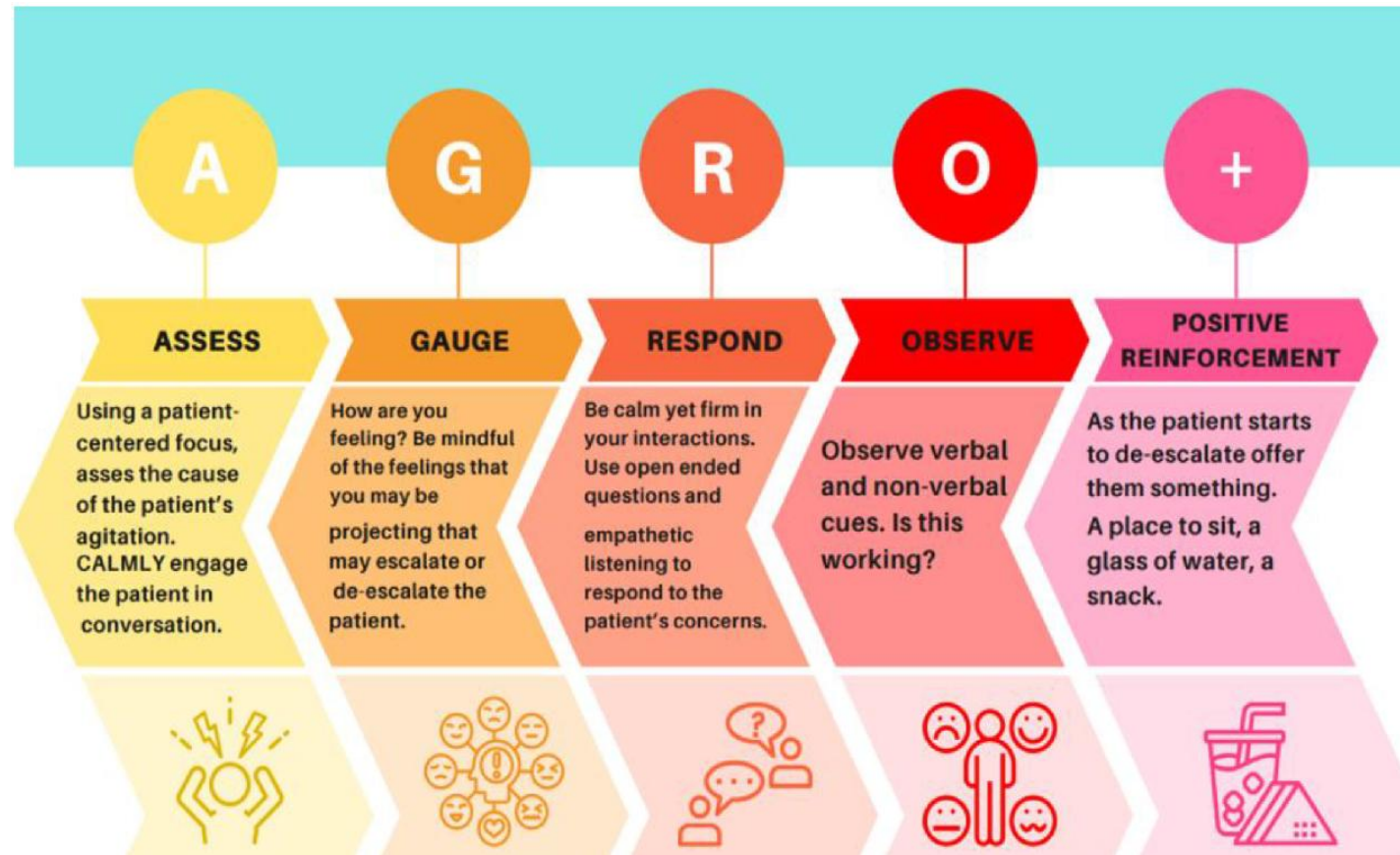


If an overdose is suspected:

- Assess the scene
- Assess the person: airway, breathing, and circulation
- Call 911
- Attempt to de-escalate the patient, if appropriate
- Stay with the person until help arrives
- Should the person suddenly become unresponsive perform CPR until help arrives.

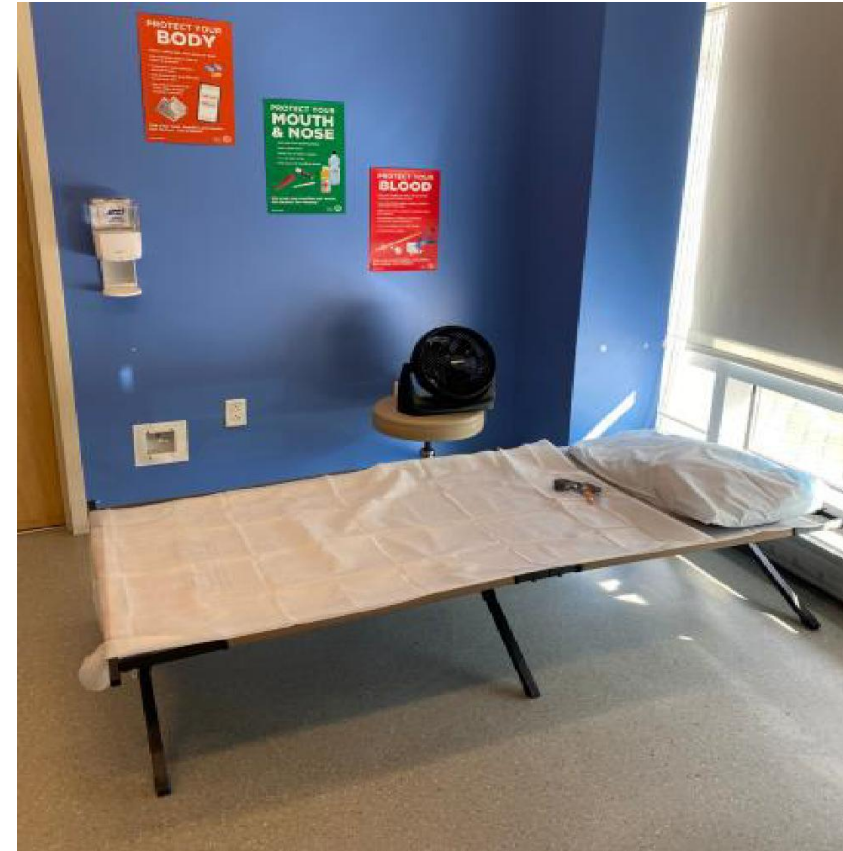
Alves et al., 2024

BEHAVIORAL DE-ESCALATION



ENSURING A SAFE SPACE

- Patients with symptoms of **overamping ideally** are promptly brought to a “**cool-down**” space (the space will look differently depending on the facility).
- **Non-pharmacological interventions to reduce symptoms:**
 - Sunglasses and ear plugs to reduce external stimuli
 - Electrolyte repletion and chewing gum to reduce dehydration
 - A cot with blankets and pillows to address symptoms of sleep deprivation



NON-MEDICAL INTERVENTION STRATEGIES FOR POLYSUBSTANCE OVERDOSE

- ◆ Spatial design is important
- ◆ Space and time, lots of time...
- ◆ Identified a safe person->empower paraprofessionals
- ◆ Redirection/distraction, affirmation/validation
- ◆ Energy absorption/release
- ◆ Stimuli control/manufactured environment
- ◆ System calming: hot/cold compresses, music, lighting
- ◆ Sensory experience: massage, pressure points
- ◆ Medical care at your organization or via a clinic/hospital system



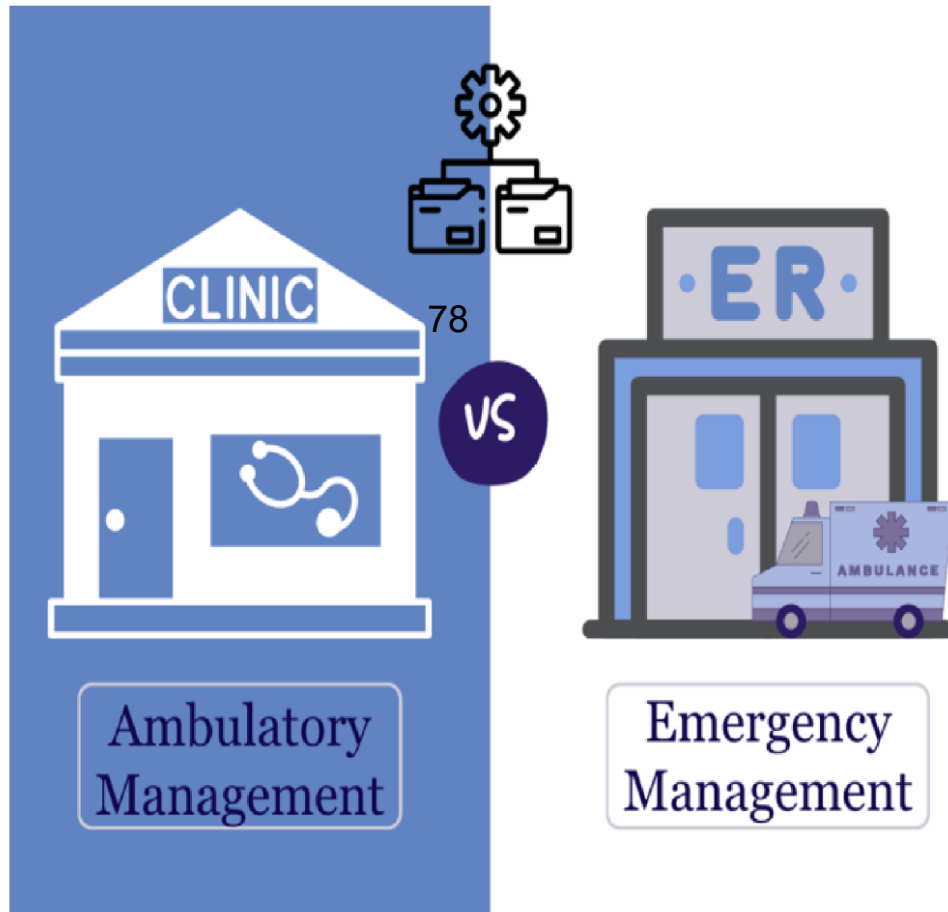
RESPONDING TO OVERAMPING

- When responding to stimulant overamping, you must assess what assistance is needed: supportive care and rest? Medical intervention? Medication intervention?
- It is beyond the scope of this training to discuss appropriate responses to all potential medical emergencies which may result due to stimulant overamping.
- However, staff should be trained to recognize and respond urgently to hyperthermia (overheating), a stroke, a seizure, and an arrhythmia/cardiac arrest/heart attack.
- In most of these situations, 911 will be called; however, while awaiting EMS, there are measures staff can take to keep the person safe, oxygenated, and cool, as appropriate.



Brent Gibson, et al. OnPoint NYC: Baseline Report

WHAT DOES THIS PERSON NEED?



What should trigger activating EMS?

- ECG changes and/or unstable angina
- Uncontrollable hyperthermia (temperature $\geq 104^{\circ}\text{F}$)
- Arrhythmia
- Refractory choreiform movements
- Hypertensive crisis with symptoms
- Seizure
- Syncope
- Respiratory distress
- Symptoms consistent with stroke, heart attack, or cardiac arrest
- Psychosis with a weapon



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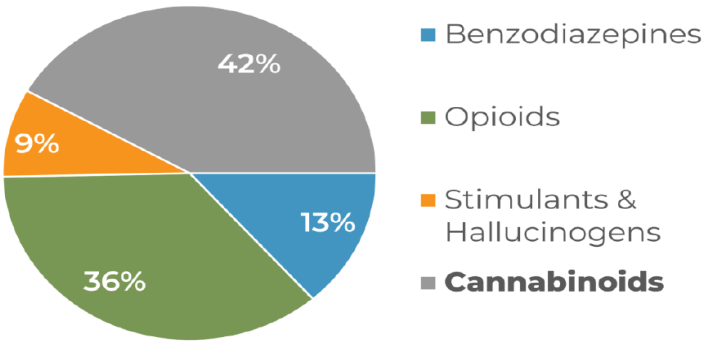
RECOGNIZING AND RESPONDING APPROPRIATELY TO A SYNTHETIC CANNABINOID OVERDOSE

SYNTHETIC CANNABINOIDS

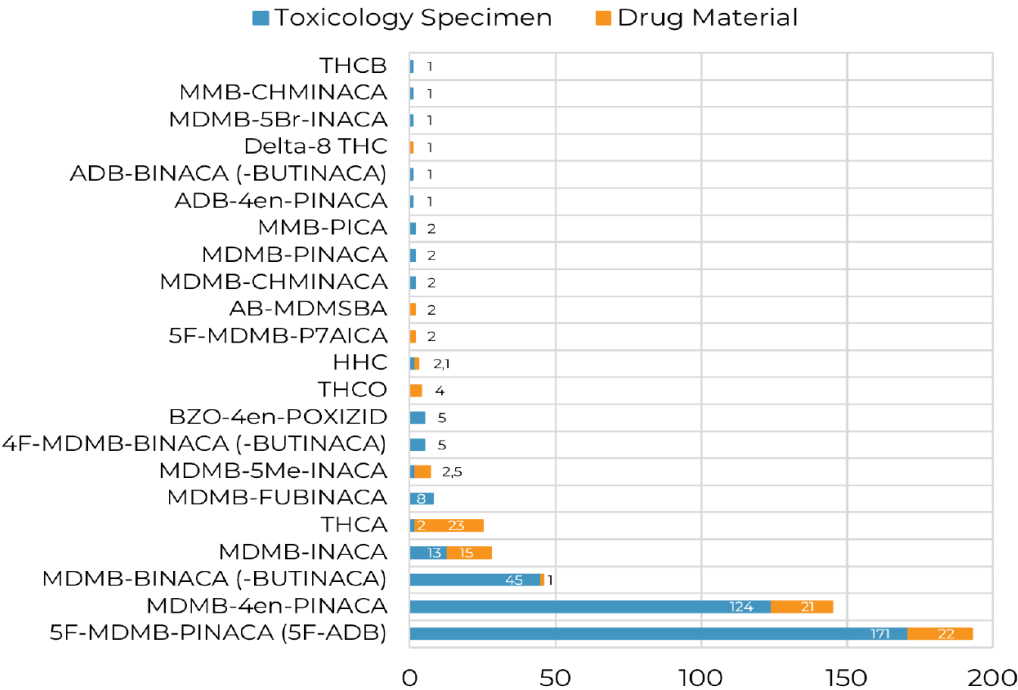
PURPOSE: This report provides up-to-date information regarding the status of NPS cannabinoid prevalence and positivity in the United States.

OVERVIEW: Novel psychoactive substances (NPS) continue to pose great challenges for forensic scientists, clinicians, and public health and safety personnel. Synthetic cannabinoids (e.g., MDMB-4en-PINACA) have been implicated in increasing hospital admissions, intoxication events, and deaths, especially in jails and prisons. Semi-synthetic cannabinoids (e.g., delta-8 THC) continue to be sold in recreational smoke and vape shops. Maintaining a current scope of analysis can be challenging, requiring comprehensive analytical methodologies and reference materials for identification(s).

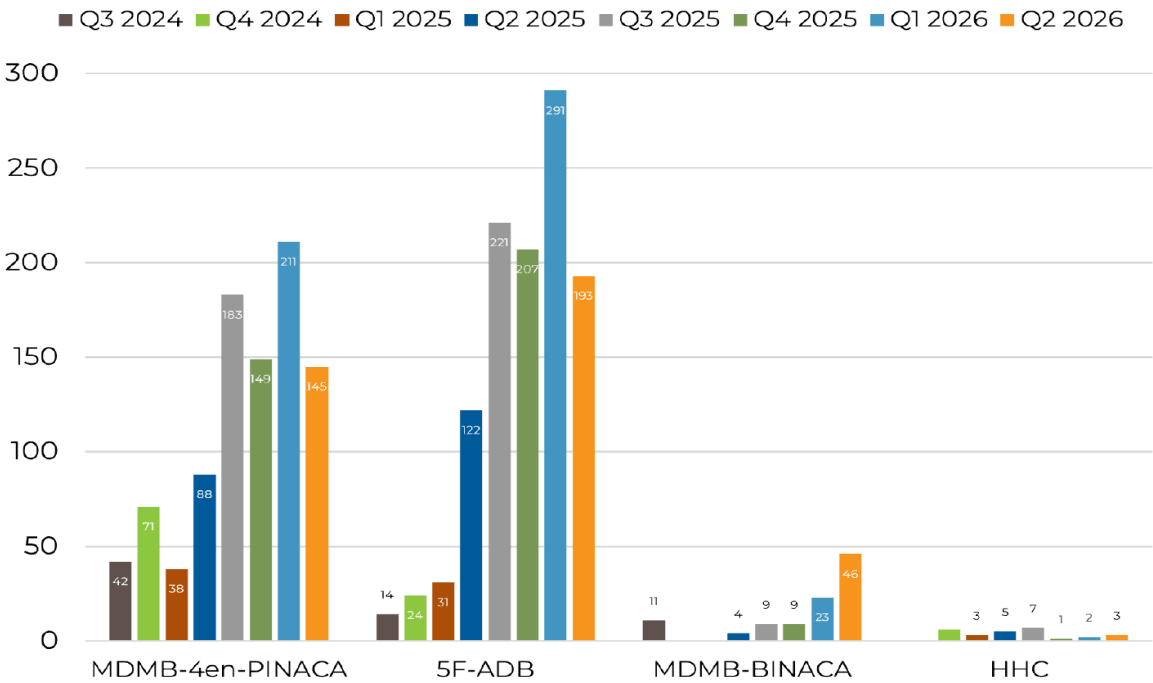
OBJECTIVE: Our laboratory utilizes novel approaches for the analysis of drugs in toxicology specimens and drug materials using comprehensive non-targeted data acquisition by gas chromatography mass spectrometry (GC-MS) and liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The scope of analysis contains more than 1,200 drugs, including a vast majority of NPS and their metabolites. This approach allows for real-time identification of novel synthetic cannabinoids and further data analysis of important trends. Specimens and sample types associated with our results stem from recreational drug materials, drug equipment, medicolegal death investigations, clinical intoxications, and/or impaired driving investigations, among other circumstances. This report summarizes the total number of NPS identifications at the CFSRE during this quarter, encompassing findings from sample-mining, data-mining, routine testing, and esoteric testing.



IDENTIFICATIONS: Q2 2026



TRENDS: Q3 2024 TO Q2 2026



SYNTHETIC CANNABINOID “OVERDOSE”

- Individuals who use synthetic cannabinoids have no way of knowing which chemicals or adulterants (including other substances like synthetic benzodiazepines) are included in their dose, unless they use drug checking.
- People experience short-lived euphoric effects with possible intense anxiety, depression, and mood swings following euphoria. Persons using synthetic cannabinoids may experience intense withdrawal symptoms.
- A variety of symptoms may occur secondary to synthetic cannabinoid use, including tachycardia (rapid heart rate), arrhythmias (abnormal heart rhythms), elevated blood pressure, heart attacks, strokes, respiratory distress, kidney injuries, seizures, gastrointestinal symptoms, severe anxiety, psychosis, agitation, and hallucinations.
- This puts people who use synthetic cannabinoids at a higher risk of overdose. An “overdose” with synthetic cannabinoids may include decreased responsiveness or lack of responsiveness.
- Supportive care with reassurance, reorientation, monitoring of vital signs, responding to seizures, and administration of oxygen (for decreased respirations or decreased SpO₂) may be needed. Unconsciousness is typically short-lived (20-40 minutes).

Riederer, A, et al. MMWR, 2016

New York State Department of Health Issues Warning that Synthetic Cannabinoids Sold in the Mohawk Valley Contain Laboratory Confirmed Synthetic Opioids that Can Create a Deadly Cocktail
Synthetic Cannabinoid Related Fatal Overdoses 3.8.23.pdf (Washington DC OCME, 2023)

de Oliveira, MC, et al. Brain Sci, 2023

SYNTHETIC CANNABINOID-INVOLVED DEATHS IN THE US, 2024

Where were select drugs of interest detected¹² in drug overdose deaths
in 2024, Overall (43 jurisdictions)?[†]

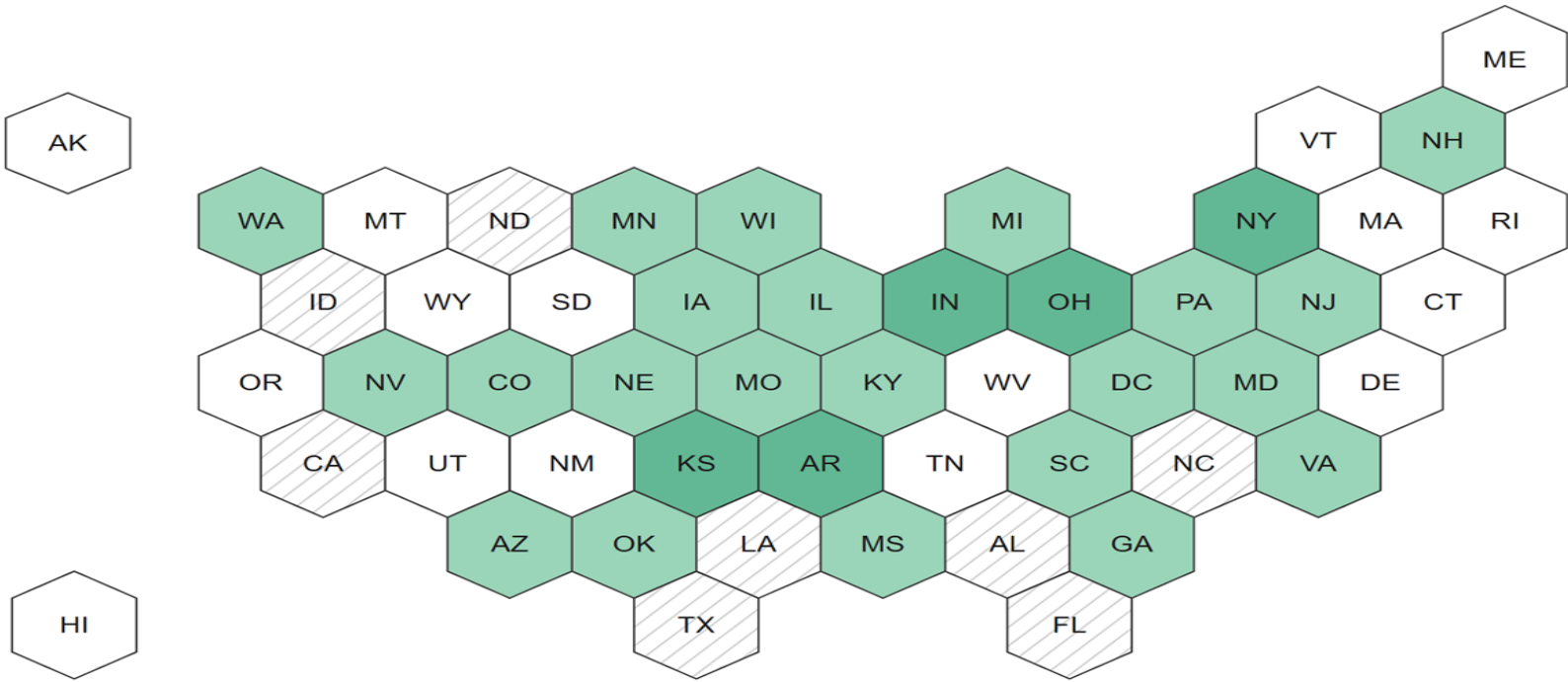
2024 ▾

Synthetic cannabinoids¹⁸ ▾

Metric: ☒ Count ☐ Percent

Overall (43 jurisdictions): 166 deaths

Color Legend



[†] Analyses of drugs detected are restricted to deaths with an available toxicology report.

2025 HEALTH ADVISORY #21: INCREASES IN SYNTHETIC CANNABINOID (K2)-RELATED EMERGENCY DEPARTMENT VISITS IN NYC

- Synthetic cannabinoids are lab-created substances that are meant to mimic the effects of THC but are associated with wide-ranging and severe adverse effects, including arrhythmias, agitation, nausea/vomiting, and seizures. While rare, synthetic cannabinoid use can result in death.
- There has been a sustained elevation in synthetic cannabinoid-related emergency department (ED) visits citywide, affecting primarily residents of Highbridge-Morrisania, Southeast Queens, and Central Harlem-Morningside Heights.
- Between January and August 2025, there were at least nine unintentional drug overdose deaths that involved synthetic cannabinoids and no other substances, an increase from at least two deaths during all of 2024.
- There have been no confirmed cases of fentanyl contamination in synthetic cannabinoid products in NYC.
- Provide supportive care to manage the symptoms of people experiencing suspected synthetic cannabinoid-related adverse effects.

*Data are from the NYC Health Department's Bureau of Vital Statistics and the NYC Office of Chief Medical Examiner. Data are provisional and subject to change.

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SUPPORTING PATIENTS AFTER AN OVERDOSE AND SUPPORTING STAFF AFTER RESPONDING TO AN OVERDOSE

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)

POST-OVERDOSE RESPONSE CARE ITEMS

- **Towels:** can be used for warmth, impromptu pillow, and to dry sweat off persons who have overdosed
- **Paper towels/napkins:** can be used to clean up bodily fluids if needed
- **Water/Pedialyte/Gatorade/Powerade:** help to rehydrate and restore lost electrolytes
- **Mouthwash:** can help the person feel refreshed
- **Plastic bags/garbage bags:** can assist in clean up
- **Hand sanitizer:** will help keep hands clean before and after overdose response
- **Baby wipes/wet wipes:** accidents can happen after naloxone administration; be compassionate
- **Gloves:** PPE can be used to protect all individuals everyone from bacteria and blood-borne pathogens
- **Medications: ibuprofen/acetaminophen/GI medications:** can soothe pain and abdominal symptoms/diarrhea that may emerge after naloxone administration due to withdrawal
- **Clean linen/Blanket:** can be used for comfort and warmth
- **Clean set of clothes:** will help the person feel more refreshed and comfortable
- **Heater/Heating pad/Fan:** can help with temperature regulation

POST-OVERDOSE RESPONSE: MENTAL AND PHYSICAL SIDE EFFECTS OF NALOXONE ADMINISTRATION AND PRECIPITATED OPIOID WITHDRAWAL

- **Extreme body temperature dysregulation** (extreme hot & extreme cold, one or the other, or simultaneously)
- **Fever/chills/goosebumps**
- **Muscle spasms, usually in the arms/hands/legs**
- **Abdominal cramps**
- **Pupil dilation**
- **Uncontrollable bodily movements** (restless legs, general restlessness)
- **Extreme malaise**
- **Nausea/vomiting/diarrhea/dehydration/headaches**
- **Yawning/teary eyes/runny nose**
- **Anxiety/general dysphoria**
- **The pain and mental anguish associated with precipitated withdrawal as well as the overdose itself can be very traumatizing for the individual; please always take care when discussing this with them and when discussing the event. Please do not disclose anyone's history of overdose unless instructed otherwise by the affected person(s). Overdosing is an extremely jarring experience. Once an overdose is reversed, try speaking to the person that overdosed with a calm/quiet demeanor. Most times people won't know they've overdosed until after it's reversed and they're notified of the situation, meaning, they likely have no idea what's going on. Meeting someone with panic while they're in this state can be detrimental to their wellbeing.**

REPETITIVE VICARIOUS TRAUMA: HOW CAN YOU SUPPORT YOUR TEAM?

COMPASSION FATIGUE RESILIENCE FRAMEWORK IN THE CONTEXT OF POST-OVERDOSE OUTREACH, MA POST-OVERDOSE OUTREACH PROGRAM STAFF INTERVIEWS

Empathy (compassion fatigue resilience constructs and sub-constructs)	
Empathic concern	Concern for others' well-being (theme and example quotes): <i>"[I was] eager to do something because I recognized the problem. I recognized people out there struggling with addiction."</i>
Empathic ability	Capacity to adopt and understand others' perspectives: <i>"I can empathize with the amount of stuff they've been through. They share a lot of trauma with us, they share a lot of what's going on in their life."</i>
Empathic response	Delivery of empathic and compassionate services: <i>"Just let them know it's an honor to speak to them. It's an honor to even be there. Thanks for opening the door is huge."</i>
Secondary Traumatic Stress	
Trauma exposure	Exposure to others' trauma: <i>"I have had situations where I went out with an officer and the person of interest actually died that morning... so that was like really difficult."</i>
Trauma exposure	Trauma exposure within personal social spheres: <i>"So one of my latest... I knew the address, which was actually close to where I grew up."</i>
Trauma exposure	Prolonged/repeated exposure to trauma: <i>"You know, over the years... you see a lot of the ugly in society. You're getting calls when people are suffering the most, at their worst... afraid, angry, upset, hurt."</i>
Compassion Fatigue Resilience 	
Self-care	Self-care practices and routines: <i>"Well, I go home and walk my dog, and exercise regularly, eat well."</i>
Detachment	Detachment from outreach experiences: <i>"And so, you know, like anybody else when you're dealing with things like that you get this cynical side, you get this hardened side to be self-protective."</i>
Social support	Social support: <i>"You gotta have little breaks together, lunches [or] thing[s] to just get away from the work for a little bit."</i>
Job satisfaction	Job satisfaction and occupational valuing: <i>"I love what I do. My experience has been great. It's rewarding for me as an individual in recovery to work with the community."</i>
Workplace support	Professional supervision and counseling support: <i>"I've sat down with [my recovery coach supervisor] and cried. It's been like, this one [post-overdose outreach visit] just hitting home, you know, it just sucks."</i>

REPETITIVE VICARIOUS TRAUMA: HOW CAN YOU SUPPORT YOUR TEAM?

Table 4. Summary of Critical Findings.

- Vicarious trauma (VT) interventions mostly targeted health care professionals and were delivered as the following types of programs, psychoeducation, mindfulness interventions, art and recreational programs, and alternative medicine therapies
- VT interventions were generally self-care based and tended to focus on general stress reduction and health promotion rather than addressing the specific effects of VT
- The VT interventions generally showed positive effect in their key outcomes. In particular, interventions delivered over the longer term in a group setting showed the most promise in addressing service providers' VT symptoms. However, future systematic evaluations are needed to determine the efficacy of such interventions, as well as investigate the efficacy of different intervention approaches

Five Core Actions

1. Promote safety
2. Promote calm
3. Promote connectedness
4. Promote hope
5. Promote self-efficacy

CASE STUDY #1

- ◆ **Introduction:** The patient is a 47-year-old male, known to you, who presents to the drop-in center at a low threshold program daily for meals, supplies, and to hang out.
- ◆ **PMH:** HIV positive, on ART; active HCV infection; bipolar disorder; anxiety disorder; TUD; SUD: hx OUD, methamphetamine use disorder, synthetic cannabinoid use disorder, hx OD x multiple times
- ◆ **Presentation:** The patient was found unresponsive on the sidewalk in front of the harm reduction program. He had been seen inside the harm reduction center's drop-in center 10 minutes earlier alert and responsive.
- ◆ **Questions:**
 - ◆ How would you respond?
 - ◆ What would you do first?
 - ◆ What would you do to support the patient?
 - ◆ What tools could assist you in your evaluation?

CASE STUDY #1 GROUP DISCUSSION

- ◆ Presentation Continued: The patient's SpO₂, RR, and HR were within normal limits. The patient was unresponsive to painful stimuli. Staff remained with the patient until he fully regained consciousness, about 15 minutes later. The patient then advised us that he had smoked synthetic cannabinoids when he stepped outside.
- ◆ Many patients may present after active substance use with loss of consciousness (with sedatives: xylazine, medetomidine, synthetic benzodiazepines; with synthetic cannabinoids, etc.) BUT have stable and adequate RR and SpO₂; therefore, naloxone is not indicated.
- ◆ Many patients co-use opioids with other substances or are on methadone or buprenorphine, so using naloxone *unnecessarily* can precipitate opioid withdrawal syndrome *unnecessarily*.
- ◆ This patient was monitored by staff with a pulse oximeter, manual count of respirations, and with oxygen on standby in case it was needed.
- ◆ The patient had no recollection of the episode.

CASE STUDY #2

- ◆ **Introduction:** The patient is a 31 yo male, known to you, who presents to the drop-in center at a low threshold program daily for meals, supplies, and to hang out.
- ◆ **PMH:** HCV s/p tx w/ SVR, OUD, MDD, hx OD x multiple times
- ◆ **Presentation:** The patient was found unresponsive in the computer station in the drop-in center. He had been seen inside the drop-in center 10 minutes earlier alert and responsive.
- ◆ **Questions:**
 - ◆ How would you respond?
 - ◆ What would you do first?
 - ◆ What would you do to support the patient?
 - ◆ What tools could assist you in your evaluation?

CASE STUDY #2 GROUP DISCUSSION

- ◆ **Presentation Continued:** The patient's SpO₂ was 83% and RR was 8/minute when he was assessed. He was unresponsive to painful stimuli. He was administered oxygen via a nasal cannula. His SpO₂ improved but his RR remained inadequate. He was administered 0.2 mg naloxone IM via titration.
- ◆ His RR normalized and his SpO₂ normalized while on administered oxygen. He remained unresponsive to verbal and tactile stimuli.
- ◆ The opioid portion of the overdose was reversed with the titrated naloxone; however, the sedative portion of the overdose continued to contribute to his unresponsiveness.
- ◆ The patient was monitored by staff with a pulse oximeter, manual count of respirations, and with oxygen until he regained consciousness, approximately 3 hours later.

SUMMARY/TAKE-AWAY MESSAGES

- The current unregulated drug supply is highly unpredictable, and the opioid supply is dominated by sedative adulterants.
- Overdose response should be nuanced, with appropriate opioid antagonist use (when indicated), and always with a compassionate overdose response in mind to cause the least physical and psychological distress to the person who overdosed.
- An appropriate overdose response for the current (and any future) drug supply focuses on responding to the signs and symptoms one is seeing in the person who has overdosed. Assess airway, breathing, and circulation and respond accordingly with a tailored response.
- Overdose response can be augmented with additional tools to better assess and support airway and breathing. These tools include a pulse oximeter, oral and nasal airways, oxygen administration, and bag valve masks.
- Overamping due to stimulants also requires a nuanced response depending on the signs and symptoms the person overamping is experiencing. Engaging in behavioral de-escalation, ensuring a safe space, and assessing for overamping-related emergencies are key elements of an appropriate response
- Synthetic cannabinoid use may result in an “overdose,” and an appropriate response includes assessing the person and providing supportive care.
- It is imperative to support patients after an overdose and support staff after they have responded to an overdose.

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QUESTIONS? THANKS!

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