



JOHNS HOPKINS
M E D I C I N E

JOHNS HOPKINS BAYVIEW MEDICAL CENTER

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June 2026

Recognition and Management of Alpha-2 Agonist Intoxication and Withdrawal

Disclosures

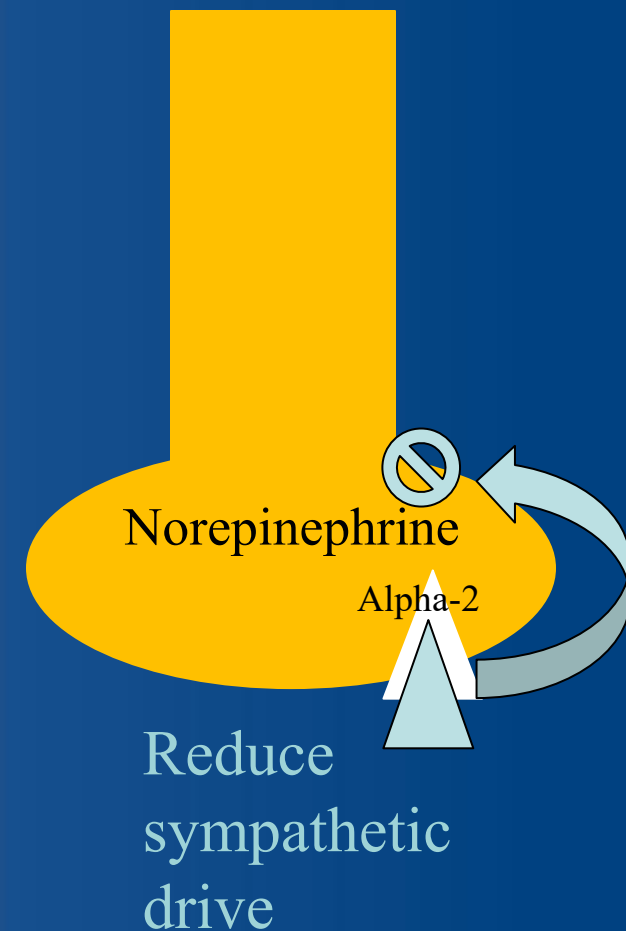
- None

Objectives

- What is an alpha-2 agonist?
- What does alpha-2 agonist intoxication look like?
- What does alpha-2 agonist withdrawal look like?
 - How do I treat it?
- What are the systems issues?

Alpha-2 Adrenergic Receptor Agonists

Receptor	Physiologic Action (Agonism)
$\alpha 1$	Constriction of vascular smooth muscle Contraction of radial muscle of the eye Contraction of the vas deferens smooth muscle
$\alpha 2$	Inhibition of norepinephrine release from presynaptic neuron Centrally induced sedation via locus ceruleus Centrally mediated pain modification via dorsal horn
$\beta 1$	Inhibition of insulin release from pancreatic β cells Increased cardiac output (increased chronotropy, dromotropy, inotropy) Increased renin release from kidney
$\beta 2$	Bronchial smooth muscle relaxation Vascular smooth muscle relaxation (vasodilation) Reduction of mast cell degranulation and histamine release
$\beta 3$	Increased adipose tissue lipolysis



Alpha-2 Adrenergic Agonists

- Used in human medicine for blood pressure, muscle relaxant and sedation
 - Eg: Clonidine, lofexidine, tizanidine, guanfacine, dexmedetomidine
- Used in veterinarian medicine for sedation
 - Xylazine, medetomidine

Xylazine and Medetomidine

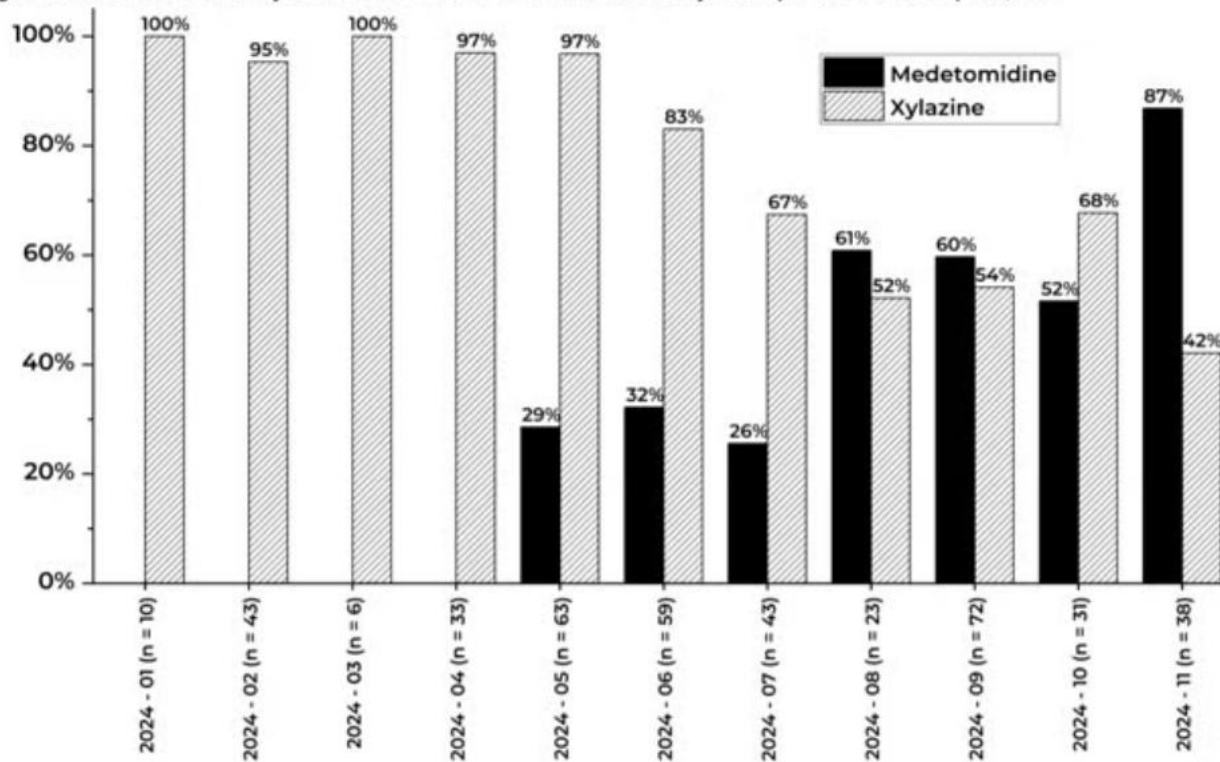
- Xylazine
 - First reported in mid 2000s in Puerto Rico and Philadelphia²
 - Dose dependent but hemodynamic effects less potent than clonidine¹
 - Associated with soft tissue wounds (became more recognized ~2020)
 - Pennsylvania scheduled xylazine in May 2024

Xylazine and Medetomidine

- Medetomidine
 - Racemic mixture of dexmedetomidine and levomedetomidine
 - ~200x more potent than xylazine¹
 - First detected in drug supply ~ 2022 in Maryland

Prevalence in Drug Supply

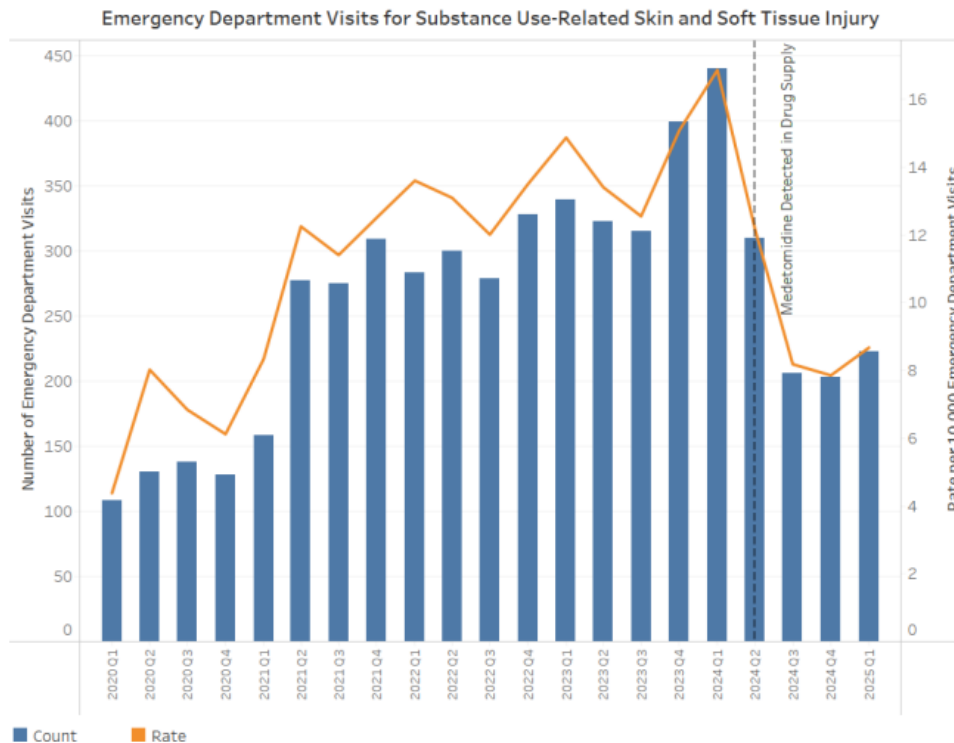
Figure 1: Prevalence of Xylazine and Medetomidine in Fentanyl Samples in Philadelphia, PA



Data source: Center for Forensic Science, Research and Education, PA Groundhogs, Philadelphia Department of Public Health

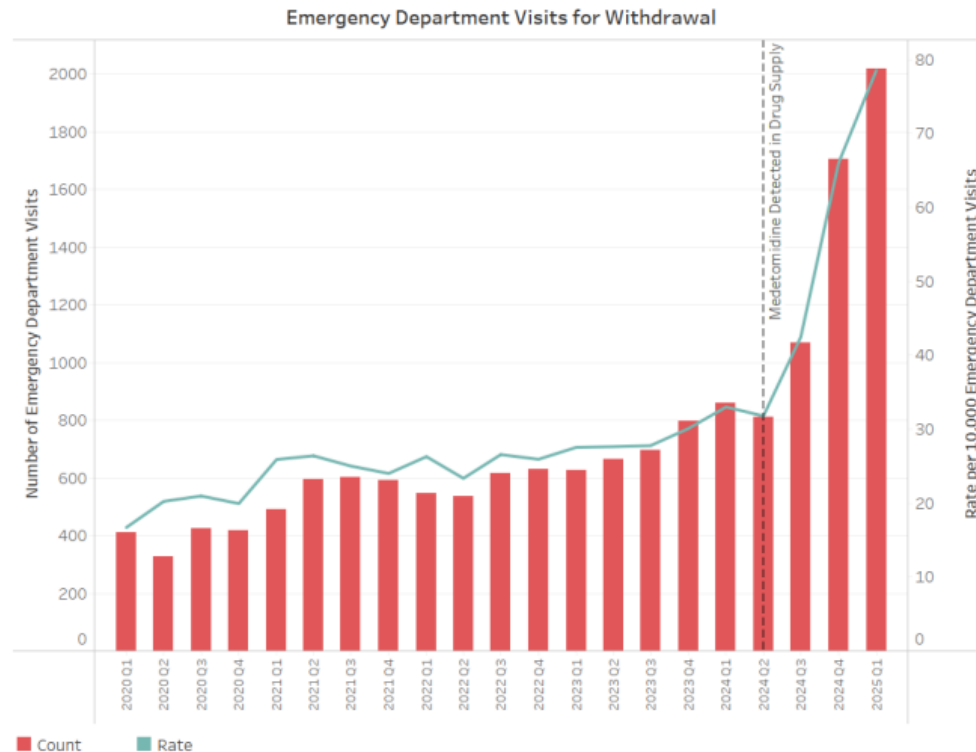
ER Visits: Skin and Soft Tissue

Despite large increases from 2020 through the beginning of 2024, emergency department visits for substance use-related skin and soft tissue injury rapidly decreased after 2024 Q1.



ER Visits: Opioid Withdrawal

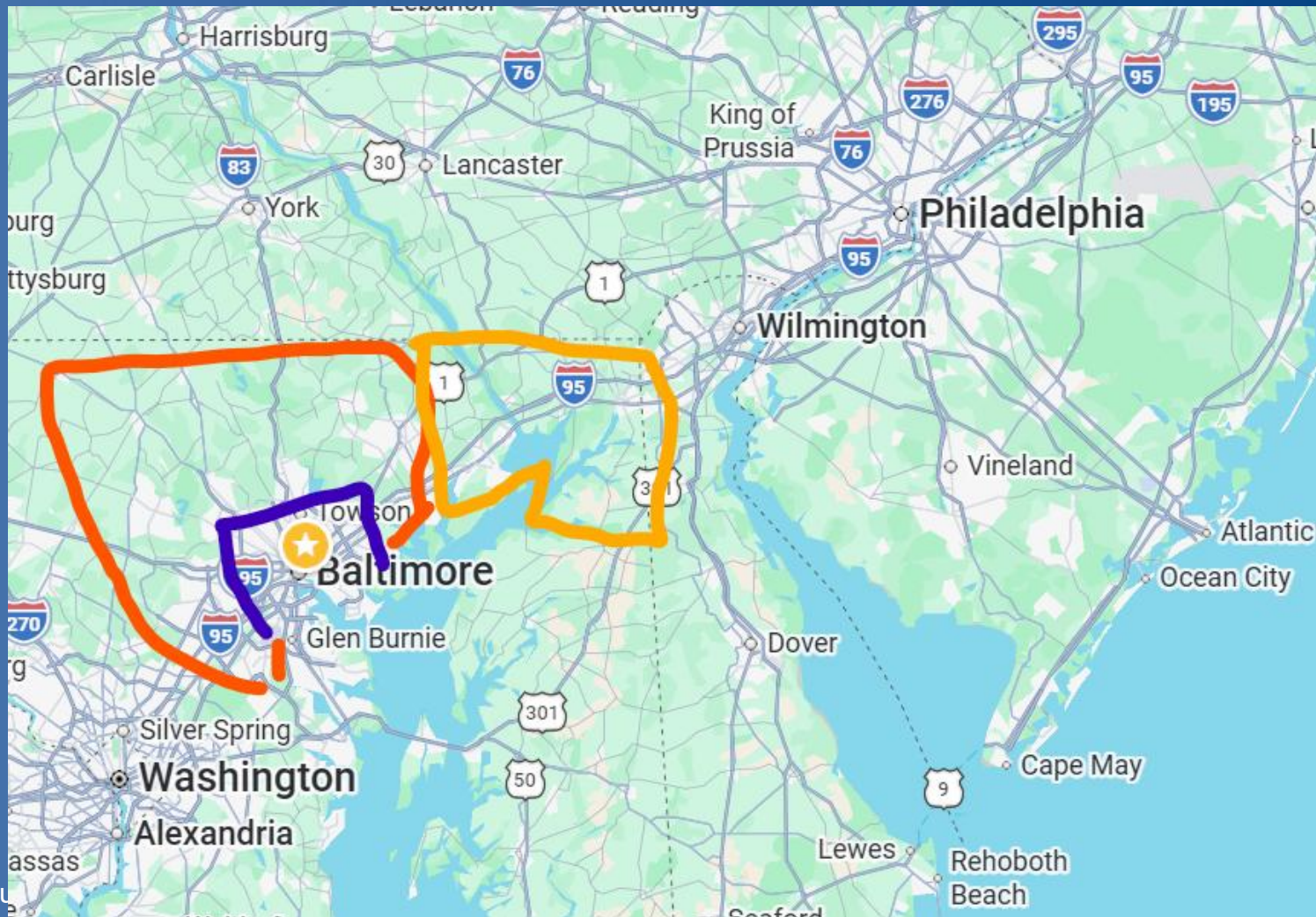
Emergency department visits for withdrawal increased substantially after medetomidine was first detected in Philadelphia's drug supply in May 2024 (2024 Q2).



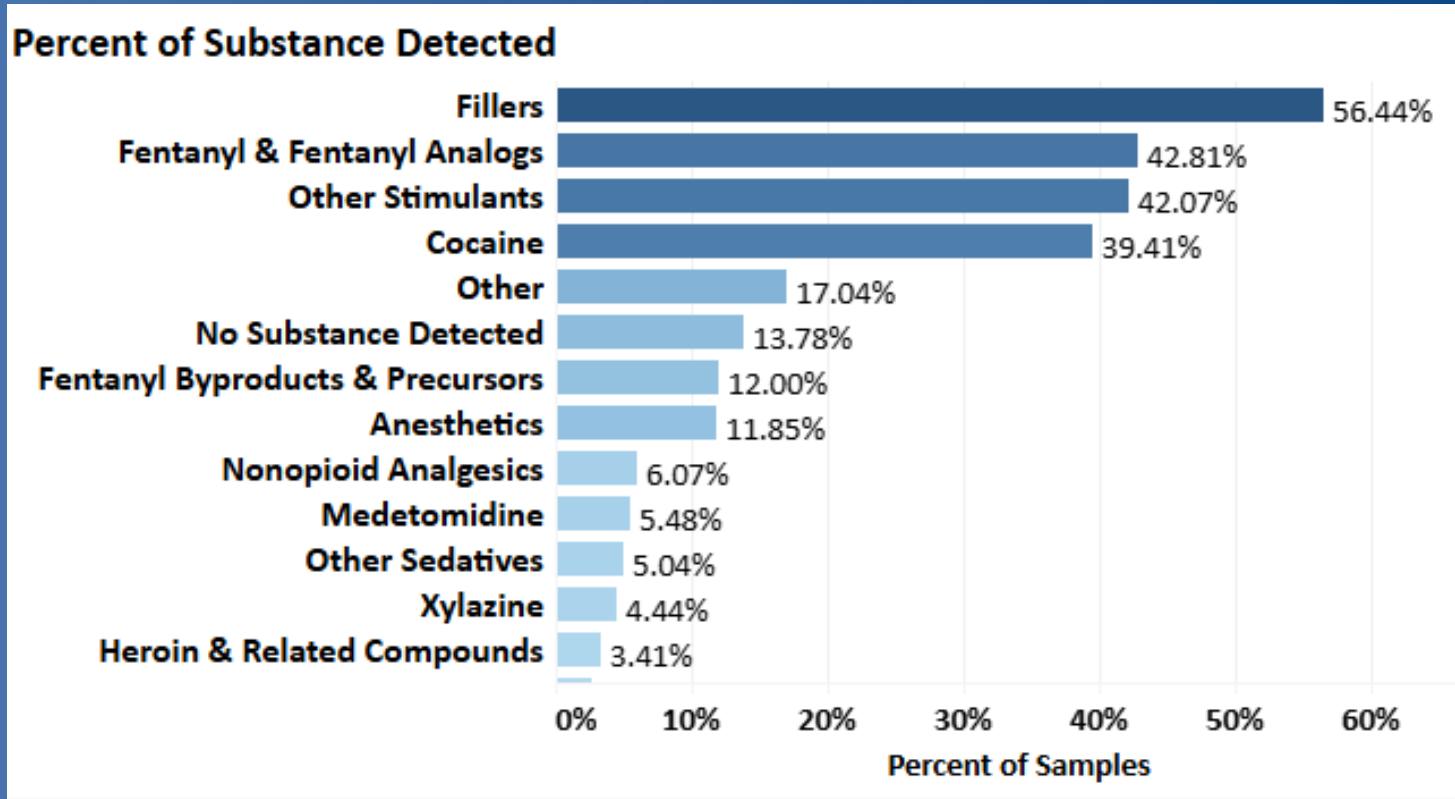
How do you know what drugs to look for?

- Drug checking- individual, local, regional and national
 - Test strips
 - Local harm reduction groups
 - Health department partners, bulletins; Poison Center; MACS!
 - NDEWS, CFSRE

Regional Trends

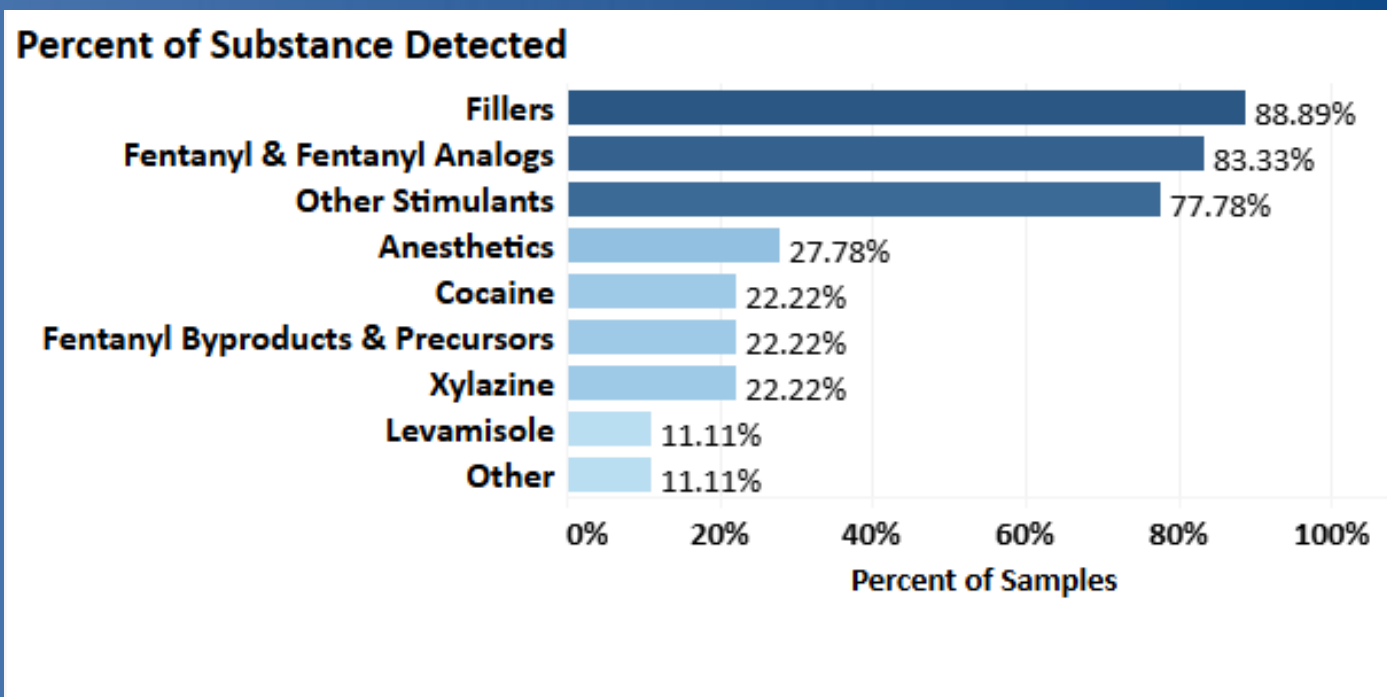


Regional Trends- Baltimore City



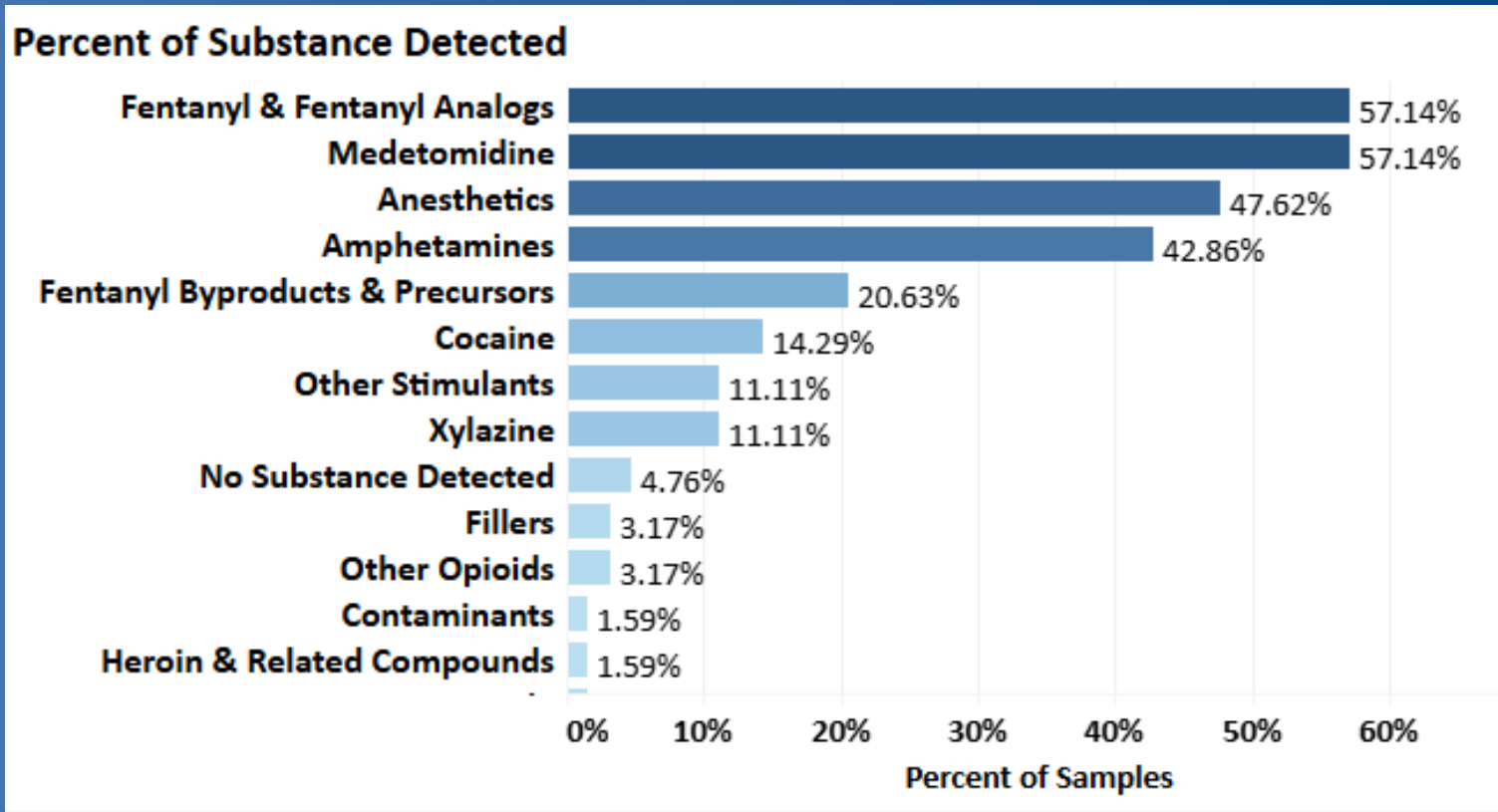
<https://health.maryland.gov/dataoffice/Pages/mdh-dashboards.aspx>

Regional Trends- Baltimore County



<https://health.maryland.gov/dataoffice/Pages/mdh-dashboards.aspx>

Regional Trends- Cecil County



<https://health.maryland.gov/dataoffice/Pages/mdh-dashboards.aspx>

It's scary out there

Tranq-Dope and Benzo-Dope in the Ohio Illicit Drug Supply

PUBLIC BULLETIN

Third overdose in three months hits Baltimore's Penn North neighborhood

WYPR - 88.1 FM Baltimore | By Scott Maucione
Published October 8, 2025 at 5:24 PM EDT



EMERGENCE OF ORPHINE ANALOGUES

DATE*	ANALOGUE
July 2020	Brorphine
Aug. 2024	5,6-Dichloro Desmethylchlorphine (SR-17018)
Dec. 2024	Chlorphine
Dec. 2024	N-Propionitrile Chlorphine (Cychlorphine)
Oct. 2025	Spirochlorphine (R-6890)
Dec. 2025	5,6-Dichloro Brorphine (SR-14968)

*Date of NPS Discovery monograph issuance.

Compound	West Coast	East Coast	All Samples	3-Month Trend (All)
Acetaminophen	77%	37%	47%	
BTMPS	23%	26%	25%	
Caffeine	6%	40%	32%	
Cocaine	13%	34%	29%	
Diphenhydramine	0%	2%	2%	
Gabapentin	3%	1%	2%	
Heroin	0%	18%	14%	
iso-PV8	0%	4%	3%	
Ketamine	3%	1%	2%	
Levamisole	0%	6%	5%	
Lidocaine	6%	44%	35%	
Medetomidine	3%	30%	23%	
Melatonin	0%	10%	8%	
Methamphetamine	42%	4%	13%	
Methocarbamol	0%	3%	2%	
Phenacetin	0%	4%	3%	
Procaine	0%	27%	20%	
Quinine	0%	30%	22%	
Tetracaine	10%	8%	9%	
Xylazine	0%	26%	19%	

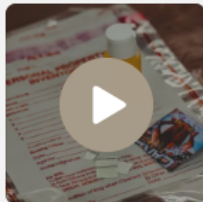
NIST



PUBLIC ALERT

DEC 2025

NOVEL BENZODIAZEPINE PHENAZOLAM INCREASING IN DETECTIONS AND PREVALENCE AMONG U.S. RECREATIONAL DRUG MARKETS



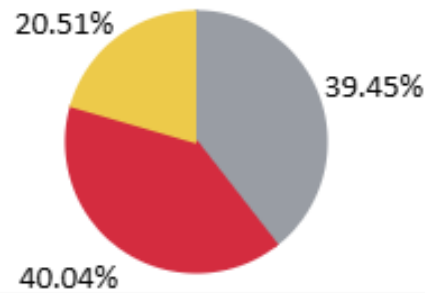
4d ago · E

A Flood of New, Deadlier Drugs




As America is beginning to wrap its arms around the fentanyl crisis, a new kind of drug epidemic is emerging. It is faster, more addictive, more lethal and powered by synthetic drugs — substances that can be made almost anywhere. Matt Richtel, a science and health reporter, and Azam Ahmed, an international investigative...

It's scary out there

Proportion of Samples that Include Expected Substances



Legend

-  Some Expected Substances
-  No Expected Substances
-  All Expected Substances

<https://health.maryland.gov/dataoffice/Pages/mdh-dashboards.aspx>

Experience at Bayview Addiction Medicine Unit (AMU)

- What is the AMU?
- October 2024 → patient with opioid use disorder (OUD) with severe withdrawal
- January 2025 → same patient admitted and suspected alternative substance; phoned a friend, connected with regional and national resources
- Working with our lab, sent 10 suspected cases and 100% were positive for medetomidine

Medetomidine intoxication, overdose

- Sedation (not reversed by naloxone)
- Bradycardia
- Hypotension

Overdose response

- Still use naloxone to restore breathing
- Most patients do not need heart rate or blood pressure support

Medetomidine Withdrawal

- Onset: 4-24 hours from last use
- Symptoms both typical opioid withdrawal and severe symptoms more specific to medetomidine/alpha-2 withdrawal
- Make sure to assess for risk of alcohol or benzodiazepine withdrawal

Medetomidine Withdrawal

Typical Withdrawal

- Body aches
- Rhinorrhea
- Lacrimation
- Yawning
- Diaphoresis

Atypical

- Severe vomiting
- Severe agitation
- Rigors
- Mutism/catatonia

Hemodynamics

- Hypertension (SBP 180-200s)
- Tachycardia (HR 130-170s)
- Occ fever

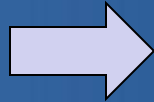
Labs

- Leukocytosis (20-25K)
- Hypokalemia
- Lactic acidosis

Withdrawal Treatment

Typical Withdrawal

- Body aches
- Rhinorrhea
- Lacrimation
- Yawning
- **COWS** in the **20s-30s**

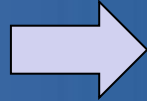


- Opioids: methadone
oxycodone,
hydromorphone,
- Discuss MOUD early

Withdrawal Treatment

Atypical

- Severe vomiting
- Severe agitation
- Rigors
- Diaphoresis
- Mutism/catatonia

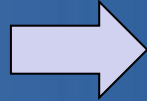


- Clonidine patch 0.3mg on admission
- Once HR >60 and SBP is ~120 we give PO clonidine 0.2-0.3mg q1-2 hours for a total dose of 0.9-1.2 and then space it out to ~q4hours
- ER or monitored setting can be more frequent/higher dosing

Withdrawal Treatment

Atypical

- Severe vomiting
- Severe agitation
- Rigors
- Diaphoresis
- Mutism/catatonia



Other Alpha-2 agonists:

- Tizanidine 4mg q6hr
- Guanfacine, longer acting

Antiemetics:

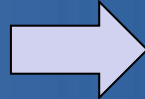
- Olanzapine
- Prochlorperazine

Don't forget opioids

Withdrawal Treatment

Atypical

- Severe vomiting
- Severe agitation
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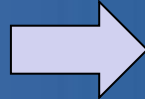
Don't forget opioids

**If nausea and vomiting is so severe that they can't tolerate PO,
start dexmedetomidine**

Withdrawal Treatment

Atypical

- Severe vomiting
- Severe agitation
- Rigors
- Diaphoresis
- Mutism/catatonia



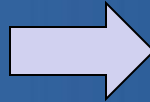
Dexmedetomidine dosing:

- “Start infusion at **0.5mcg/kg/hr**. Titrated, by nursing, no more than **0.4mcg/kg/hr** every 20 minutes up to **1.5mcg/kg/hr**. **Doses > 1.5mcg/kg/hr** should be **provider driven** to a maximum of **2.4mcg/kg/hr**. Titrate to SBP <160.”
- Some places doing higher loading dose

Withdrawal Treatment

Atypical

- Severe vomiting
- Severe agitation
- Rigors
- Diaphoresis
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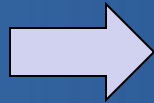


- Adjunctive medications:
ketamine (in the 0.1-
0.3mg/kg/hr range),
propofol
- If still agitated, consider
BZD or phenobarbital

Withdrawal Treatment

Hemodynamics

- Hypertension (SBP 180-200s)
- Tachycardia (HR 130-170s)
- Occ fever



- Clonidine, dexmedetomidine should improve these
- Targeted BP meds like nicardipine, esmolol as would be used for hypertensive emergency

- <https://penncamp.org/medetomidine/>

Clinical Recommendations for Managing Medetomidine Withdrawal

You can download our ICU medetomidine-fentanyl withdrawal management strategy here.

Complications of withdrawal

- NSTEMI
- PRES
- Seizure
- Severe electrolyte disturbances
- Aspiration
- Intubation

What are the system implications?

- Very high ICU rates and costs¹
 - What can be done to reduce ICU level care?
 - How do we communicate about new drugs with other departments, other hospitals, with patients?
- High return to use
 - What can be done to reduce return to use?

What we don't know

- What are the long-term effects of medetomidine?
 - So far, no association with severe wounds like xylazine
- How can we predict who will have severe withdrawal or not?
 - PICU data
- Reversal agent?
 - Atipamazole
- What is the next drug?

Summary

If it doesn't look like typical withdrawal, ask a friend, check the local drug supply

The drug supply is dangerous, unpredictable; impacts patients and health care system

Medetomidine intoxication- sedation, bradycardia. Still use naloxone if suspected opioid overdose

Medetomidine withdrawal- it is severe. Treat aggressively

Questions?

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