



Medetomidine: An Emerging Adulterant Reshaping Toxicity and Withdrawal Management

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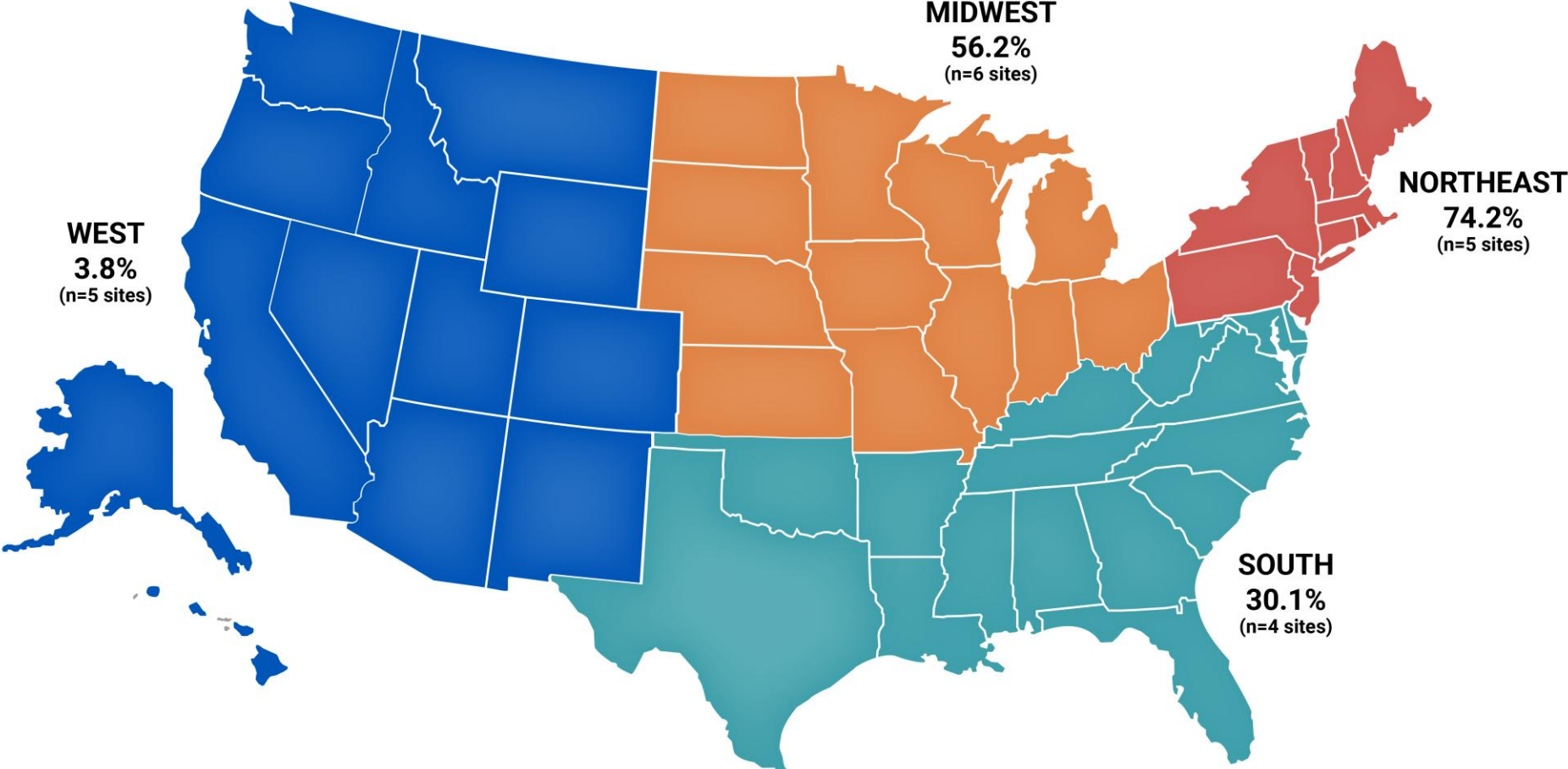
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Objectives

- **Describe** the emergence of medetomidine as an illicit drug adulterant and its impact on overdose toxicity and withdrawal presentations.
- **Recognize** the clinical features of medetomidine toxicity and differentiate medetomidine withdrawal from opioid, benzodiazepine, and other sedative withdrawal syndromes.
- **Apply** evidence-informed strategies for early, aggressive management of medetomidine withdrawal.
- **Identify** system-level challenges posed by medetomidine and outline approaches to multidisciplinary coordination.

Medetomidine Detection-2025

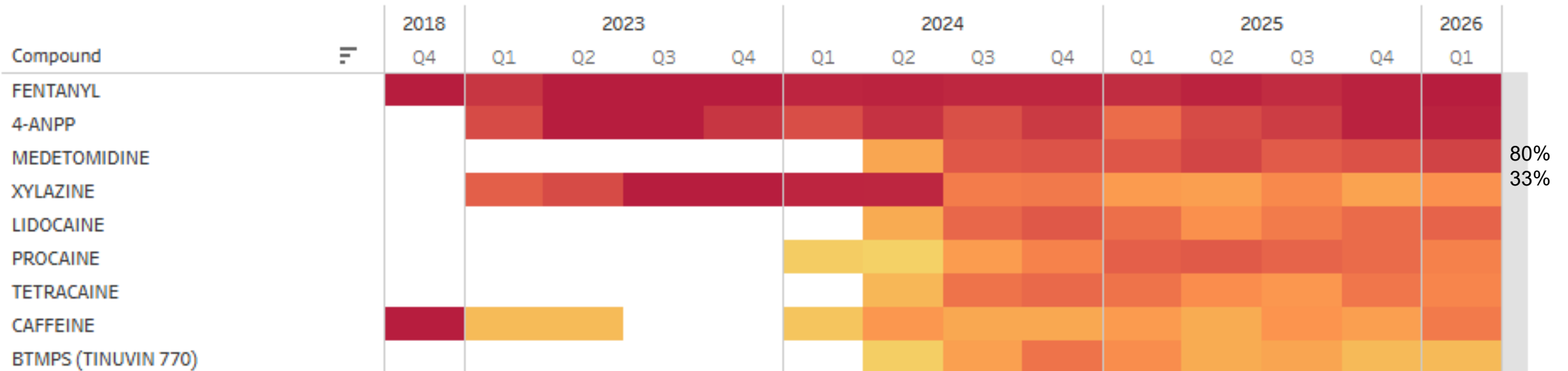


<https://www.cdc.gov/han/php/notices/han00527.html>

PA Drug-Checking Data

PA Groundhogs Adulterant Report

ADULTERANTS FOUND IN PA STREET DRUGS SOLD AS FENTANYL

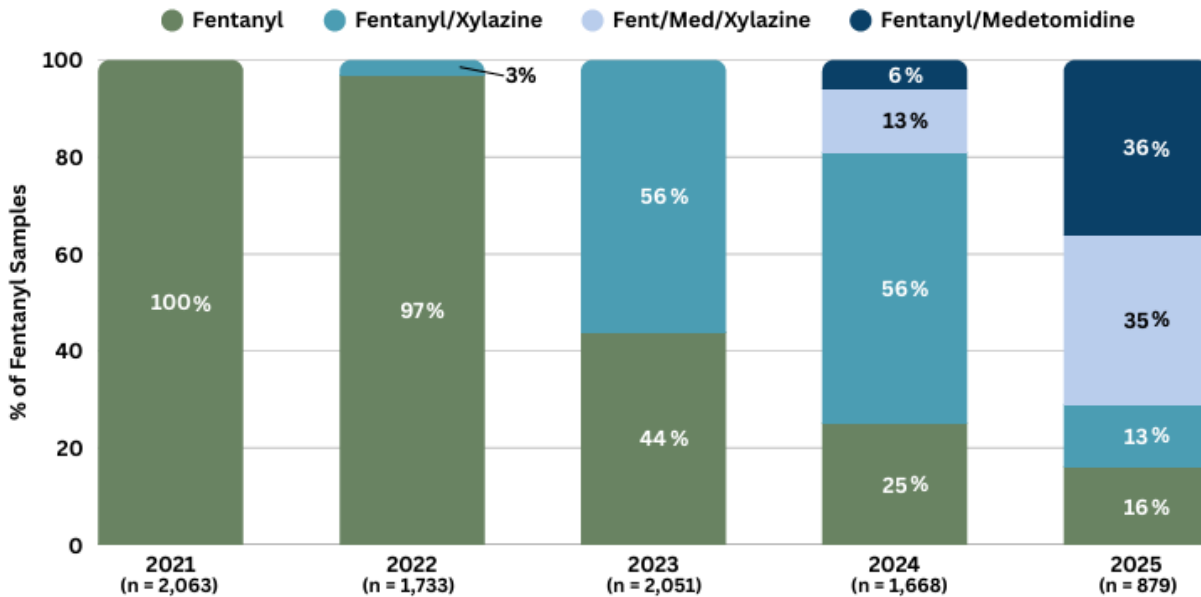


[DATA | PAGroundhogs](#) Accessed 4/15/26

Allegheny County Adulterants

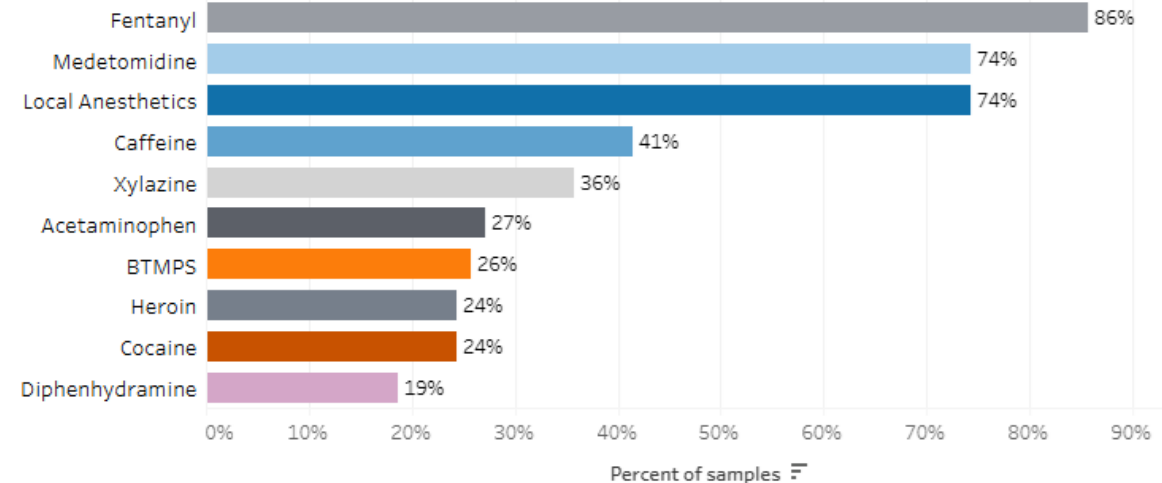
1/1/26-4/15/26

Percent of Fentanyl Samples Containing Medetomidine and Xylazine, 2021 - 2025



Top Substances Found in Samples People Submitted Expecting to Contain Fentanyl
Fentanyl was found (in any amount) 86% of the 70 tested samples.

-Use "Select Expected Substance" to see results for specific expected substances, or pick "Any Expected Substance" for all samples.
-Because samples often contain multiple substances (both at primary and trace amounts), percentages will exceed 100%.

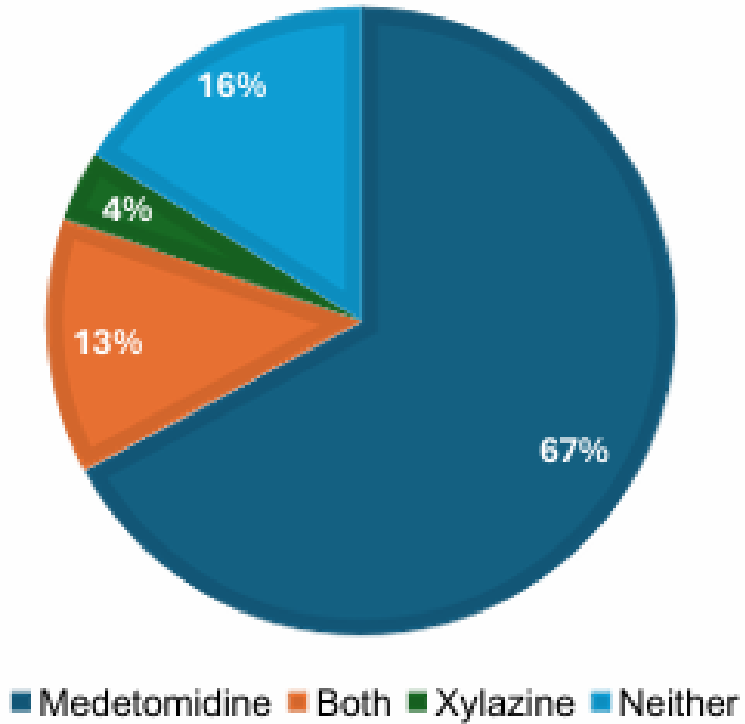


1. [medetomidine brief](#) Accessed 3/20/2026
2. [Workbook: Substance Monitoring Dashboard](#) Accessed 4/15/2026

Philadelphia County Drug Checking Data

1/2025-6/2025

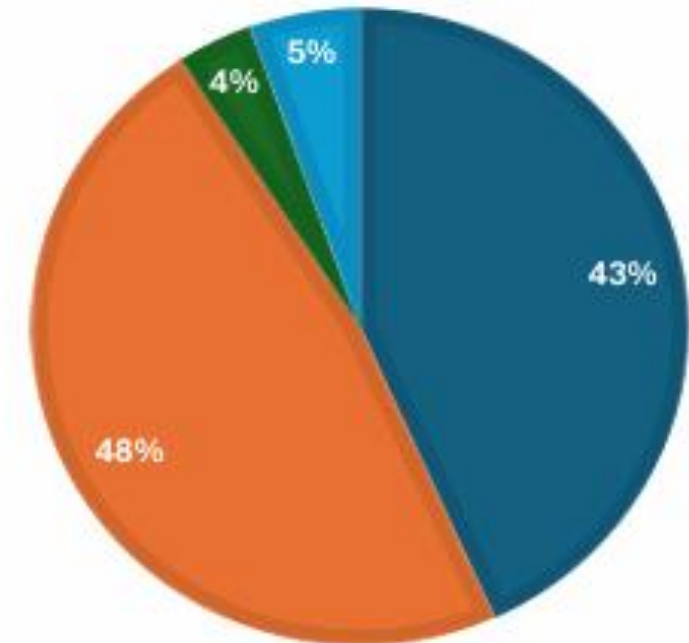
Figure 1. Sedatives in Samples with Fentanyl or Heroin as the Primary Drug



10/2025-12/2025

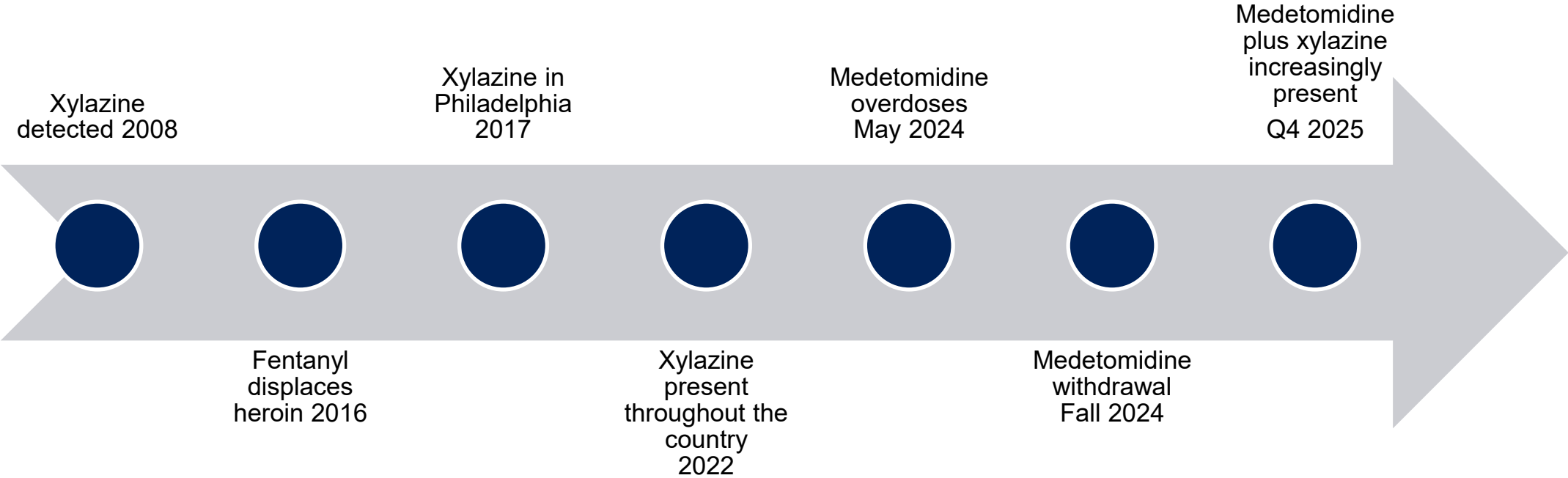
Figure 1. Sedatives in Samples with Fentanyl or Heroin as the Primary Substance

- Medetomidine Only
- Both Medetomidine & Xylazine
- Xylazine Only
- Neither Medetomidine or Xylazine



<https://www.substanceusephilly.com/reports>. Accessed 4/15/2026

Timeline of Adulterants



Growing Public Health Recognition



Morbidity and Mortality Weekly Report (*MMWR*)

Search



Notes from the Field: Suspected Medetomidine Withdrawal Syndrome Among Fentanyl-Exposed Patients — Philadelphia, Pennsylvania, September 2024–January 2025

Weekly / May 1, 2025 / 74(15);266–268



Morbidity and Mortality Weekly Report (*MMWR*)

Search

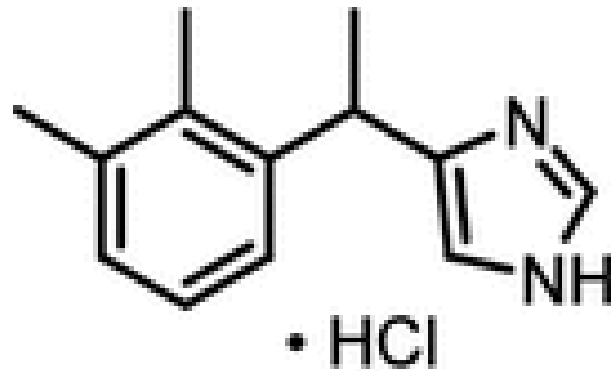


Notes from the Field: Severe Medetomidine Withdrawal Syndrome in Patients Using Illegally Manufactured Opioids — Pittsburgh, Pennsylvania, October 2024–March 2025

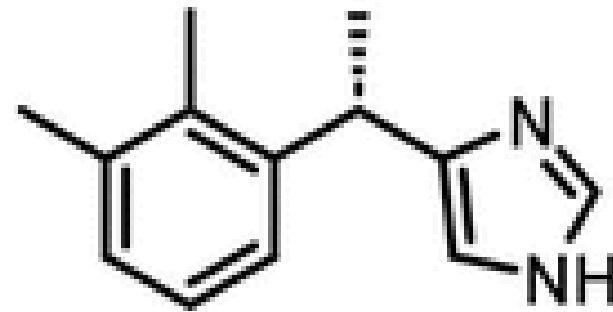
Weekly / May 1, 2025 / 74(15);269–271

Medetomidine

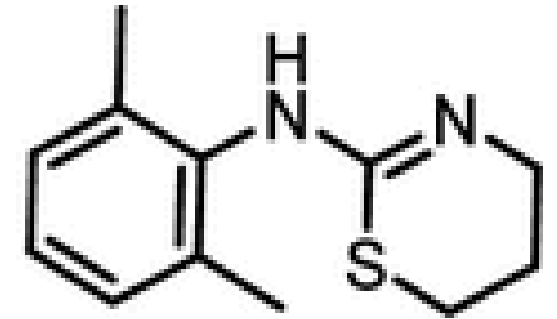
- Medetomidine is a racemic mixture of levo- and dexmedetomidine
- FDA-approved veterinary anesthetic
- Shares structural elements with other alpha-2 agonists



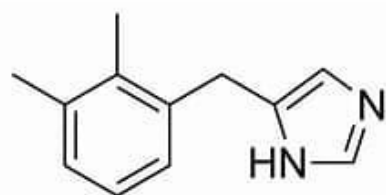
Medetomidine, 1



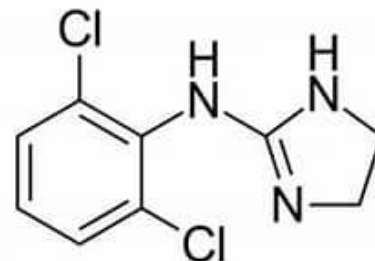
Dexmedetomidine, 2



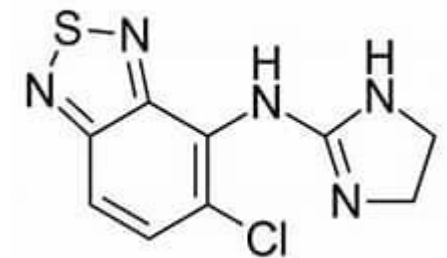
Xylazine, 3



detomidine

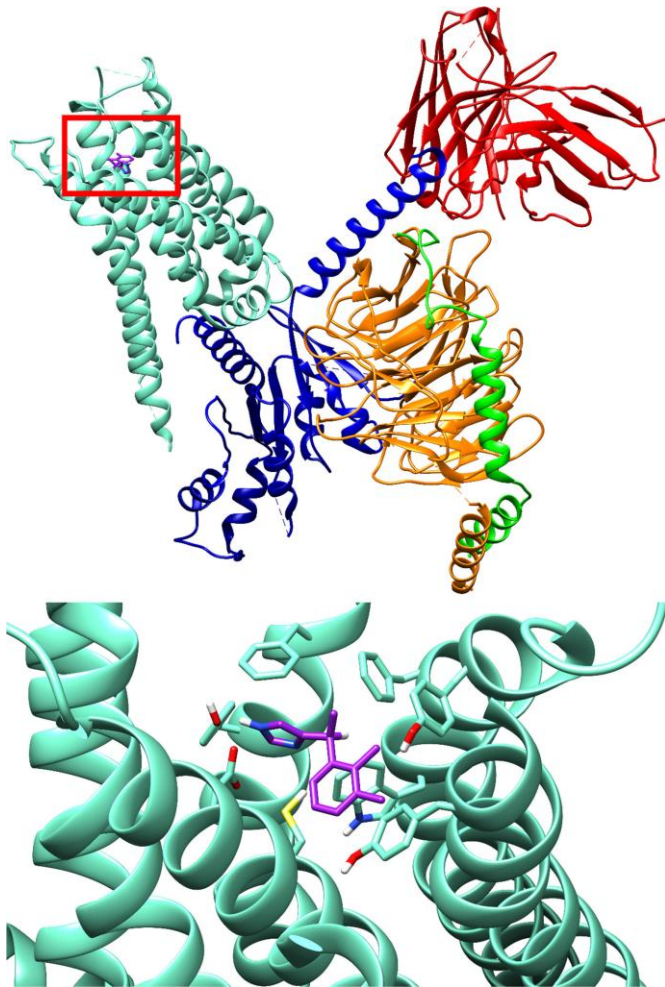


clonidine



tizanidine

Medetomidine Pharmacodynamics



- Medetomidine is a highly selective ligand for the alpha-2 receptor

K_i (nM)

compound	α_1	α_2	selectivity ratio (α_2/α_1)
medetomidine	1750 \pm 567	1.08 \pm 0.23	1620
xylazine	30300 \pm 1720	194 \pm 35.3	160
clonidine	713 \pm 109	3.20 \pm 1.18	220

de Andrade 2024

Pharmacokinetics

Absorption

- IV, SL, buccal, intranasal
- Extensive first-pass effects (16% bioavailability)

Distribution

- Highly protein bound
- Crosses BBB and placenta
- $V_d = 1.31-2.46$ L/kg

Metabolism

- Hepatic metabolism
- 99% inactive metabolites

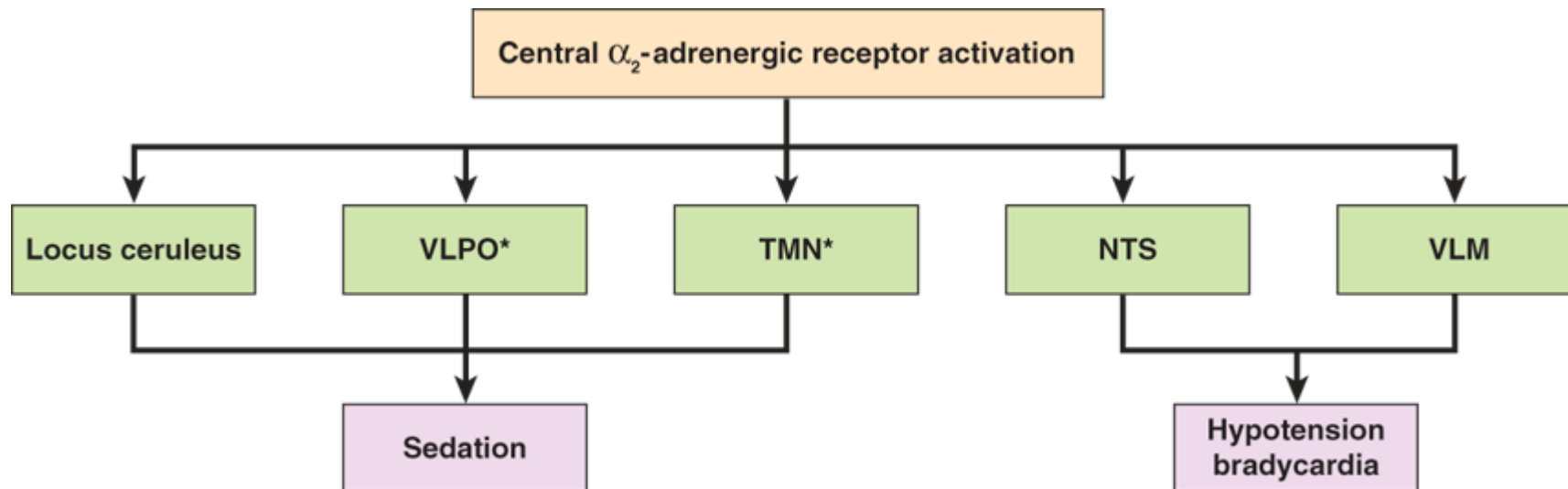
Elimination

- Half-life: 2.1-3.1 hours (Prolonged with hepatic impairment)
- 94% urinary excretion of metabolites

de Andrade Horn P, Berida TI, Parr LC, Bouchard JL, Jayakodiarachchi N, Schultz DC, Lindsley CW, Crowley ML. Classics in Chemical Neuroscience: Medetomidine. ACS Chem Neurosci. 2024 Nov 6;15(21):3874-3883. doi: 10.1021/acscchemneuro.4c00583. Epub 2024 Oct 15. PMID: 39405508; PMCID: PMC11587509.

Mechanism

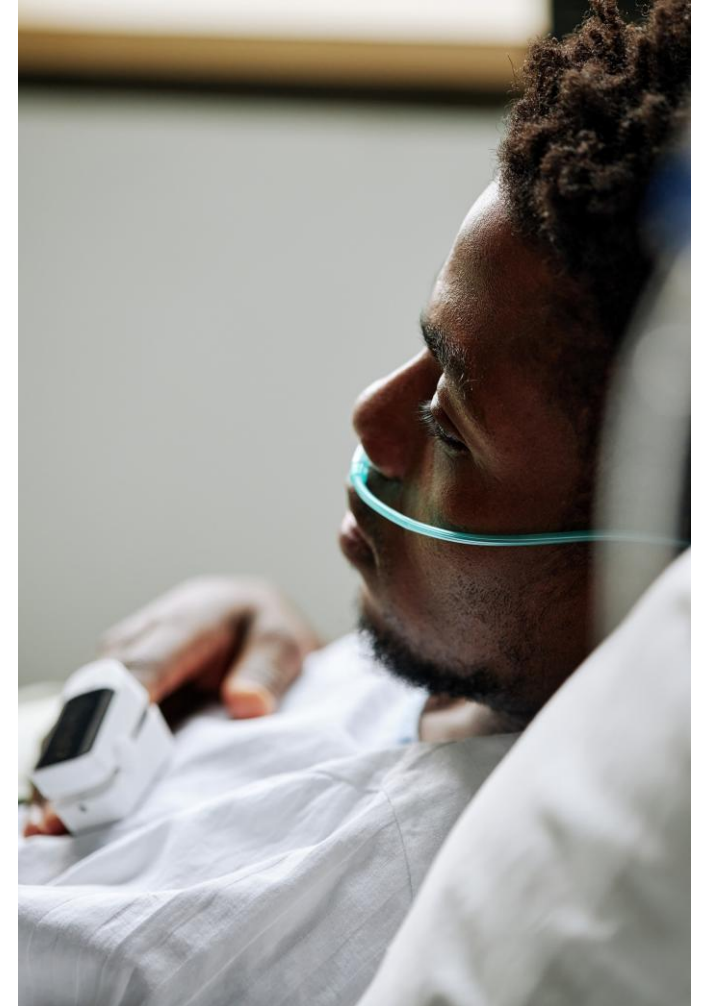
- Alpha-2 receptor effects
 - Peripheral effects
 - Initial vasoconstriction with increased SVR
 - Central effects
 - Inhibits sympathetic output → bradycardia and hypotension
 - Sedation



Source: L.S. Nelson, M.A. Howland, N.A. Lewin, S.W. Smith, L.R. Goldfrank, R.S. Hoffman: Goldfrank's Toxicologic Emergencies, Eleventh Edition Copyright © McGraw-Hill Education. All rights reserved.

Acute Toxicity

- Typically in conjunction with opioid toxicity
- Symptoms persist after opioid reversal
 - Prolonged sedation
 - Miosis
 - Sinus bradycardia
 - 30s-40s commonly observed
 - Hyper/hypotension
 - α -2 agonist toxicity can cause initial hypertension followed by hypotension
 - SBP 70s-80s
 - Bradypnea



1. Nayani 2025
2. Nham 2024

Acute Toxicity-Management

Naloxone

- Naloxone does not reverse medetomidine-induced sedation
- **Naloxone should still be given to treat opioid toxicity**

Respiratory

- Most patients require only supplemental oxygen
- Few require mechanical ventilation

Cardiovascular

- Most cases of hypotension respond to fluid resuscitation alone without vasopressors
- Some require pressors
- Avoid treating bradycardia in the setting of hypertension

Additional Considerations

- Rhabdomyolysis
- Co-occurring toxicity or infectious pathology

Atipamezole

- Not approved for human use
- Likely to be associated with greater harm than benefit

Testing

- Nearly always found in conjunction with fentanyl
- There are no rapid clinical medetomidine tests available
- Liquid Chromatography-Mass Spectroscopy (comprehensive drug screening)
 - Able to identify medetomidine
 - Medetomidine presence is transient
 - Medetomidine metabolites (3-OH-medetomidine and medetomidine glucuronides) only identified through additional directed testing
 - Unavailable in nearly all clinical settings
- Drug checking
 - Medetomidine test strips are available

1. Huo 2025
2. Ostrowski 2025
3. <https://pagroundhogs.org/news/f/pag-releases-new-adulterant-report>. Accessed 5/2/2025

Pharmaceutical Dexmedetomidine Withdrawal

- Most common after 3 days of sedation (reported as early as 24 hours)
- Higher peak doses and rates have higher risk
- Limited evidence to suggest utility of clonidine and guanfacine to facilitate weaning

Symptoms Experienced	Negative Withdrawal (n = 15)	Positive Withdrawal (n = 27)	p
Individual withdrawal symptoms, n (%)			
RASS > +1	0	9 (33)	0.02
Confusion Assessment Method ICU +	3 (20)	25 (93)	< 0.01
Systolic blood pressure > 140 mm Hg or mean arterial pressure > 90 mm Hg	1 (7)	13 (48)	0.01
Heart rate > 90 beats/min	9 (60)	23 (85)	0.13
WAT-1 ≥ 3	0	3 (11)	0.54

1. Bouajram RH, Bhatt K, Croci R, Baumgartner L, Puntillo K, Ramsay J, Thompson A. Incidence of Dexmedetomidine Withdrawal in Adult Critically Ill Patients: A Pilot Study. *Crit Care Explor.* 2019 Aug 9;1(8):e0035. doi: 10.1097/CCE.0000000000000035. PMID: 32166276; PMCID: PMC7063945.
2. Rajendraprasad S, Wheeler M, Wieruszewski E, Gottwald J, Wallace LA, Gerber D, Wieruszewski PM, Smischney NJ. Clonidine use during dexmedetomidine weaning: A systematic review. *World J Crit Care Med.* 2023 Jan 9;12(1):18-28. doi: 10.5492/wjccm.v12.i1.18. PMID: 36683967; PMCID: PMC9846870.
3. Feters MB, Diep C, Ran R, Kloosterboer A. Effect of Enteral Guanfacine on Dexmedetomidine Use in the ICU. *Crit Care Explor.* 2022 Nov 1;4(11):e0785. doi: 10.1097/CCE.0000000000000785. PMID: 36349291; PMCID: PMC9632248.

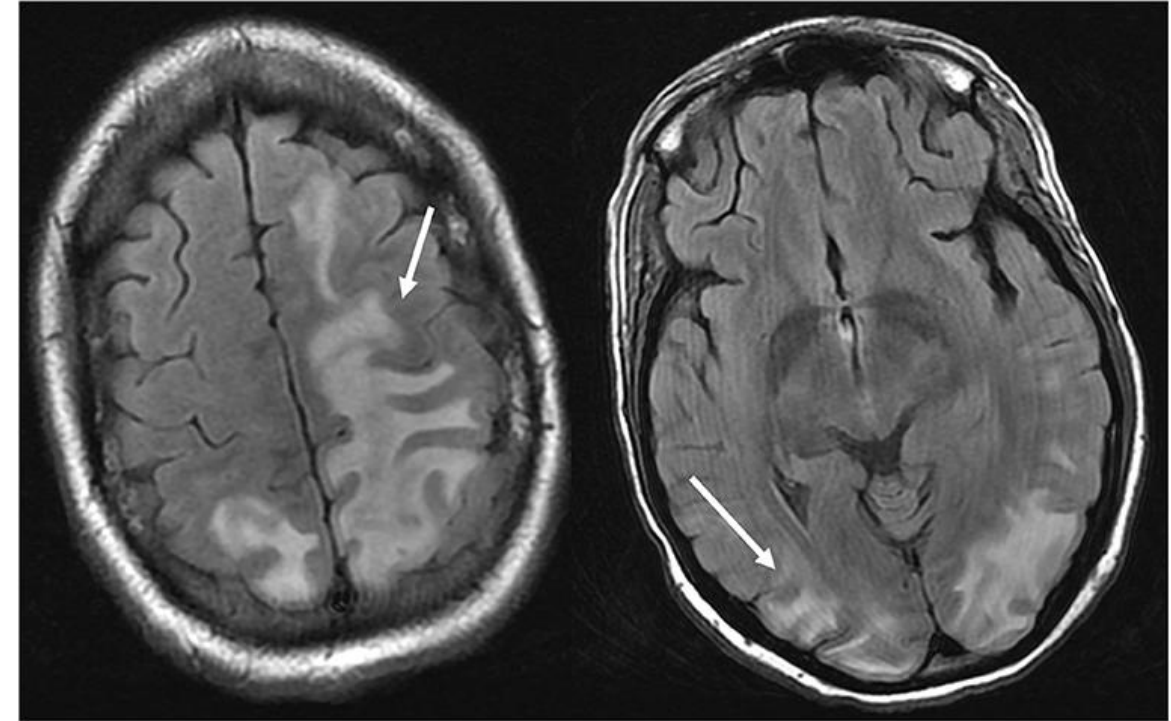
Medetomidine Withdrawal-Clinical

- Rapid Onset (often within 4-6 hours)
- Severe nausea and vomiting
- Progressive sinus tachycardia (to 170s+)
- Progressive severe hypertension
 - SBP: 170-230s
 - DBP 120-140s
- Anxiety, diaphoresis, and tremor
- Myoclonic jerks and coarse tremor
 - No definitive evidence of true seizures
- Encephalopathy/delirium
- ~77-90% admitted to ICU



Medetomidine Withdrawal-Findings

- Anion gap metabolic acidosis
- Elevated lactic acid levels
- Hypokalemia
- QTc prolongation
- Myocardial injury with troponin elevations
- Posterior Resolving Encephalopathy Syndrome (PRES)



1. Huo 2025
2. Ostrowski 2025
3. Anderson 2020

Medetomidine Withdrawal-Management

- **Alpha-2 agonists**

- Mild-Moderate

- Clonidine 0.3mg q15 minutes x 3 doses
 - Clonidine 0.2-0.3mg q2 standing AND PRN COWS (5/15)
- Guanfacine IR 2mg PO q8h standing
- Transdermal clonidine 0.3mg

- Severe and/or unable to tolerate PO

- Dexmedetomidine

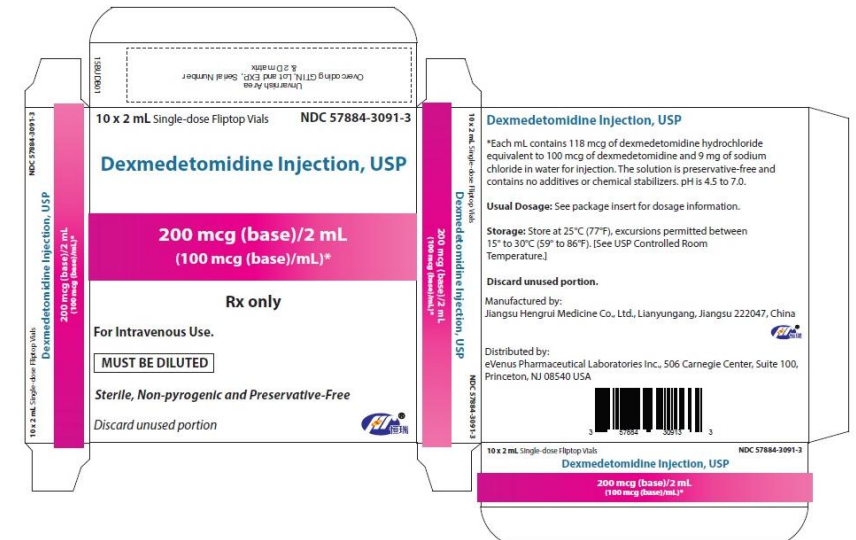
- Loading dose 1 mcg/kg IV over 10 min
- Followed by continuous infusion 0.5-2.4 mcg/kg/hr titrated to effect

- Continue/resume PO meds as tolerated

- 24-72 hours and clinical improvement → transition to PO α -2 agonists only

- Taper guanfacine (2mg PO BID, 1mg PO TID, 1mg PO BID, 1mg PO QD)

- Discharge with alpha-2 agonist?



1. Lynch 2026
2. <https://fda.report/DailyMed/6f6c592a-6c87-461c-929f-77cba42029c8>. Accessed 5/6/2025

Medetomidine Withdrawal-Management

- **Opioid withdrawal and MOUD Initiation (pathways vary)**
 - Overlapping symptoms
 - Methadone induction
 - Methadone IV or PO if tolerated
 - Monitor QTc
 - Buprenorphine Induction
 - Approaches vary
 - Recommend microdose pathway
 - COWS score unreliable in this population



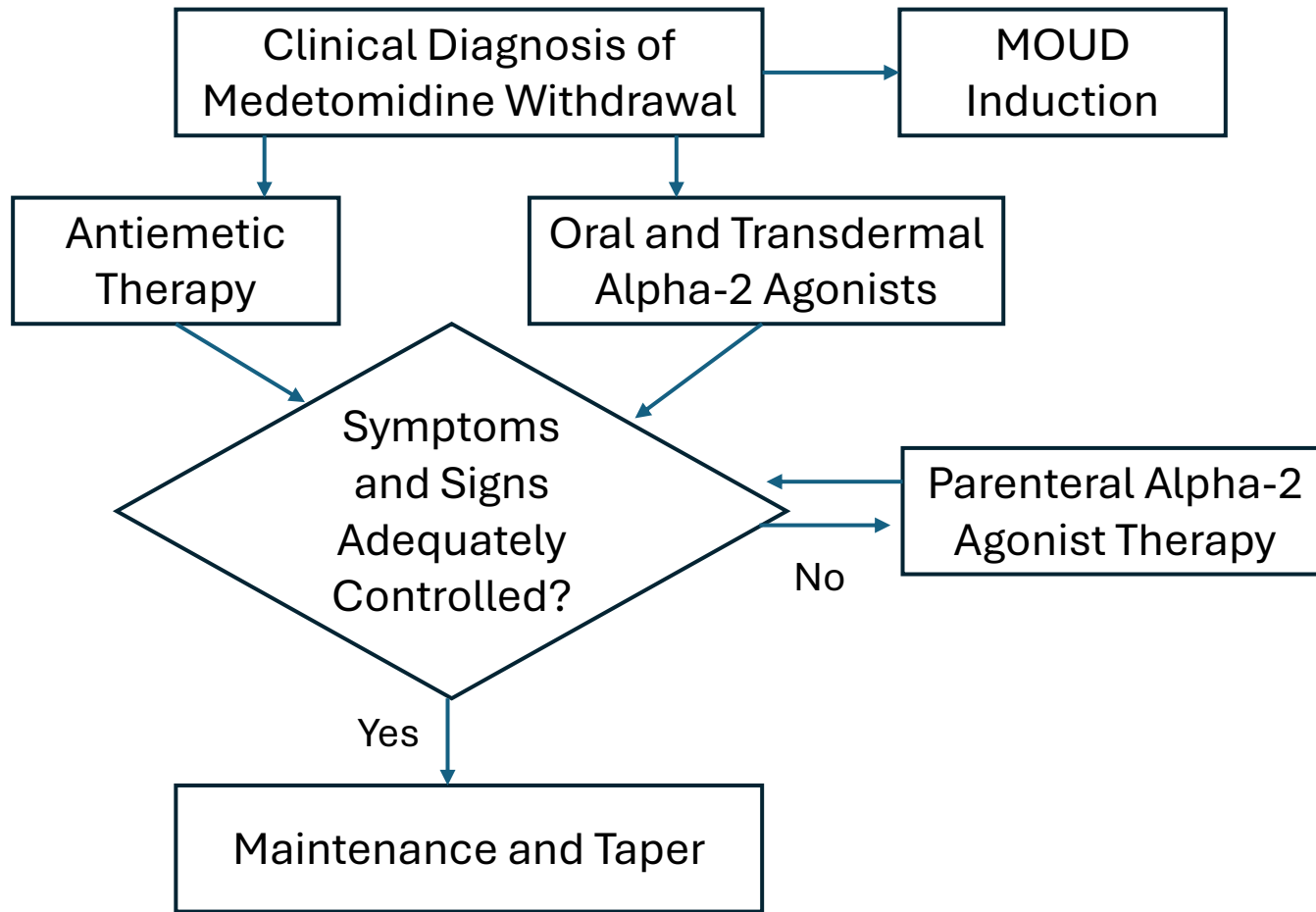
1. O'Rourke 2022
2. <https://www.npr.org/sections/health-shots/2018/10/05/653360644/addiction-treatment-gap-is-driving-a-black-market-for-suboxone>. Accessed 5/6/2025

Medetomidine Withdrawal-Management

- Supportive
 - IV fluids and electrolyte replacement
 - Antiemetics
 - Ondansetron seems minimally effective
 - Dopamine antagonists seem more effective
 - Droperidol, prochlorperazine, olanzapine
 - Timethobenzamide and transdermal scopolamine can be considered
 - Antihypertensive adjuncts
 - Co-occurring syndromes or extreme agitation
 - Benzodiazepines +/- barbiturates for suspected GABA agonist withdrawal
 - Ketamine



UPMC Medetomidine Withdrawal Treatment Guideline



Medetomidine withdrawal:

- Onset within hours of last illicit substance use
- Nausea and vomiting
- Tremor, myoclonic jerks, anxiety, diaphoresis
- Tachycardia and hypertension
- Encephalopathy
- Minimal or no response to GABA and opioid agonists

Antiemetic therapy:

- Ondansetron rarely effective
- Prochlorperazine 10mg IV/IM/PO, repeat as needed
- Droperidol 2.5-5mg IV/IM, repeat as needed
- Olanzapine 5-10mg IV/IM, repeat as needed

Oral and Transdermal Alpha-2 Agonists

- Clonidine 0.3mg PO; repeat up to 2 additional doses in hour 1 as loading dose (total of 0.9mg)
- Transdermal clonidine 0.3mg weekly
- Guanfacine 2mg PO q8 hours
- Clonidine 0.2-0.3mg PO q2 hours for COWS of >5 or >15, respectively
- Tizanidine 2mg PO q8 hours can be considered
- Benzodiazepines/barbiturates for additional sedation if needed

Parenteral Alpha-2 Agonist Therapy:

- Dexmedetomidine
 - 1 mcg/kg IV bolus
 - 0.5-1.5 mcg/kg/hr IV infusion titrated to Riker 3-4 or RASS -1-0 (or sedation if scores not recorded)
 - For severe cases: ↑ up to 2.4 mcg/kg/hr
- IV Dexmedetomidine can typically be weaned with overlapping oral regimen over 24-72 hours
- Benzodiazepines/barbiturates or ketamine for agitation uncontrolled with dexmedetomidine if needed

Maintenance and Taper:

- PO regimen can typically be weaned after 3-5 days:
 - As PRN clonidine needs resolve, wean guanfacine to 2mg PO BID x 1 day, then 1mg PO TID x 1 day, then 1mg PO BID x 1 day, and 1mg PO once x 1 day and remove clonidine patch
- Other symptom-triggered medications as needed

Impact

- Severity may preclude admission to residential facility or outpatient management
 - Increased ED and inpatient utilization for opioid withdrawal management
 - ICU capacity
- No established predictive tools
 - High index of suspicion
 - Diagnosis is clinical
- Extended observation in ED
- Careful monitoring as symptoms progress rapidly
- Early, aggressive treatment



Emergency Department and Hospital Utilization

- Evaluation of UPMC Mercy ED visits and dispositions for patients with opioid use disorder/withdrawal
- 2023 (no medetomidine) vs. 2025
- Limited by Primary Diagnosis
- Clear increases in:
 - Overall volume
 - Percent requiring hospitalization
 - Percent admitted to ICU

Emergency Department Primary Diagnosis of Opioid Withdrawal

	ED Visits	Admissions (%)	ICU Admissions (% of Admitted Patients)
2023	85	9 (10.6)	0
2025	214	73 (34.1)	29 (39.2)
Percent Difference	↑ 151.8%	↑ 221.7%	↑ ∞

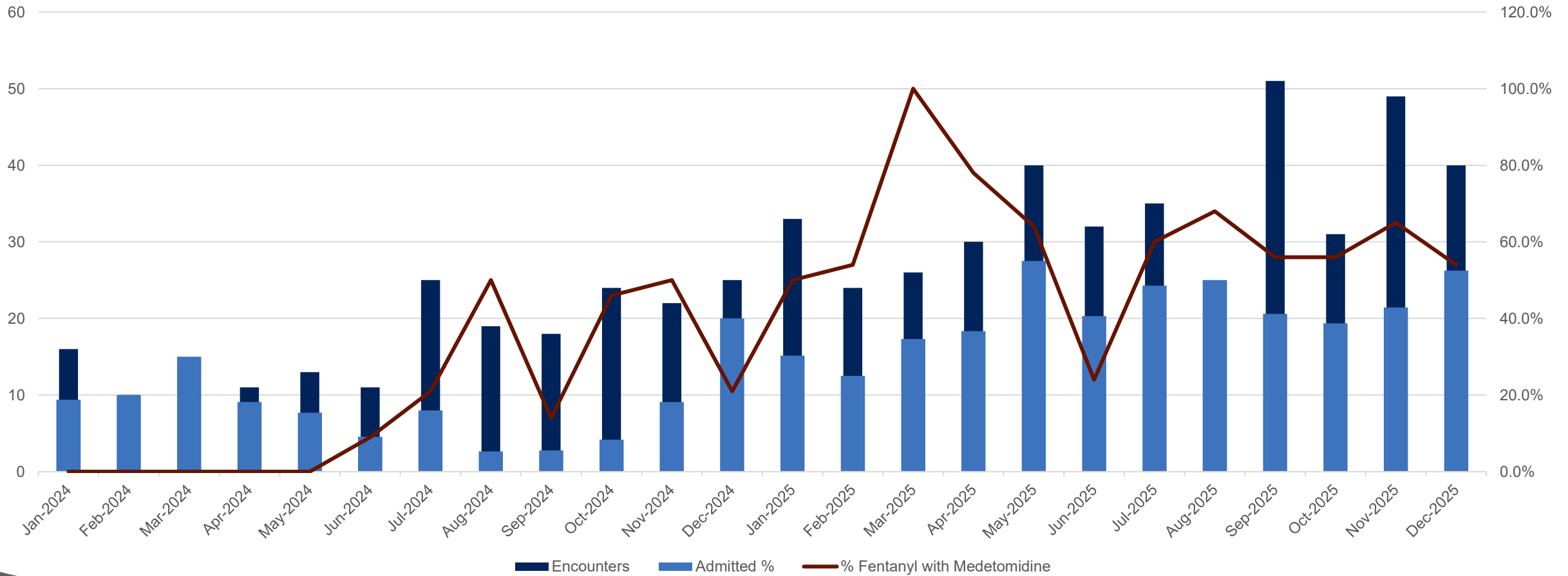
Emergency Department Primary Diagnosis of Untreated Opioid Use Disorder or Opioid Withdrawal

	ED Visits	Admissions (%)	ICU Admissions (% of Admitted Patients)
2023	412	47 (11.4)	3 (6.4)
2025	747	196 (26.2)	52 (26.5)
Percent Difference	↑ 81.3%	↑ 129.8%	↑ 314.1%

Threshold Response Hypothesis

Differing threshold prevalences are likely needed to observe acute toxicity and severe withdrawal

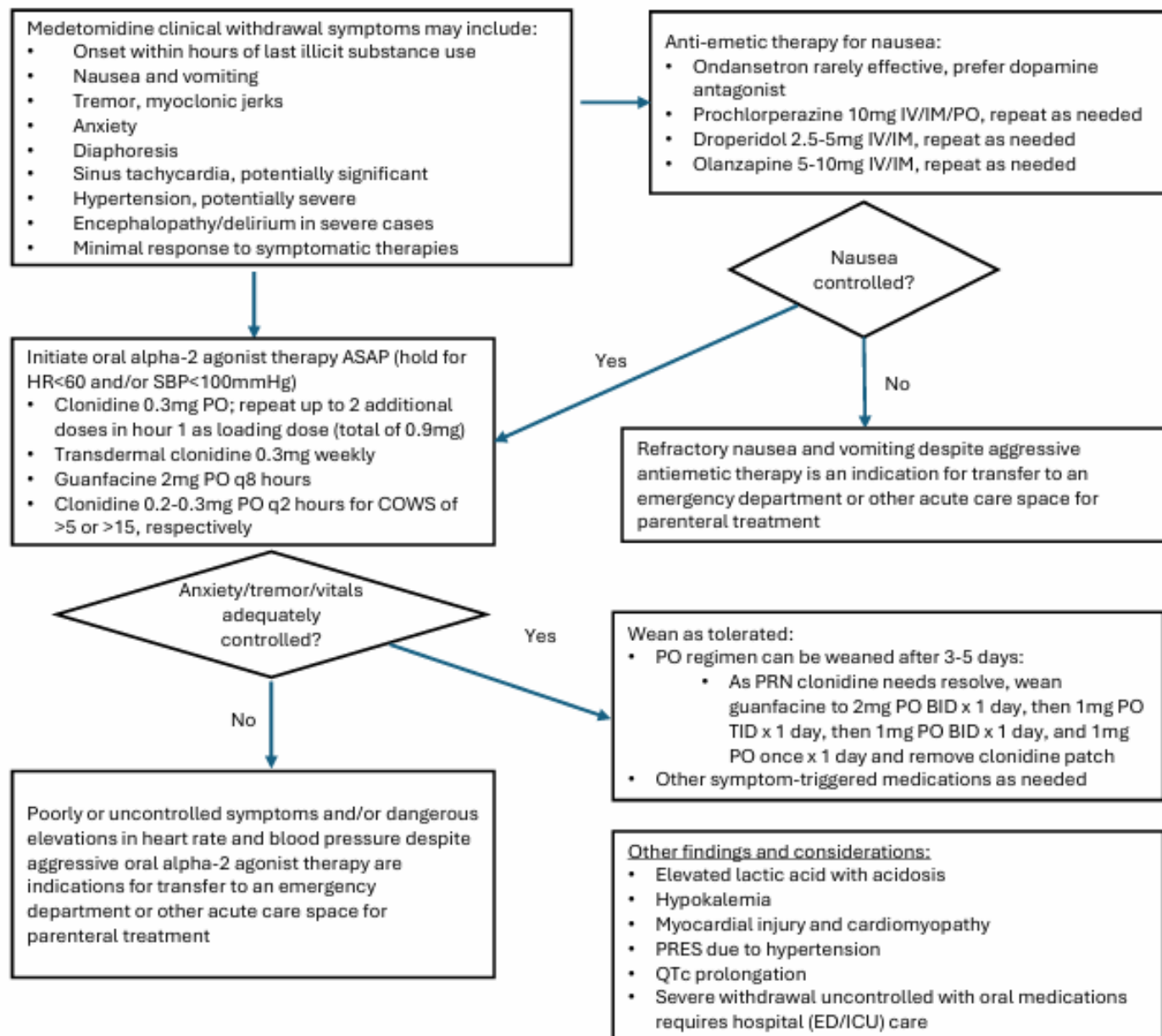
UPMC Allegheny County ED Encounters for Opioid Withdrawal



Suggested Approach To Assessment

- **Understand local drug supply**
 - Is medetomidine present in >10-20% of the supply?
- **Potential predictors of severe withdrawal**
 - History of complicated opioid withdrawal requiring ICU care/dexmedetomidine
 - Repeated toxicity with prolonged sedation/bradycardia
 - Drug checking confirming medetomidine exposure
 - Persistent bradycardia after opioid use
- **Early management (outside hospital)**
 - Aggressive PO α -2 agonists and antiemetics
 - Close monitoring and/or guidance for signs and symptoms of progressive withdrawal
- **Refer to ED if...**
 - Refractory nausea/vomiting
 - Progressive tachycardia, hypertension, or change in mental status

UPMC Medical Toxicology Outpatient Medetomidine Withdrawal Treatment Guideline



Future Considerations

1. Is there a role for long-acting alpha-2 agonists or antagonists after completion of withdrawal?
2. Is there a separate alpha-2 agonist addiction or are the effects a complication of underlying opioid use disorder alone?
3. Are there alternative therapies that could improve withdrawal treatment including avoiding hospitalization or ICU need?
 - a) IN/SL dexmedetomidine?
 - b) IV clonidine
4. What will be the next impactful high potency opioids and/or adulterants?

Summary

- The drug supply, both primary drug and adulterants, continue to evolve
- Rapid identification of emerging substances can drive clinical response
- Potent adulterants can cause new/different toxicity and withdrawal syndromes
- The substance use treatment system has needed to rapidly adapt to changes in clinical care associated with drug evolution
- Primary prevention, harm reduction, and easy access to SUD treatment is critical

Thank you!

The End