DDAP TECHNICAL ASSISTANCE WEBINAR

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- Registered attendees will join with their cameras and mics off.
- You can engage with the presenter using **chat, reactions**, or **Q&A** features.
- Organizers choose when to let attendees turn on their cameras or unmute.
- All slides and recordings will be shared post webinar.
- Any unanswered questions will be followed up.

Pennsylvania
Department of Drug and Alcohol Programs

MAY 11, 2026

Emerging Drug Trends: Medetomidine and Clinical Considerations for Treatment Providers

DDAP TECHNICAL ASSISTANCE WEBINAR

Welcome & Opening Remarks

DR. LATIKA DAVIS-JONES, PHD, MPH, MSW

Secretary, Pennsylvania Department of Drug and Alcohol Programs

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Disclaimer to Learners

The contents of this presentation reflect the views of the presenter, and they do not necessarily reflect the official views or policies of the Department of Drug and Alcohol Programs or the Commonwealth of Pennsylvania.

Learning Objectives

By the end of this session, participants will be able to:

- Recognize key clinical effects and withdrawal symptoms associated with medetomidine exposure
- Identify risks and management considerations for patients presenting with medetomidine withdrawal
- Apply current guidance to support safe and appropriate responses within treatment settings
- Identify when escalation of care and coordination with hospital-based providers is needed

Clinical Overview & Treatment Considerations

DR. MICHAEL LYNCH, MD, FACEP, FACMT

UPMC LIFE CHANGING MEDICINE

Emerging Drug Trends: Medetomidine and Clinical Considerations for Treatment Providers

Michael Lynch, MD FACEP FACMT
UPMC Health Plan Quality and Substance Use Disorder Services Senior Medical Director
Director, UPMC Medical Toxicology Telemedicine Bridge Clinic
Associate Professor
Division of Medical Toxicology, Department of Emergency Medicine
University of Pittsburgh School of Medicine

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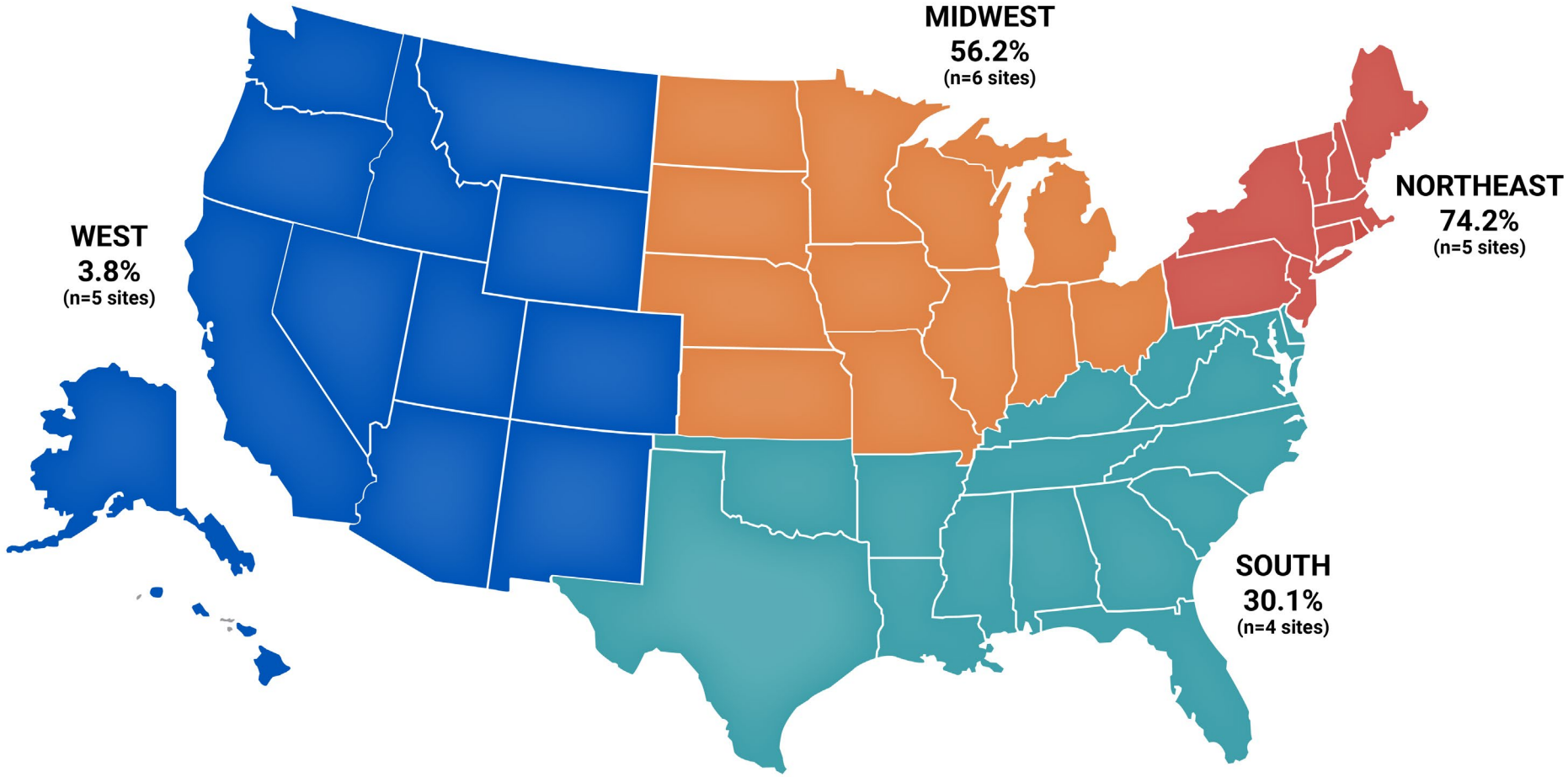
Medetomidine Detection-2025



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

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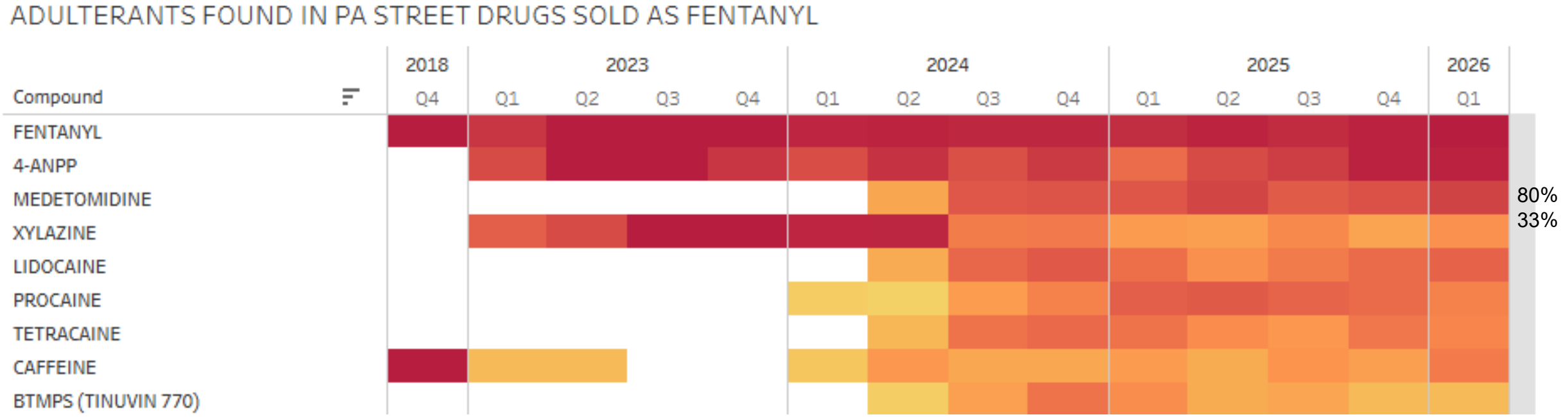
PA Drug-Checking Data

PA Groundhogs Adulterant Report



DATA | PAGroundhogs Accessed 4/15/26

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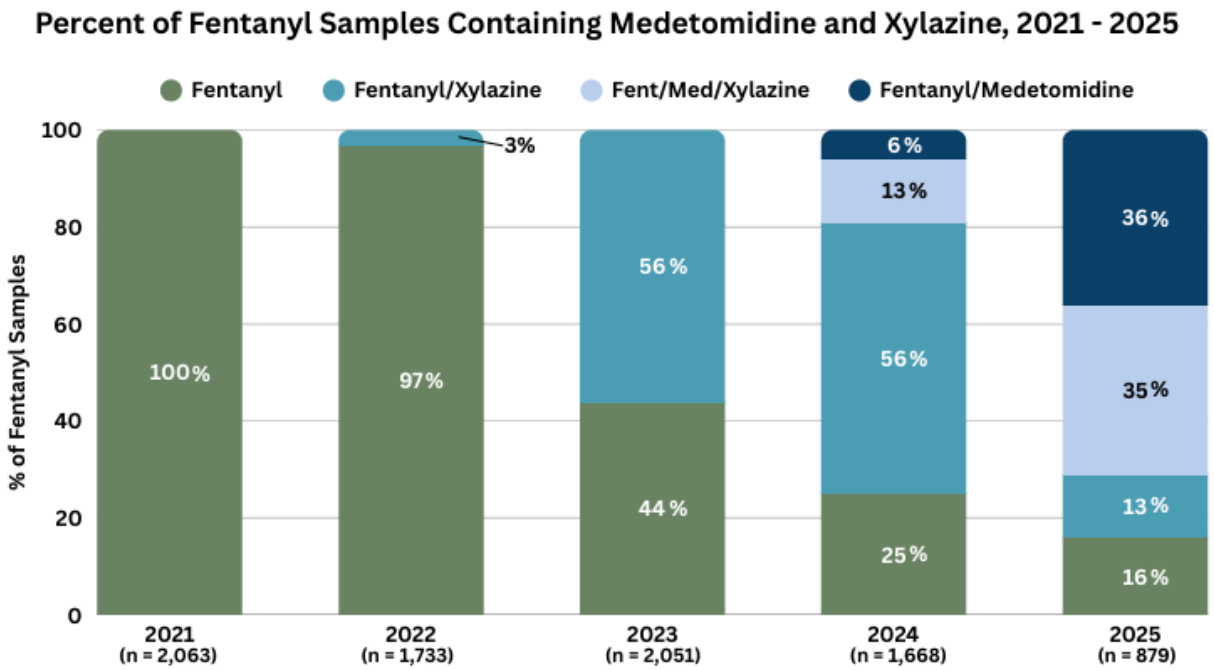
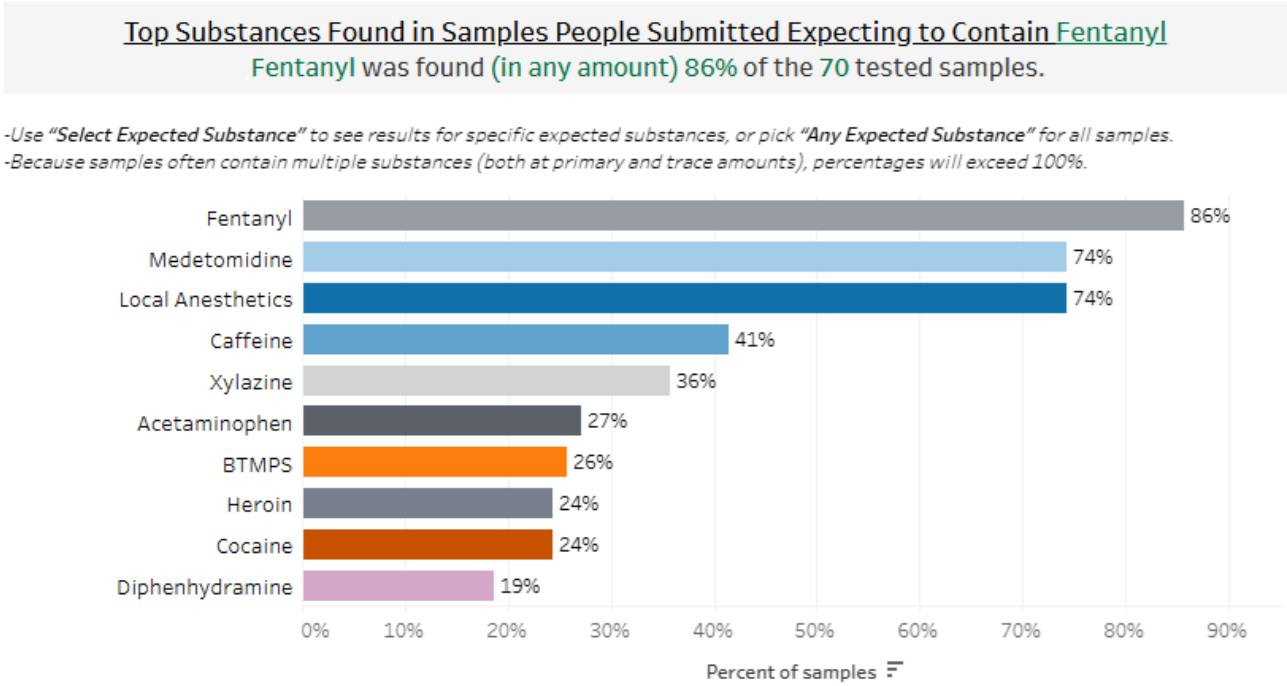
Allegheny County Adulterants



1/1/26-4/15/26



1. medetomidine brief Accessed 3/20/2026
2. Workbook: Substance Monitoring Dashboard Accessed 4/15/2026

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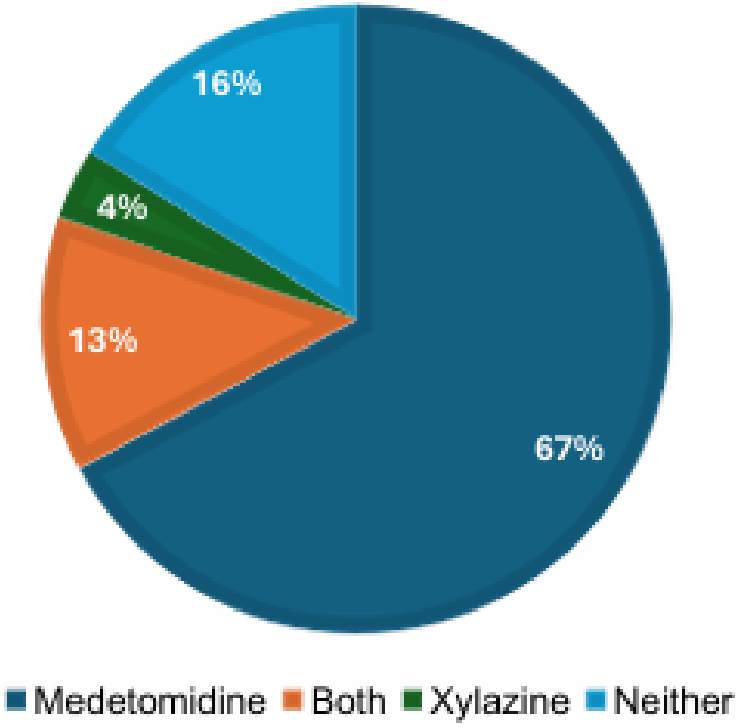
Philadelphia County Drug Checking Data

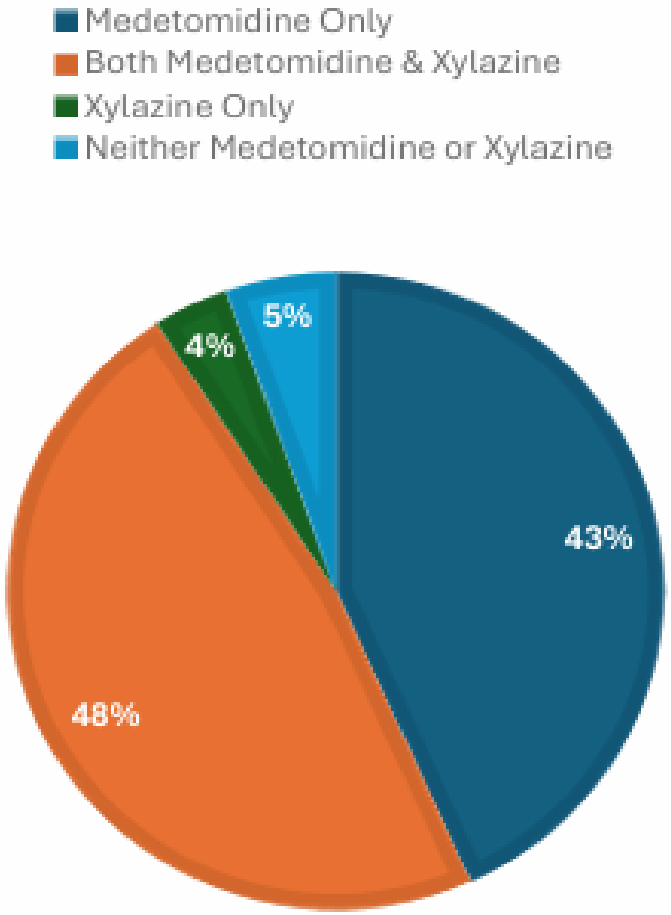
1/2025-6/2025

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



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

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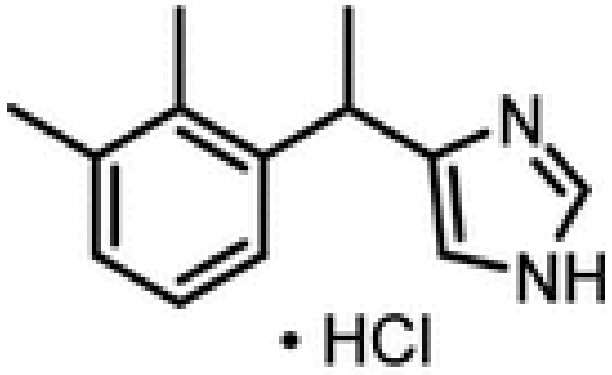
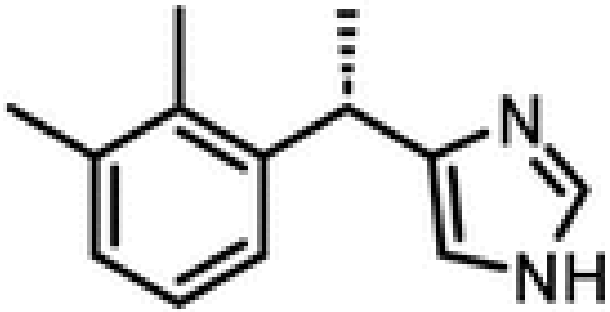
Medetomidine

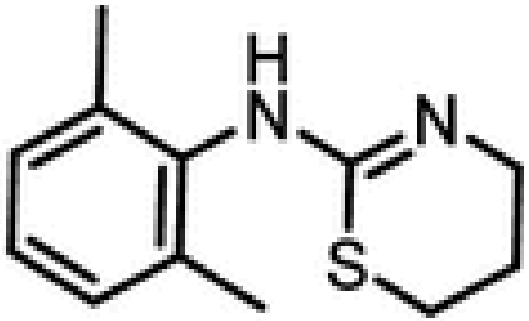
- Medetomidine is a racemic mixture of levo- and dexmedetomidine
- FDA-approved veterinary anesthetic
- Shares structural elements with other alpha-2 agonists



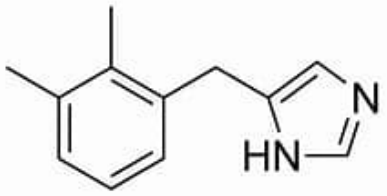
Medetomidine, **1**



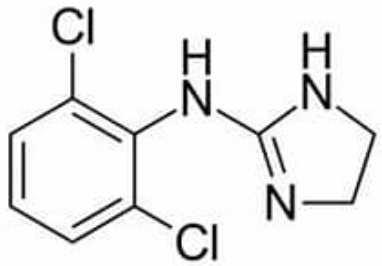
Dexmedetomidine, **2**



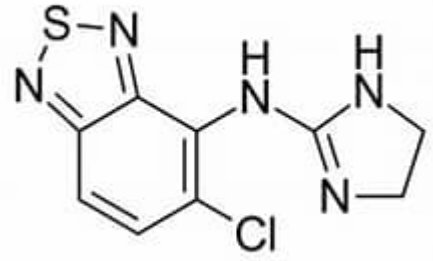
Xylazine, **3**



detomidine



clonidine

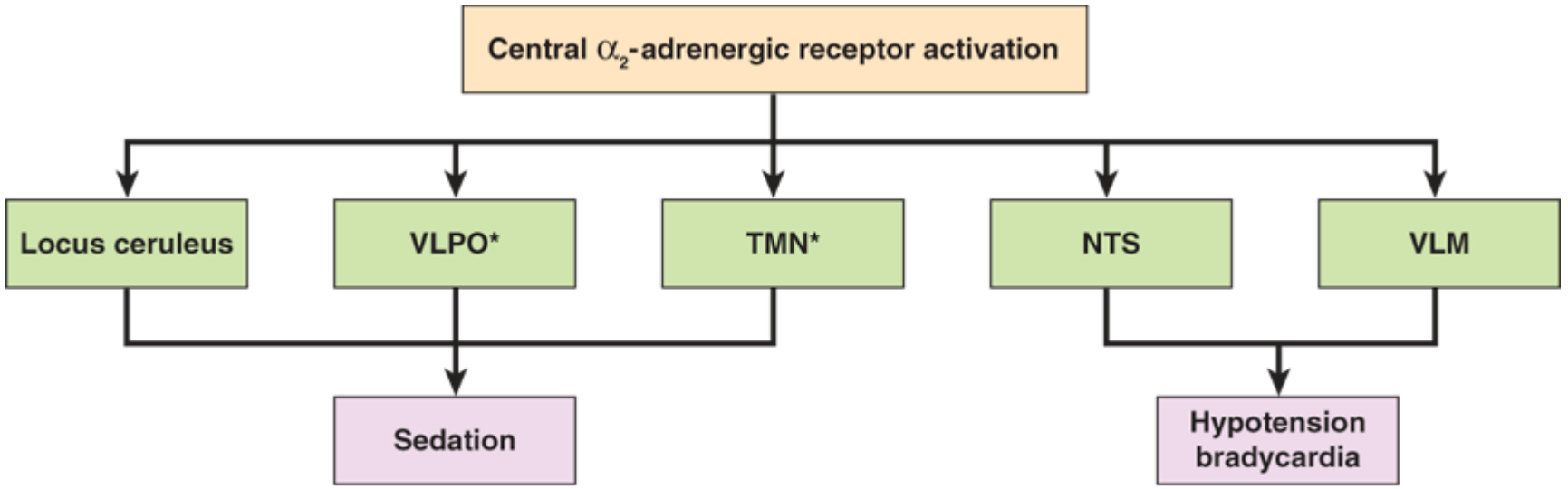


tizanidine

de Andrade 2024

Mechanism

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

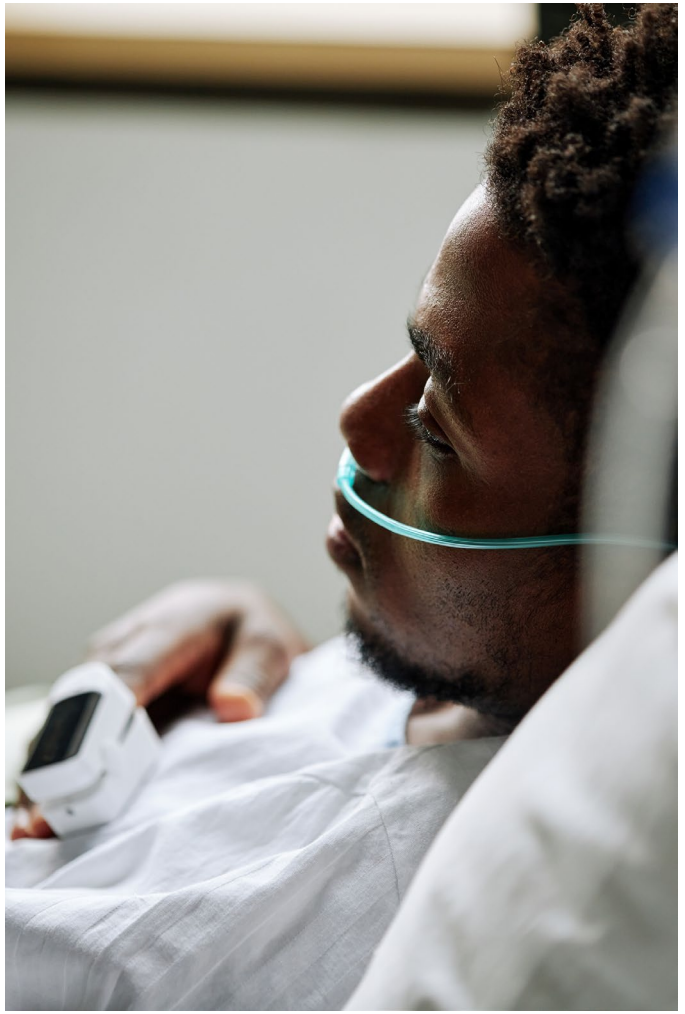


Source: L.S. Nelson, M.A. Howland, N.A. Lewin, S.W. Smith, L.R. Goldfrank, R.S. Hoffman: Goldfrank's Toxicologic Emergencies, Eleventh Edition

de Andrade 2024

Acute Toxicity

- Typically seen 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

1. Nayani 2025
2. Nham 2024

Testing

- 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

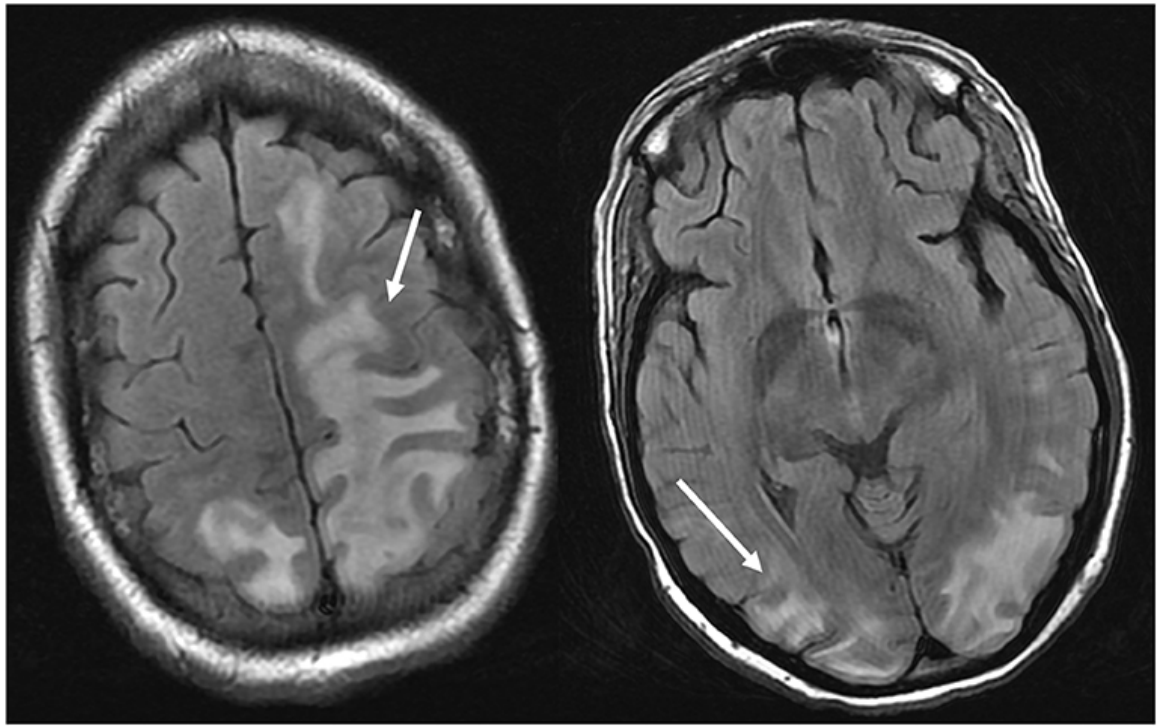
Medetomidine Withdrawal-Clinical

- 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

1. Huo 2025
2. Ostrowski 2025
3. London 2026

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

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Medetomidine Withdrawal-Management

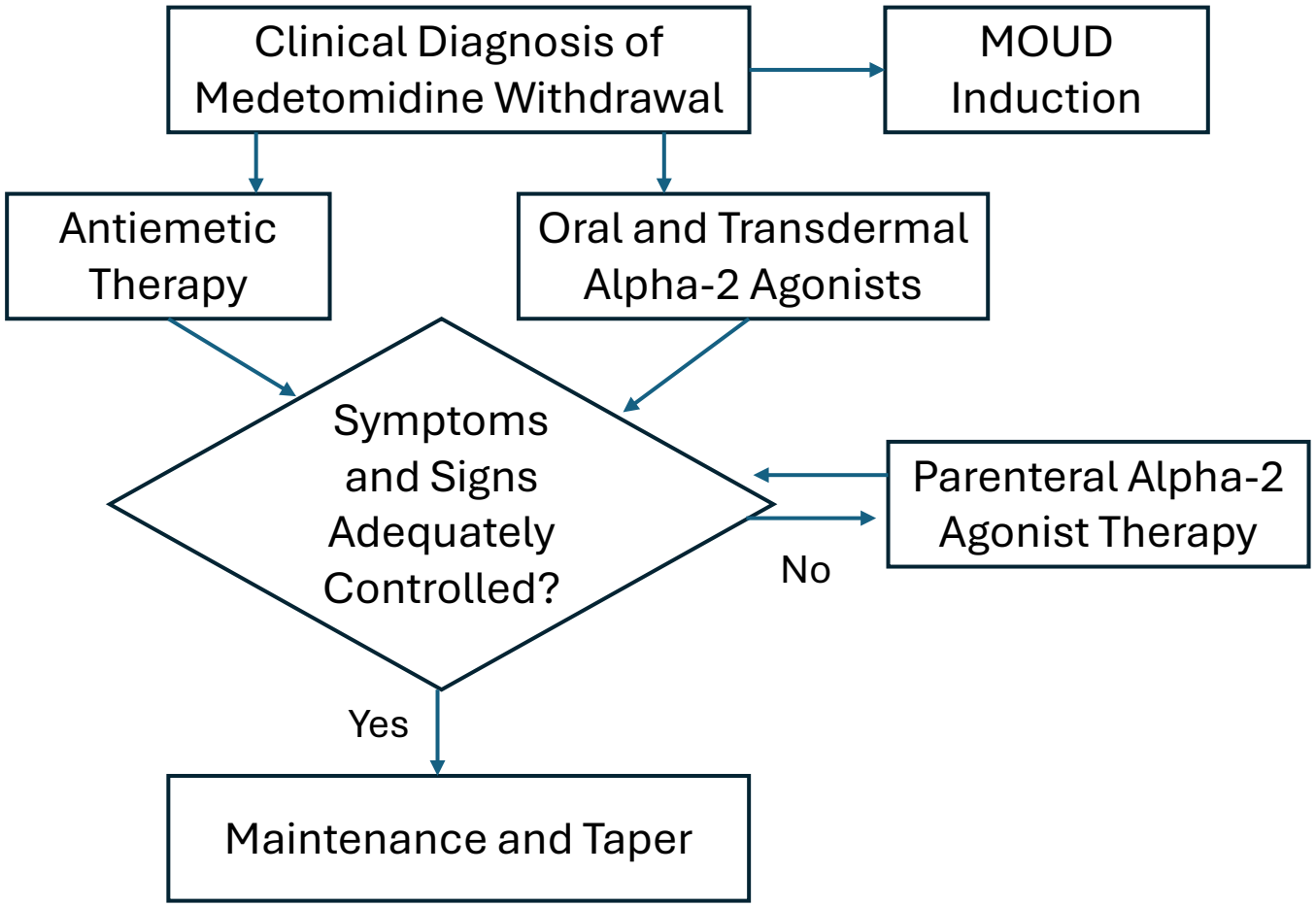
- **Opioid withdrawal and MOUD Initiation (pathways vary)**
  - Overlapping symptoms
  - Methadone induction
    - Methadone IV or PO if tolerated
      - Monitor QTc
  - Buprenorphine Induction
    - Approaches vary
    - Recommend microdose pathway
    - COWS score unreliable in this population

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
- Benzodiazepiness/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

Lynch MJ, Pizon AF, Yealy DM. Emergence of Medetomidine in the Illicit Drug Supply: Implications for Emergency Care and Withdrawal Management. Ann Emerg Med. 2026 Jan 22:S0196-0644(25)01434-9. doi: 10.1016/j.annemergmed.2025.12.004. Epub ahead of print. PMID: 41575403.

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

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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%	↑ ∞

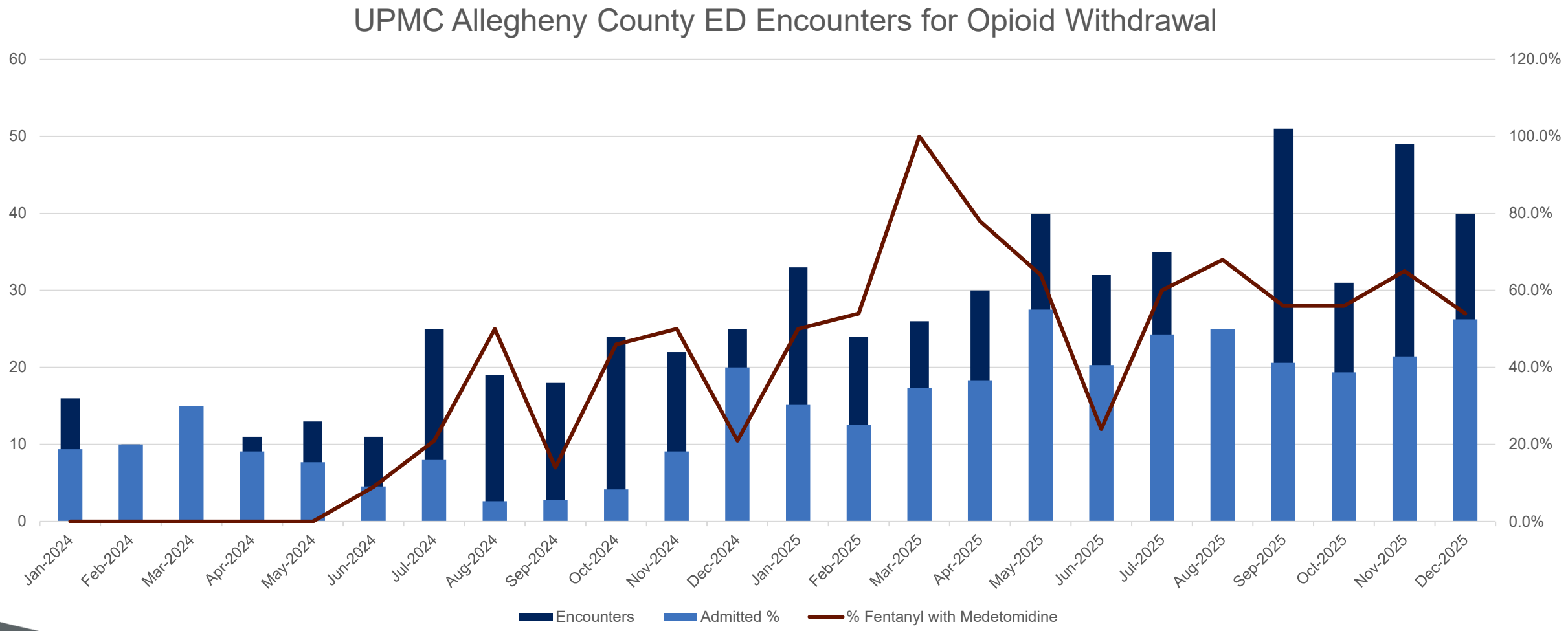
Emergency Department Primary Diagnosis of Untreated Opioid Use Disorder or Opioid Withdrawal

	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%

Lynch MJ et al. Increased Healthcare Utilization and Acuity Associated with Medetomidine. Poster Presentation. 57th Annual American Society of Addiction Medicine Annual Meeting. 4/2026.

Threshold Response Hypothesis

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



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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

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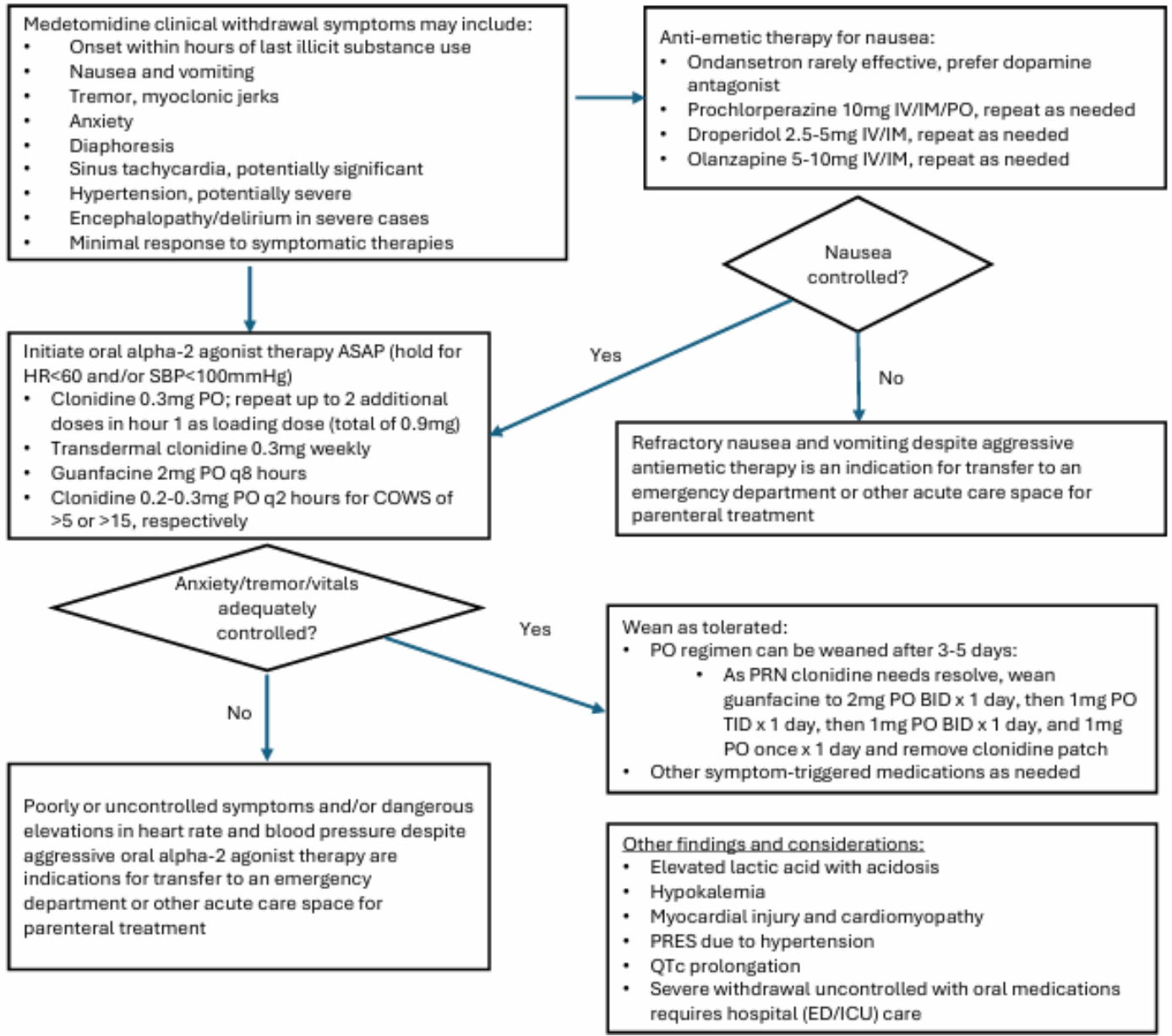
UPMC Medical Toxicology Outpatient Medetomidine Withdrawal Treatment Guideline



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, continues 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!

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Q&A

Closing Remarks

Thank you!

- The recording and presentation slides will be available in the Technical Assistance Webinar library on the DDAP website within the next few weeks.
- Responses to all questions will be compiled into a Q&A document and posted in the Webinar Library alongside the slides and recording.
- **Have additional questions?** Submit them using the Inquiry Form.

Next Technical Assistance Webinar

Monday, July 6, 2026 at 10:00 AM

Fireside Chat with Behavioral Health Managed Care Organizations (BH-MCO)

Medetomidine Trainings

- UPenn's An Emerging Adulterant in Philadelphia: Medetomidine Withdrawal in People Who Use Fentanyl webinar on 4/23/2025
- Department of Health's Medetomidine - Addressing Health Care Concerns & Identifying Best Practices webinar on 3/10/2026. The recording will be posted on Train PA.
- CDC Webinar: Clinical Implications of Medetomidine Mixed with Opioids
- IRETA's Medetomidine: An Emerging Adulterant Reshaping Toxicity and Withdrawal Management webinar on 4/15/2026. The recording and webinar slides will also be available in the webinar library on the IRETA website soon.
- **Upcoming Training:** ASAM Training on Tuesday, June 23: Managing Opioid Withdrawal in the Era of Medetomidine

Medetomidine Clinical Resources

- CDC Health Alert: Medetomidine in the U.S. Illegal Fentanyl Supply Increasing Risk for Overdose and Severe Withdrawal Syndrome
- PA DOH: Clinical Resources for Emerging Adulterants
- ASAM Fact Sheet for Clinicians: Medetomidine: Rising Adulterant in the Illicit Drug Supply
- Penn Medicine: Clinical Recommendations for Managing Medetomidine Withdrawal
- Philadelphia Health Update: Responding to overdose and withdrawal involving medetomidine
- Philadelphia Department of Public Health: Medetomidine Resource Page

Risk Reduction Resources

- DDAP: Overdose Prevention Program
- DOH: Naloxone Resources
- PDA: Naloxone Copay Assistance Program
- Prevention Point Pittsburgh & NEXT Distro: Mail-To-Home Program
- PA Harm Reduction Network: Resources
- PA Groundhogs: Drug Checking Program