

## Health Alert

### Hospitals and behavioral health providers are reporting severe and worsening presentations of withdrawal among people who use drugs (PWUD) in Philadelphia

12/10/2024

#### SUMMARY POINTS

- Symptoms of worsening and severe withdrawal include: intractable vomiting, excessive diaphoresis, hypertensive emergency, waxing and waning hypoactive encephalopathy, tremor, and tachycardia.
- Worsening and severe presentations of withdrawal are likely due to changes in illicit fentanyl, and the increasing prevalence of medetomidine in illicit fentanyl.
- Although opioid withdrawal is often safely managed in outpatient, residential, and non-hospital treatment settings, adulterants such as medetomidine may necessitate higher levels of care for intoxication and withdrawal management. The treatment strategies listed here may require hospital or ICU level monitoring and support.
- Treatment strategies include aggressive management of opioid withdrawal with methadone and hydromorphone, and alpha-2-agonist withdrawal with clonidine.
- PWUD with these symptoms may be at risk of aspiration, and non-oral treatment modalities can be used to reduce risk of aspiration.

Drug-related morbidity and mortality remains high in Philadelphia, where more than 1,400 individuals died from unintentional overdoses in 2022 and thousands more experienced non-fatal overdoses and adverse drug side effects. Complicating the clinical care of people who use drugs (PWUD) is the constantly changing illicit drug supply.

In November, the Philadelphia Department of Public Health received reports from hospital and behavioral health providers of PWUD presenting with atypical and severe withdrawal symptoms requiring intensive care unit (ICU) level of care. In addition, the onset of symptoms has been described as a rapid transition from intoxication to withdrawal, which have complicated triage of PWUD to the appropriate level of care.

Below is a summary of the observed changes in withdrawal symptoms, emerging strategies and recommendations for treatment.

#### Reported symptoms include:

- Intractable vomiting
- Excessive Diaphoresis
- Hypertensive emergency
  - Hypertension has been described as persistent despite aggressive treatment and rebound hypertension has been observed when attempting to wean anti-hypertensives within 48 hours of presentation.
- Waxing and waning hypoactive encephalopathy
  - Hypoactive encephalopathy has been described as somnolence or stupor and has been incorrectly interpreted as uncooperative behavior.
  - Hypoactive encephalopathy may be associated with posterior reversible encephalopathy syndrome (PRES) in the setting of hypertensive emergency.
- Tremor
  - The tremor observed among patients with more severe presentations of withdrawal has been described as teeth chattering, facial twitching, body shaking, and rigor.

- Tachycardia
  - o Has been described as occurring with quick onset after initial presentation with bradycardia.

### Emerging treatment strategies

- Initial treatment:
  - o Prioritize early initiation of aggressive management of opioid withdrawal starting with an initial methadone 40mg dose and then up to an additional 20mg on day 1 (60mg max; either as an additional 20mg dose or 10mg q4h x2) and standing 2-3mg IV hydromorphone pushes every 2 hours.
    - For patients who cannot take oral medications, IV methadone formulations are being used in ICU settings.
  - o Early initiation of alpha-2-agonist therapy with maximum tolerated doses of clonidine.
    - Apply 3 x 0.3mg clonidine patches and initiate oral clonidine with hold parameters for hypotension or bradycardia.
    - Tizanidine or guanfacine can be used as an alternative to clonidine.
  - o Escalation to dexmedetomidine titrated to a maximum of 1.5 mcg/kg/hr for persistent hypertension and alpha-2-agonist withdrawal. Especially in patients unable to tolerate PO medications due to vomiting and/or altered mental status.
    - Dexmedetomidine is often only available in the intensive care unit, but intermediate units piloting dexmedetomidine to a maximum of 0.7 mcg/kg/hr have expanded access to the medication on inpatient floors.
  - o Early screening for alcohol and benzodiazepine use and withdrawal. Maintain a high index of suspicion for concurrent alcohol and benzodiazepine withdrawal.
- Additional treatment:
  - o Ketamine to treat co-occurring pain.
    - Hospitals offering oral Ketamine formulations have been able to expand access to the medication on inpatient floors.
    - Hospitals developing protocols for administering ketamine without consulting anesthesia have been able to expand access to the medication on inpatient floors.

### Recommendations

- In the outpatient setting, there should be a low threshold to refer patients who are experiencing withdrawal to a higher level of care if they are exhibiting waxing and waning altered mental status, severe hypertension, intractable vomiting, rapid changes in heart rate, or tremor beyond what is expected in opioid withdrawal.
- The Clinical Opioid Withdrawal Scale may not accurately measure the severity of withdrawal symptoms due to difficulty assessing all symptoms among patients with waxing and waning hypoactive encephalopathy.
- Adding sedating agents, such as benzodiazepines, early in treatment may complicate clinical assessment for improvement in hypoactive encephalopathy and should be avoided unless concomitant benzodiazepine or alcohol withdrawal is suspected.
- Clinical indicators of treatment success may include vital sign normalization and improved mental status.
- Given patients are presenting with hypoactive encephalopathy, there is a potential risk of aspiration by administering oral medications and limited benefit of utilizing patient-controlled analgesia. Treatment strategies using medications that can be administered via non-oral routes can avoid risk of aspiration.
- PWUD who present in severe withdrawal may have co-occurring critical diagnoses that may be missed by attributing all symptoms to withdrawal. Clinicians should keep a high index of suspicion for other critical diagnoses, such as infection and exacerbation of co-morbid chronic illness.

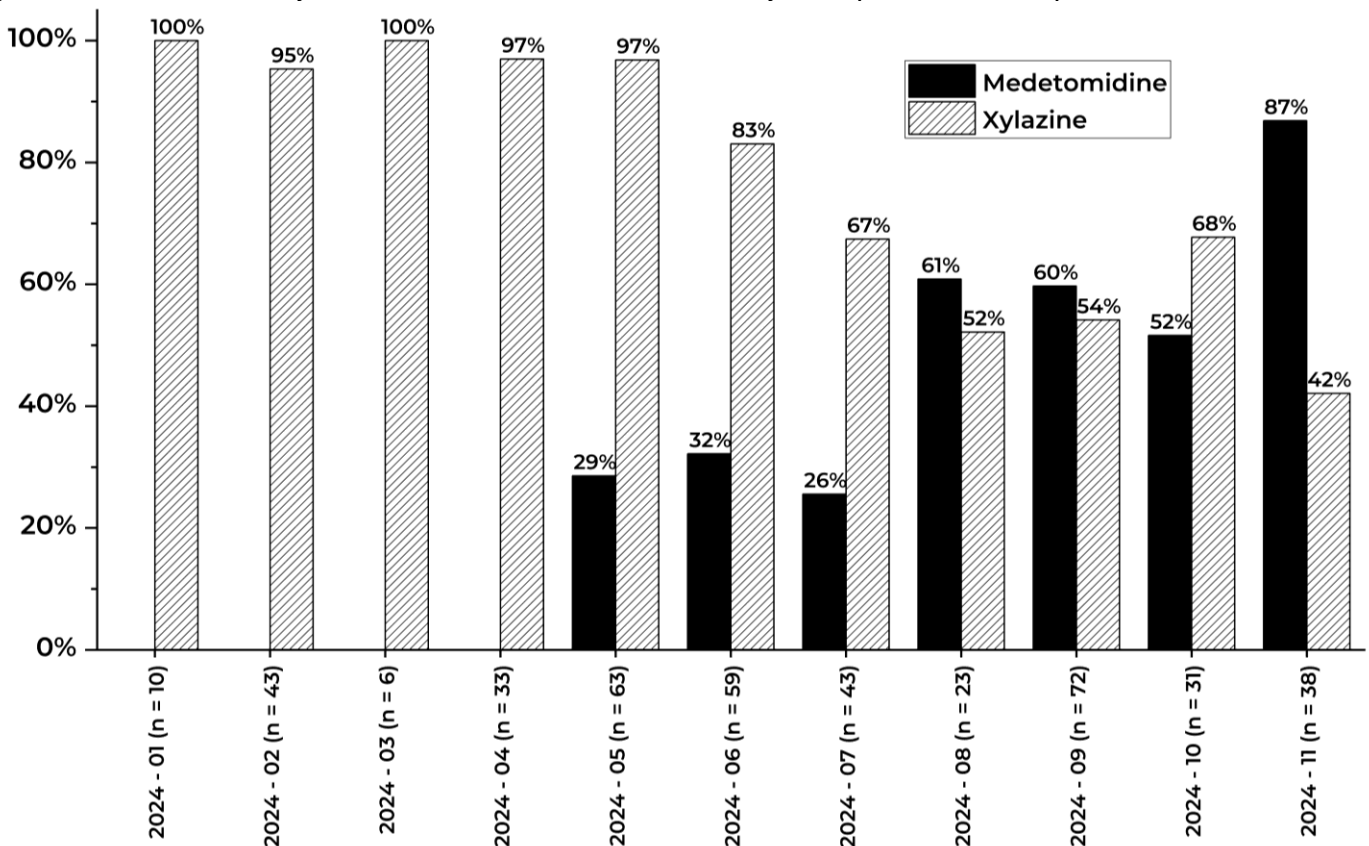
- Given the severity of withdrawal symptoms are increasingly requiring ICU level of care, hospitals and health systems may consider strategies to expand access to medications such as ketamine and dexmedetomidine at lower levels of inpatient care.

**Changes in adulterants in illicit fentanyl**

Worsening and more severe presentations of withdrawal among PWUD are likely due to changes in Philadelphia’s illicit fentanyl supply. In May 2024, [Medetomidine](#) was first detected in Philadelphia’s illicit drug supply, and has now surpassed xylazine as the most common veterinary alpha-2-agonist adulterant in illicit fentanyl samples. (see Figure 1) Medetomidine is a more potent sedative than xylazine. Medetomidine is also similar to dexmedetomidine. Withdrawal syndromes from abrupt discontinuation of dexmedetomidine in the hospital setting have been described in the literature and mirror the worsening and severe presentations of withdrawal among PWUD in Philadelphia.<sup>1,2</sup> However, there is currently no established association between reports of more severe presentations of withdrawal with medetomidine use.

The Philadelphia Medical Examiner’s Office (MEO) initiated toxicology testing for medetomidine on May 18, 2024. Since then, medetomidine has been detected in 46 overdose decedents. All decedents who had toxicology testing positive for medetomidine were also positive for fentanyl. Of all overdose deaths since May 18, 2024, with finalized toxicology testing by MEO, 13.5% had medetomidine detected and 18.25% of decedents with finalized toxicology that was positive for fentanyl during this period also had medetomidine detected.

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

## **Resources**

### **Substance Use Disorder Treatment**

- Behavioral Health Services Initiative (uninsured): 1-215-546-1200
- Community Behavioral Health (Medicaid): 1-888-545-2600
- CareConnect Warmline: 484-278-1679
- DBHIDS Medication Assisted Treatment: <https://dbhids.org/services/addiction-services/mat/>
- SAMHSA National Helpline: 800-662-HELP (4357)

**Recommend patients try not to use alone.** If that is what they are doing, then provide resources:

- Never Use Alone: 877-696-1996
- The Brave App – free to download on app stores
- Canary App – free to download on app stores

**Learn how to get and use naloxone** – [www.substanceusephilly.com](http://www.substanceusephilly.com)

**Get naloxone & fentanyl test strips for free and confidentially** – <https://nextdistro.org/philly>

**Learn how to use fentanyl test strips:**

- <https://www.cdc.gov/stopoverdose/fentanyl/fentanyl-test-strips.html>
- <https://www.youtube.com/watch?v=GmhE6UOZ9YY>

**Take a wound care training** - <https://www.substanceusephilly.com/healthcare-providers>

## **References:**

1. Haenecour AS, Seto W, Urbain CM, Stephens D, Laussen PC, Balit CR. Prolonged Dexmedetomidine Infusion and Drug Withdrawal In Critically Ill Children. *J Pediatr Pharmacol Ther JPPT Off J PPAG*. 2017;22(6):453-460. doi:10.5863/1551-6776-22.6.453
2. Pathan S, Kaplan JB, Adamczyk K, Chiu SH, Shah CV. Evaluation of dexmedetomidine withdrawal in critically ill adults. *J Crit Care*. 2021;62:19-24. doi:10.1016/j.jcrc.2020.10.024