Lucas County Substance Use Response Coalition Meeting

Wednesday, May 7, 2025
1:30 P.M.
Lucas County EMS Training Center, 2127 Jefferson Ave, Toledo, OH 43604

Agenda:

Call to Order & Welcome- Tony Dible, Toledo-Lucas County Health Department

1. Announcements & Introductions
2. Roundtable Discussion Topics
    - Trends and Data Updates on Populations You Serve.
        i. How are you addressing it?
    - Planning for August Coalition Meeting (Overdose Awareness Month).
        i. Interested in inviting local leaders (City Council, Mayor's Office, County Commissioners)
        ii. Develop an agenda for their attendance (what topics should be covered, what questions do we have for them, what do we want to showcase as a coalition, etc.)
    - Additional Topics (Time Permitting)
3. Organizational Updates

Next Coalition Meeting:
August 6, 2025, 1:30pm
Location: Lucas County EMS Training Center / Zoom

Lucas County Substance Use Response Coalition

For questions and other inquiries, please email opiateresponse@co.lucas.oh.us

Toledo-Lucas County Health Department
Stay informed. Stay healthy.
Public Health
Prevent. Promote. Protect.

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Lucas County EMS Training Center
1:30 p.m. Wednesday, May 7, 2025

Print Name	Signature	Organization	Email (Please print clearly!)	Check if 1st Time Attendee
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Angelia King				

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Print Name	Signature	Organization	Email (Please print clearly!)	Check if 1st Time Attendee
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Tasha Hollis		ProMedica	tasha.hollis@promedica.org	✓

SHAWN MCMAHON

Revised 8/2/19

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    - Trends and Data Updates on Populations You Serve.
        i. How are you addressing it?

- Xylazine is increasingly being mixed in local drug supply, being found co-mixed in most drugs sold it Toledo. Testing strips for Xylazine are available at TLCHD and NOSS. Mahj will be sharing Xylazine presentation from RX Summit.
- UMIDAP - Professionals working in SUD should be trained on mental health
- Mercy Mothers – A lot a cocaine use disorder recently
- Team Recovery – new detox just opened last week. Seeing a lot of cocaine and meth, some K2. Increasingly seeing Kratom.
- MHSRB – are agency's around addressing youth marijuana use? Lots of parents asking.
    - Sophia Quintera working in some TPS schools and Ohio Guidestone has a virtual group. Danielle at UTMC also looking into this topic.
- Unison – lots of cocaine use disorder. Seen a surge in clients in last couple months.
- Ohio Guidestone – number 1 issue is alcohol use disorder, with a significant amount of cocaine addiction as well.
- Harbor – noticing many youth using marijuana with prescription pills. Some people seeking benzos.
- Arrowhead – noticeable drop in fentanyl addiction, also seeing lots of cocaine and meth addiction currently.
- Northwest Ohio Hospital Council – Pathways – noticing some grants disappearing that focus on minority populations. Many caseworkers and health educators working directly with families.
- Sophia Quintera – provides resources and education to the Old South End in Hispanic communities. Seeing lots of alcohol use disorder.

- Opportunity Project – Toledo Legal Aid Society – works with people with mental health / SUD issues while within criminal justice system. Next pieces are education, housing and employment. Seeing clients reporting lots of cocaine, meth use, as well as buying street suboxone and misusing this.
- ProMedica Hospital – slight reduction of OD in their hospital, with most ODs from fentanyl or methadone.
- New Concepts – seeing more youth seeking services for various SUD
- TFRD – uptick in THC, gummy use, especially in pediatrics. Increasing mental health calls, sometimes hand in hand with drug use. While overall OD runs have been down in Q1 of 2025, April was a significantly elevated month.
    - 77% of AMA patients received a leave behind kit
- Talbot – also seeing people testing positive for suboxone that are not prescribed, seeing decrease in fentanyl use, increase in cocaine.

Notable Trends Discussed in Meeting Included:

- Noticeable drop in fentanyl positivity / use among providers
- Youth resources of high interest and a priority for partners
- TFRD April Fatality uptick notable
- New ORH standard – naloxone must be on the premises of Ohio Recovery Houses
- Dexmetotomodine a notable drug in the supply / one to monitor moving forward
- Uptick in reported benzo use among treatment providers

- **Planning for August Coalition Meeting (Overdose Awareness Month).**
    i. **Interested in inviting local leaders (City Council, Mayor's Office, County Commissioners)**
    ii. **Develop an agenda for their attendance (what topics should be covered, what questions do we have for them, what do we want to showcase as a coalition, etc.)**
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3. Organizational Updates

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D.A.R.T. 2025 STATISTICS

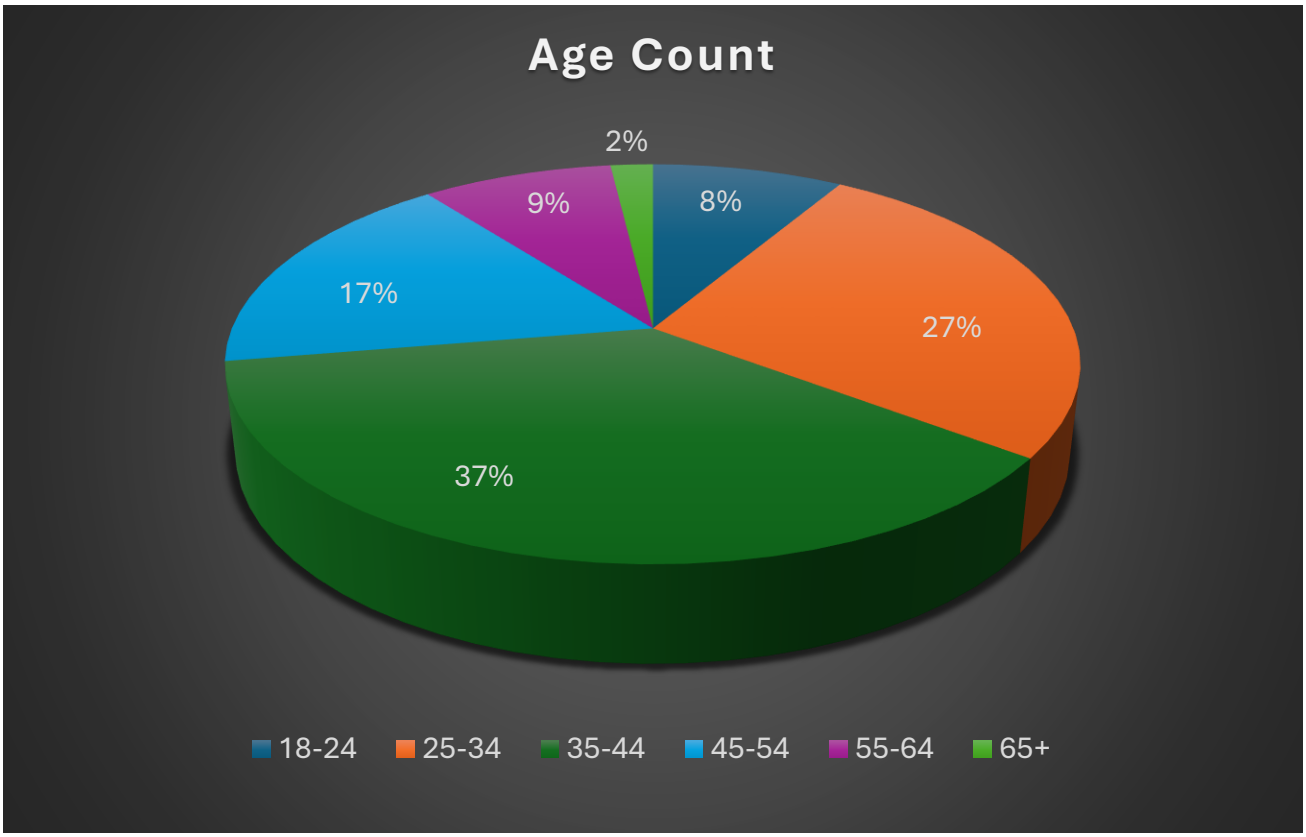
KEY:

A = New Clients B = OD's Created C = Interactions

D = Referrals to Tx E = Connections to Tx F = Notes

Year To Date Totals = 2025

A	B	C	D	E	F
92	27	556	26	71	1,071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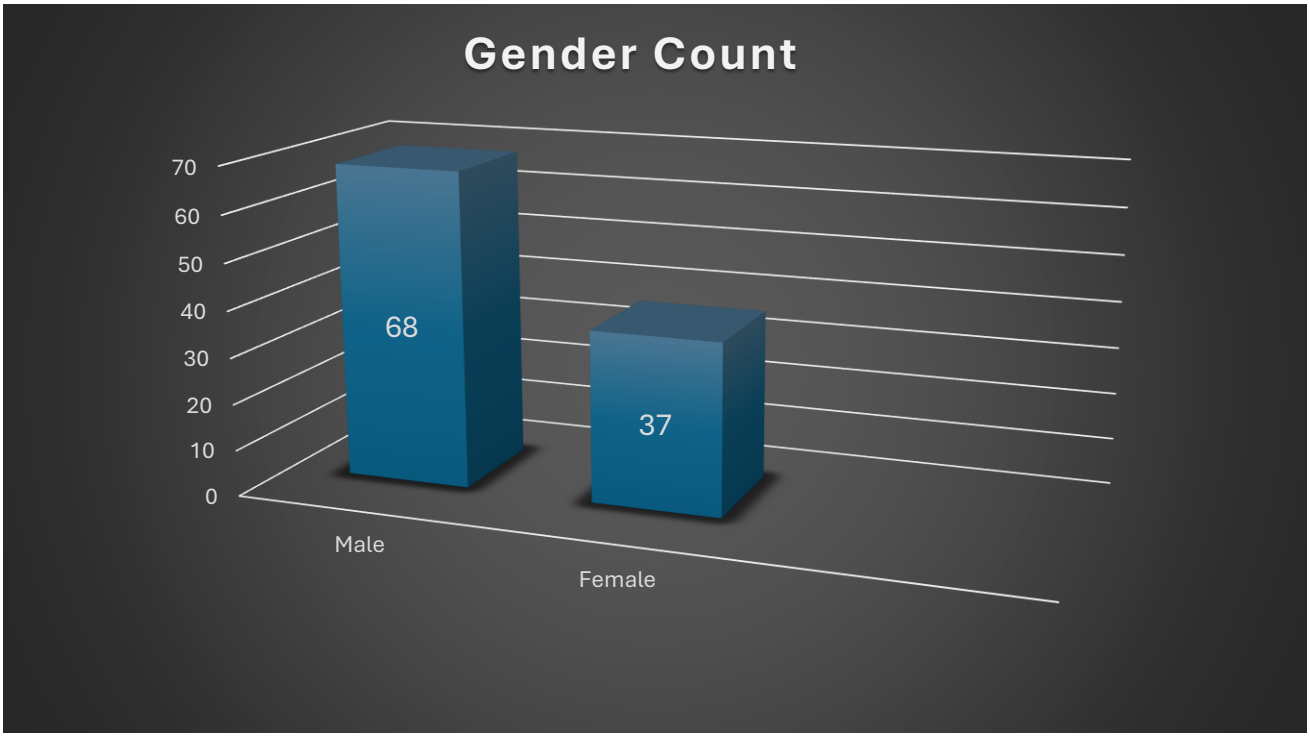
8%
17%
27%
37%
18-24
25-34
35-44
45-54
55-64
65+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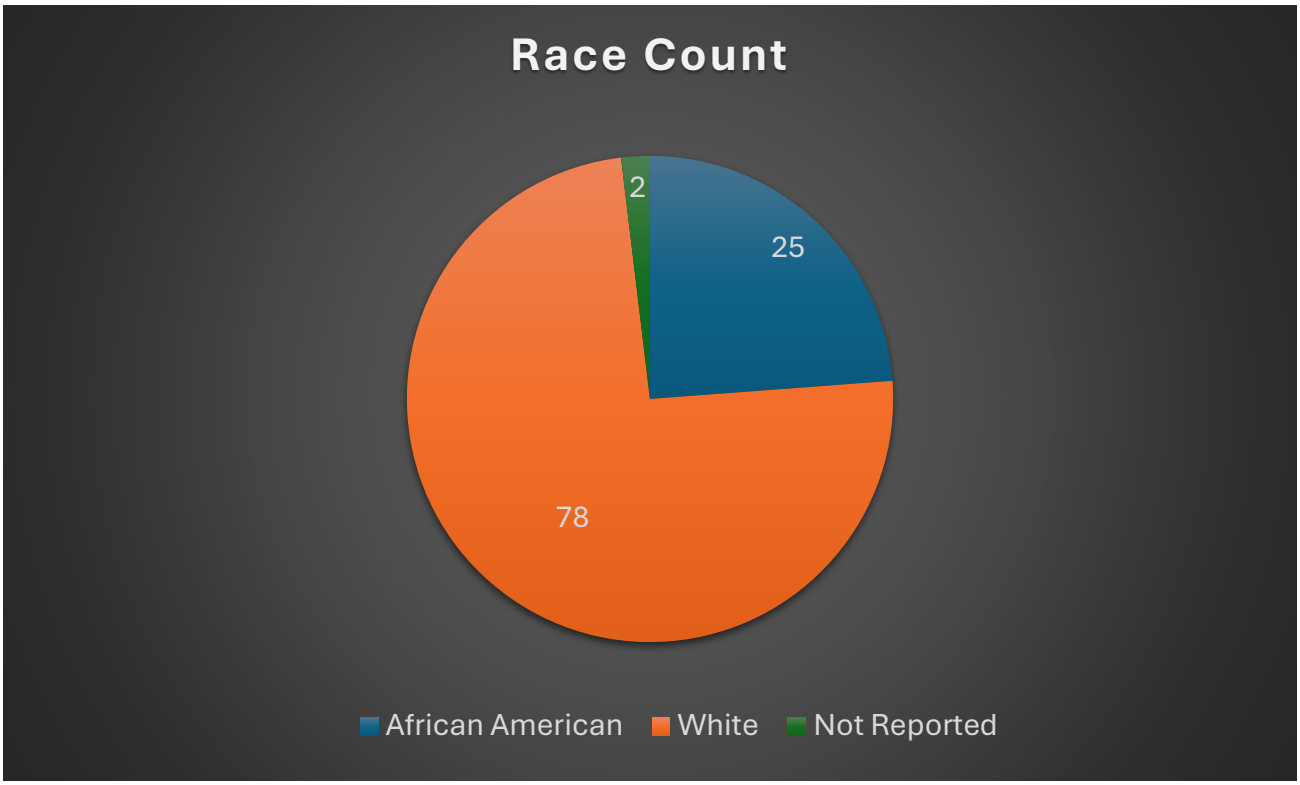
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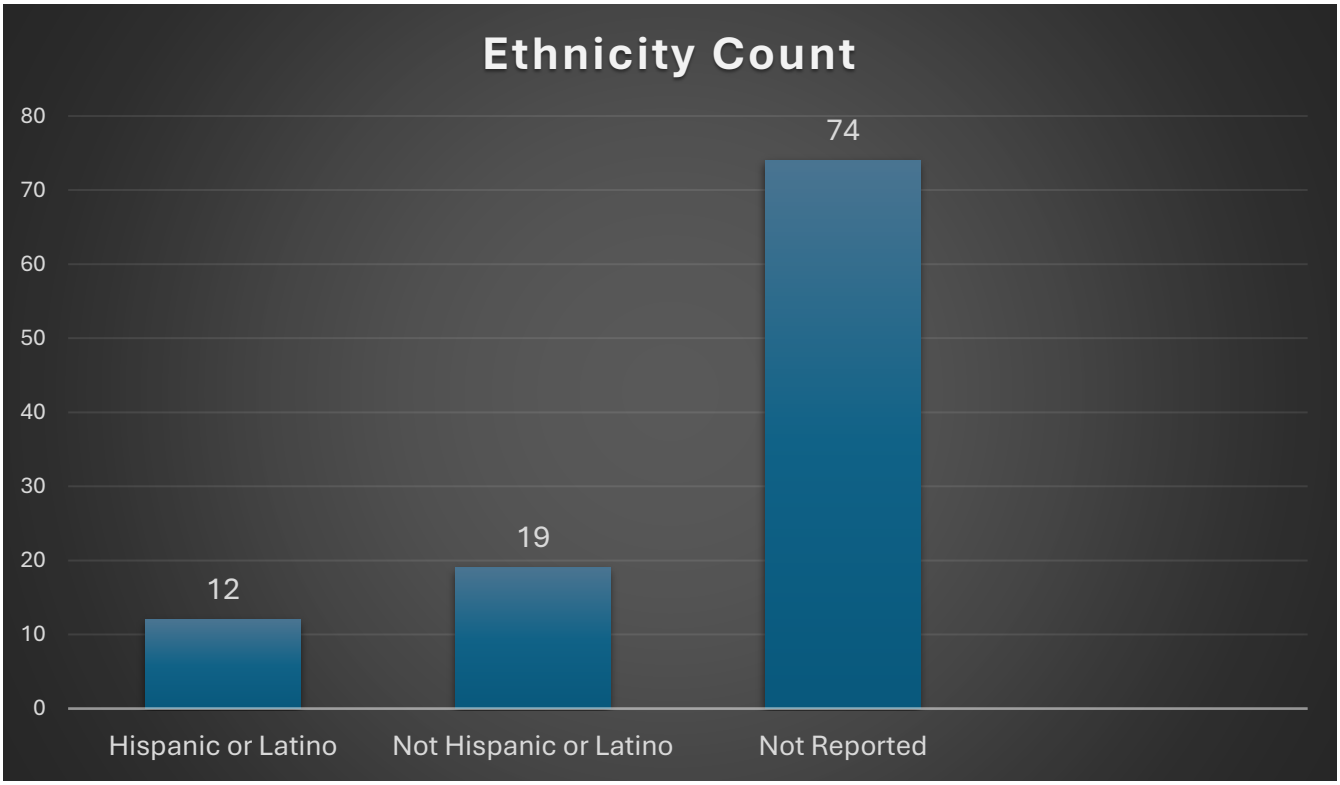
African American
White
Not Reported


Ethnicity Count
80
70
60
50
40
30
20
10
0
12
19
74
Hispanic or Latino
Not Hispanic or Latino
Not Reported

Anthony Dible

From: Geneva Krieger <GKrieger@Harbor.org>
Sent: Wednesday, May 7, 2025 2:17 PM
To: Anthony Dible; chelsea.diedrich@uhsinc.com
Subject: Adolescent Rehabilitation Facilities

Abraxas Youth and family Services | ~110 miles Away
(800) 680-5747 | 2775 OH-39, Shelby, OH 44875
https://abraxasyfs.org/abraxas-ohio.html

The Buckeye Ranch | ~145 miles Away
(614) 875-2371 | 5665 Hoover Rd, Grove City, OH 43123
https://www.buckeyeranch.org/our-services/residential-treatment/

Foundations for Living (Visions Program for dual diagnosis) | ~115 miles Away
(419) 589-5511 | 1451 Lucas Rd, Mansfield, OH 44903
https://foundationsforliving.net/programs-services/specialty-programs/mental-health-substance-use-visions-program/

Geneva Krieger, BA-QMHS, Army Veteran
She/Her/Hers
CCBHC Care Coordinator

419-469-7194 419-297-6619 www.harbor.org
gkrieger@harbor.org

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Talbot
Health Services

SUMMER PARTY

CELEBRATING SOBRIETY

JULY 12TH

732 MAIN ST TOLEDO, OH 43605

12:00PM – 4:00PM

FUN FOR THE WHOLE FAMILY!

- **Refreshments Table**
- **Delicious Food Trucks**
- **Arts and Crafts Corner**
- **Games and Contests**
- **Bounce Houses for Kids**
- **Raffle Prizes and Giveaways**
- **Ice Cream and Treats**

ADMISSION IS FREE! JUST COME WITH A SMILE AND YOUR FESTIVE SPIRIT

for resource table information
please reach out to
Jdressel@talbothealthservices.com

Toledo Fire and Rescue Department Overdose Statistics (Q1)

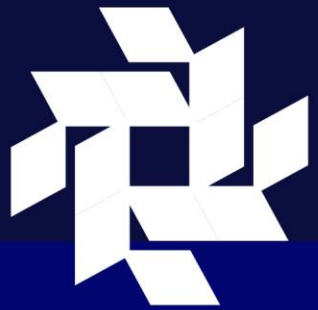
	Q1 2023 Opiate OD's	Q1 2024 Opiate OD's	Q1 2025 Opiate OD's
TOTAL	298	238	136

	Q1 2023 Fatalities	Q1 2024 Fatalities	Q1 2025 Fatalities
TOTAL	45	23	13

Notable Q1 2025 Trends:

- Time of day with highest OD: 2300 (6)
- Day of week with highest OD: THUR. (36)
- Date with highest number: 26 Mar (7)

- Number of AMA (Against Medical Advice) Patients: 31
- Number of LIB (Leave it Behind) naloxone kits provided: 24
- Percentage of AMA patients that received LIB kit: **77%**



Rx and Illicit Drug Summit

Rx and Illicit Drug Summit

Xylazine Withdrawal: Managing Uncharted Territory

William J. Lynch Jr. BS Pharm, RPh

Adjunct Faculty, Rowan University School of Osteopathic Medicine-Department of Emergency Medicine
Advanced Clinical Pharmacist, Jefferson Health System
Camden County NJ Addiction Awareness Task Force
Preceptor Jefferson, Rutgers, Saint Joseph's Colleges of Pharmacy
atTAcK addiction Advisory Board Member
Central Virginia Overdose Working Group
HIDTA Marijuana Impact Group Pharmacy Internship Preceptor
International Academy on the Science & Impact of Cannabis (IASIC)

Moderated by: Danielle Perkins
Member, Operation UNITE Board of Directors

Faculty Disclosures

- William J. Lynch Jr. BS-Pharm, RPh, has no financial relationships to disclose relating to the subject matter of this presentation
- Danielle Perkins has no financial relationships to disclose relating to the subject matter of this presentation

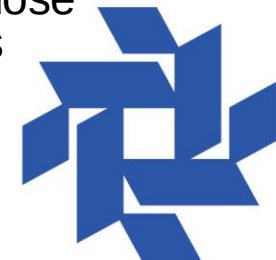
Reference.

Faculty Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity.
- This activity has been independently reviewed for balance.
- This CME activity includes brand names for participant clarity purposes only. No product promotion or recommendation should be inferred.

Learning Objectives

- Discuss the identification and progression of the xylazine overdose toxidrome and subsequent withdrawal syndrome, identify these signs and symptoms earlier, and intervene most appropriately.
- Discuss practical modality of care to use in treating their own xylazine patients, including early recognition of the withdrawal syndrome and appropriate medications to better manage overall patient outcomes. Medications and the dosages employed for xylazine withdrawal management to be reviewed will include, but not limited to dexmedetomidine, clonidine, tizanidine, guanfacine, olanzapine, lorazepam, phenobarbital and gabapentin. When these medications should and should not be used will be discussed.
- Identify strategies derived from collaborative efforts among first responders and across multiple medical disciplines, to effectively address this xylazine overdose withdrawal syndrome that can be shared within their respective communities upon returning home.



Disclaimer

The information presented by:

William J. Lynch Jr., BS-Pharm, RPh

are the information/opinions of this individual alone

and do not reflect the opinions of any of his affiliations or organizations.

Acknowledgements: Thank You!

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- Past President, Delaware Society of Health System Pharmacists

Major Brian V. Blazovic, MD
- Attending Family Medicine Physician, United States Army, Joint Base Elemendorf-Richardson, Anchorage AK
- Former Family Medicine Chief Resident, United States Army, Fort Hood Texas

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Carson M. Grier
- atTAcK addiction Advisory Board Member

Ryan M. Gray
- atTAcK addiction Advisory Board Member

Acknowledgements: Thank You!
ONDCP HIDTA NMI/MIG Pharmacy Internship Program

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Rutgers University Ernest Mario School of Pharmacy/HIDTA NMI Pharmacy Intern

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Saint Joseph's University Philadelphia College of Pharmacy/HIDTA NMI Pharmacy Intern

Old Adage

IT IS GOOD
TO LEARN FROM YOUR MISTAKES!!

IT IS BETTER…
TO LEARN FROM SOMEONE ELSE'S!!!!

LESS PAINFUL!!

Xylazine Situation

- Xylazine adulteration of drug supply has exploded over last few years across the US
- Documented cases seen in Philadelphia PA & Southern New Jersey area since 2006
- Increasing emergence of xylazine accompanied by horrific necrotizing wounds that are extremely difficult to manage
- Important to overall improved management of these patients is recognition & treatment of a xylazine overdose & specifically the xylazine withdrawal syndrome
- Recognition & management of xylazine withdrawal is critical in taking care of these patients, their wounds, & having them ultimately obtain an overall better outcome by receiving better treatment

Xylazine Toxidrome

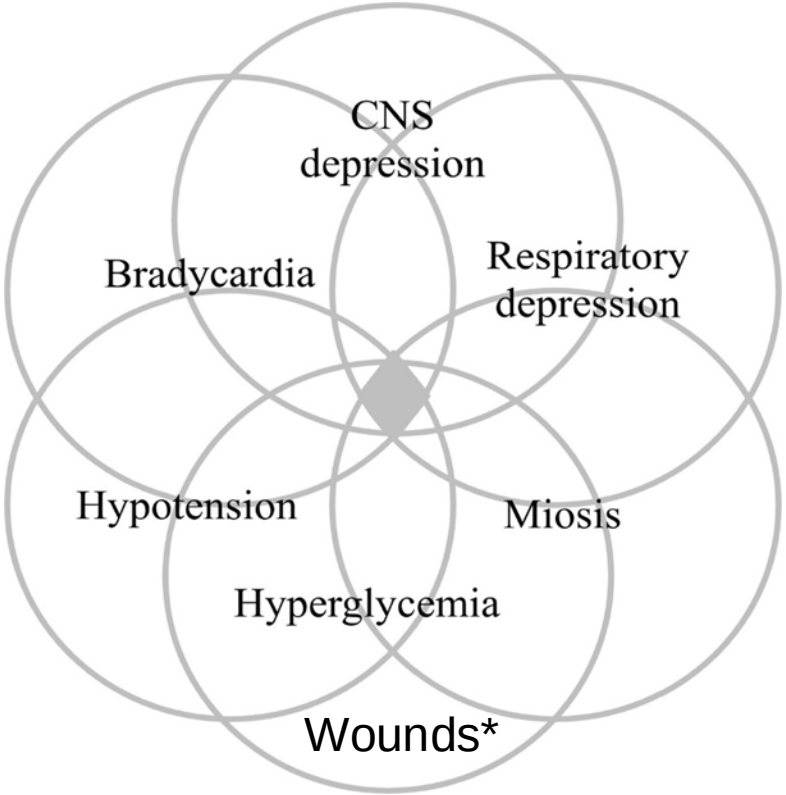


Fig. 2. General Toxidrome for Xylazine

Ruiz-Colón K, Chavez-Arias C, Díaz-Alcalá JE, et al. Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: A comprehensive review of the literature. *Forensic Sci. Int.* 2014;240:1-8. doi:10.1016/j.forsciint.2014.03.015.

Xylazine Toxidrome Summary by System

Central Nervous System	
Areflexia	Dysmetria
Asthenia	Hyporeflexia
Ataxia	Miosis
Blurred Vision	Slurred Speech
Disorientation	Somnolence
Drowsiness	Staggering
Dysarthria	Coma

Xylazine Toxidrome Summary by System

Respiratory	Cardiovascular	Endocrine
Apnea	Hypotension	Hyperglycemia
Dyspnea	Bradycardia	
Shallow Breathing	Premature Ventricular Contraction	

Xylazine Case Treatment Options

- **Acute Overdose**
  - Supportive Care:
    - **Xylazine is NOT an opiate**
      - ***Naloxone SHOULD BE ADMINISTERED!!!***
        - Synthetic opioid era → Higher doses naloxone
        - Higher dose of naloxone → Higher risk of naloxone-induced non-cardiogenic pulmonary edema
        - No recommended maximum dose
    - Study published on Substance Abuse Treatment, Prevention, & Policy
      - Proposed reasonable range:
        - **4-6 mg IM** OR **8-12 mg Intranasal**
      - Approximates increases of 2–3 fold from current recommended doses

Moss, R.B., Carlo, D.J. Higher doses of naloxone are needed in the synthetic opioid era. *Subst Abuse Treat Prev Policy.* 2019;14(1):1-6. doi:10.1186/s13011-019-0195-4.
Marco CA, Trautman W, Cook A, et al. Naloxone Use Among Emergency Department Patients with Opioid Overdose. *J. Emerg. Med.* 2018;55(1):64-70. doi:10.1016/j.jemermed.2018.04.022.

Xylazine Treatment Concerns

- Medicine is catching up/unaware of the problem
  - How to Recognize & Treat Xylazine:
  - Overdose
  - Withdrawal
  - Wounds

- **Even when patients treated with OUD MAT**
  - ***We are not treating xylazine symptoms/withdrawal!!***

- Participants may be unaware that they are even using xylazine

- Difficult to place patients, not accepted into treatment/detox with open wounds/pain management &/or withdrawal issues

Identification of wounds early/decreasing:

- Infection
- Progression
- Morbidity
- Mortality
- **Withdrawal**

Xylazine Withdrawal Syndrome

- Poorly Defined
- In addition to withdrawal from other substances
- Often not recognized
- Increased agitation/extreme anxiety/dysphoria/shaking/chills
- Rebound Hypertension
  - Can become critically elevated if untreated
- Heart Arrythmias/Conduction Abnormalities
- Psychiatric Symptoms
  - Tactile Sensations/Head Zaps/Hallucinations
  - Cannot sit still/hypermobility
- Withdrawal Not Recognized/Not or Poorly Controlled
- **Reason sign out AMA**
- Symptoms may be protracted/last weeks-months
- Long term use reported to lead to decline in IQ scores in some cases

Xylazine Withdrawal Symptoms

- Anxiety
- Agitation
- Restlessness
- Pain
- Tachycardia
- Insomnia/Nightmares/Flashbacks
- Muscle Spasms
- Rebound hypertension
- Diarrhea
- Nausea/Vomiting

Withdrawal Tx = Wound Tx

Treating Withdrawal

IS

Treating the Wounds!!

Xylazine Pharmacokinetics in Patients Testing Positive for Fentanyl & Xylazine

Methods

- Xylazine quantified in serial remnant plasmas collected from 28 patients
- Starting at initial patient encounter & continuing for up to 52 hours from presentation
- Using LC-MS/MS to calculate terminal half-life for xylazine
- Xylazine metabolites identified by product ion scanning & multiple reaction monitoring
- Used to estimate relative abundance of xylazine metabolites in 74 collected plasma samples

Results

- Median terminal half-life for xylazine was calculated to be 12.0 h (range: 5.9–20.8)
- Oxo-xylazine & sulfone-xylazine metabolites detected in all plasma specimens that contained xylazine

Conclusions

- **Half-life of xylazine in humans is longer than previously observed in animal studies**
- Furthers current understanding of expected duration of effects in individuals who use fentanyl mixed with xylazine & the window of detection
- Both oxo-xylazine & sulfone-xylazine appear to circulate in plasma for as long as xylazine

Lin,Y. et al. *Xylazine Pharmacokinetics in Patients Testing Positive for Fentanyl and Xylazine.* Clinical Chemistry, Volume 71, Issue 2, February 2025, Pages 266–273, https://doi.org/10.1093/clinchem/hvae163

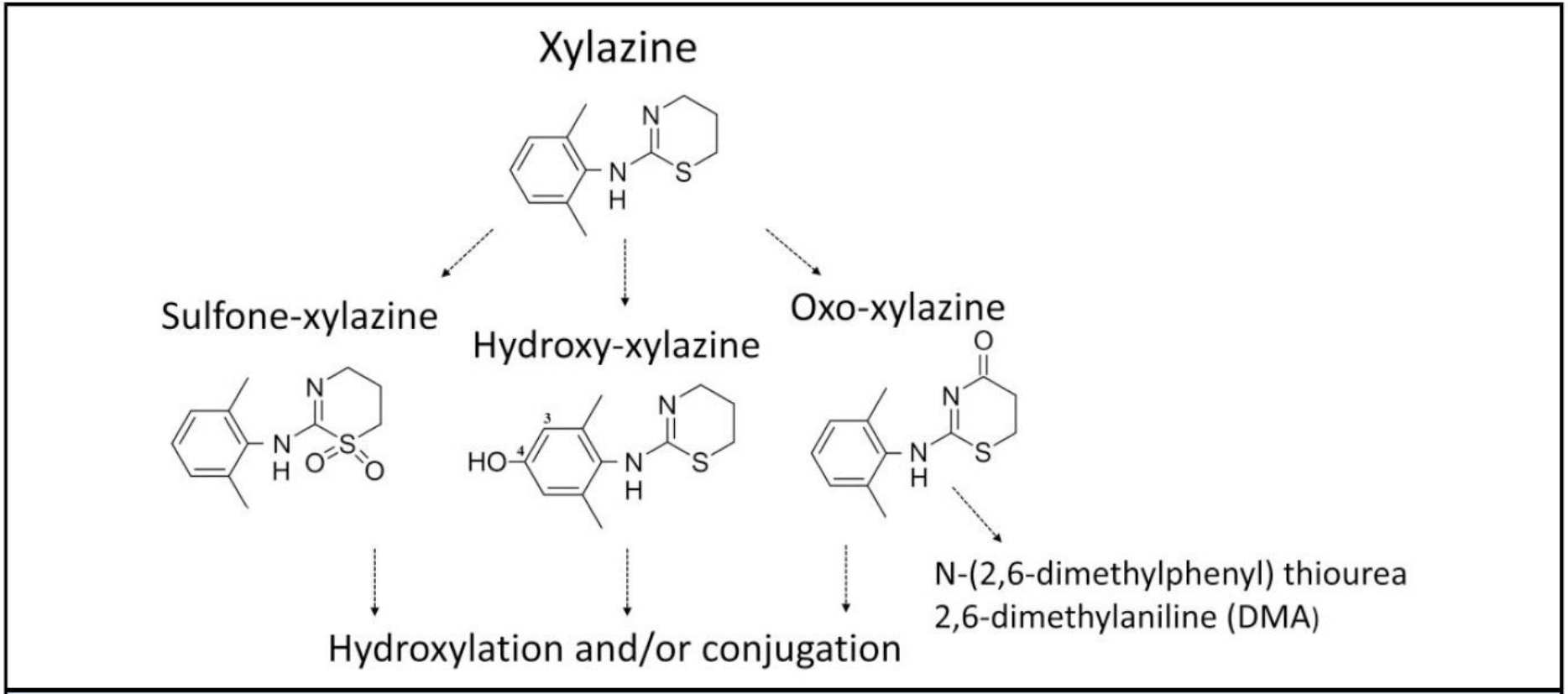


Fig. 1. Structure of xylazine and metabolites. N-(2,6-diemthylphenyl) thiourea and 2,6-dimethylaniline were not identified in this study but previously reported (6, 7).

Lin,Y. et al. *Xylazine Pharmacokinetics in Patients Testing Positive for Fentanyl and Xylazine.* Clinical Chemistry, Volume 71, Issue 2, February 2025, Pages 266–273, https://doi.org/10.1093/clinchem/hvae163

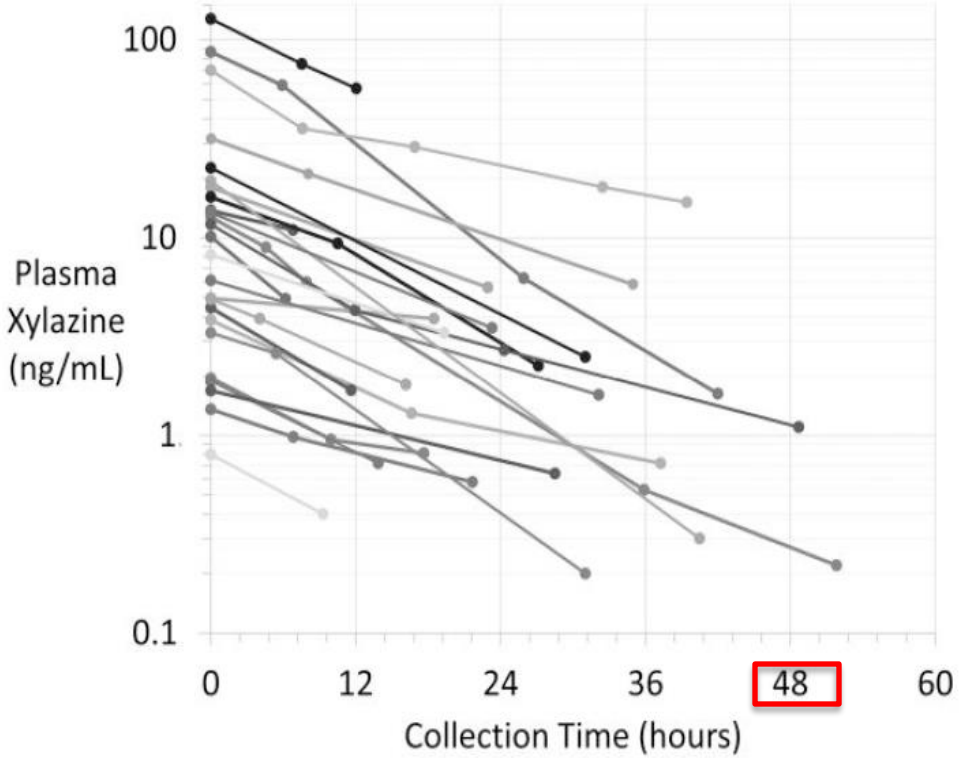


Fig. 3. Xylazine plasma concentration (log scale) vs collection time in 28 patients.

Lin,Y. et al. *Xylazine Pharmacokinetics in Patients Testing Positive for Fentanyl and Xylazine.* Clinical Chemistry, Volume 71, Issue 2, February 2025, Pages 266–273, https://doi.org/10.1093/clinchem/hvae163

Half Life Range
5.9 to 20.8 hrs

Median:12.0 hrs

Outlier: 53.3 hrs

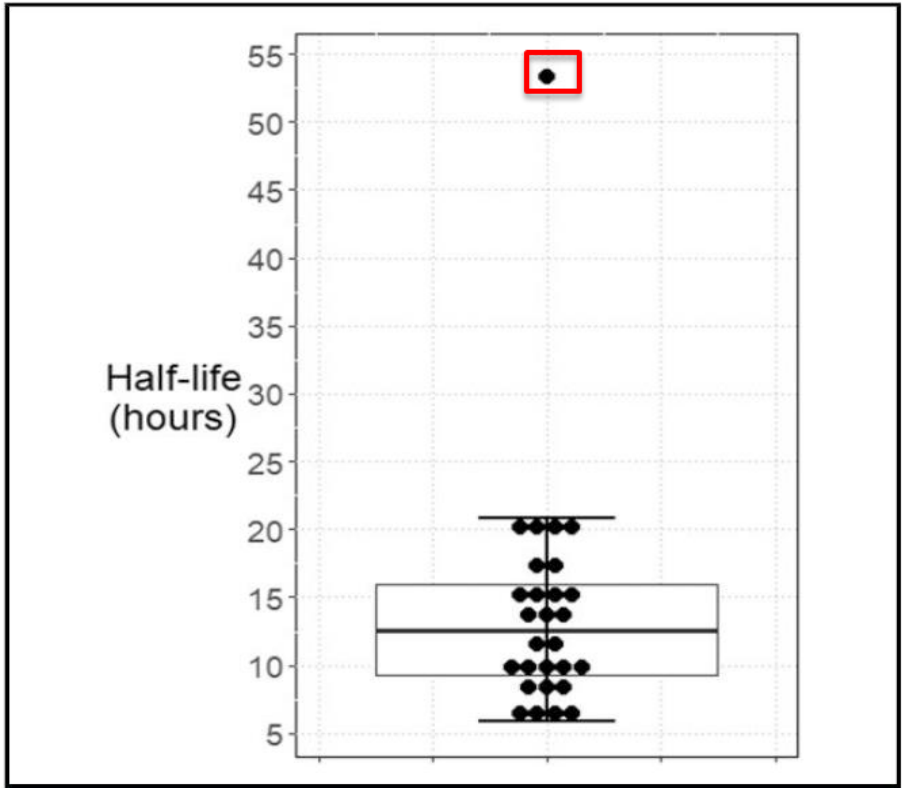
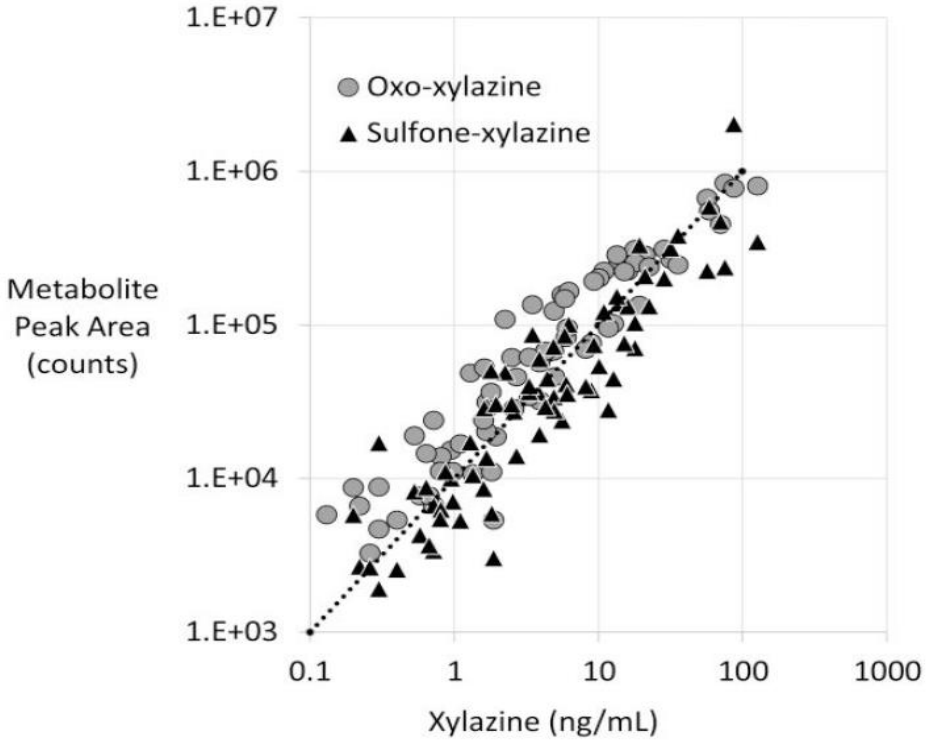


Fig. 4. Boxplot of xylazine half-life in 28 patients.

Lin,Y. et al. *Xylazine Pharmacokinetics in Patients Testing Positive for Fentanyl and Xylazine.* Clinical Chemistry, Volume 71, Issue 2, February 2025, Pages 266–273, https://doi.org/10.1093/clinchem/hvae163



Biological Effects, Duration, Pharmacological Activities of Xylazine Metabolites are Unknown

Fig. 5. Semi-log plot of metabolite peak area signal (counts) vs xylazine concentration (ng/mL) in 28 patients. The dashed line represents the relationship between xylazine peak area and xylazine concentration ($y = 10\,000x$).

Lin,Y. et al. *Xylazine Pharmacokinetics in Patients Testing Positive for Fentanyl and Xylazine.* Clinical Chemistry, Volume 71, Issue 2, February 2025, Pages 266–273, https://doi.org/10.1093/clinchem/hvae163

Medications to Consider for Treatment

ALL MEDICATIONS ARE OFF LABEL/NOT FDA APPROVED

WITH REGARDS TO TREATING XYLAZINE WITHDRAWAL

α-2 Agonist Replacement for Xylazine Withdrawal Management

Dexmedetomidine **OFF LABEL USE/NOT FDA APPROVED**

- ***"Go to Agent"***
- *α-2 agonist*
- ICU Sedation
- Dosing: 0.2 to 1.5 mcg/kg/hour
- Titrate by 0.2/kg/hour every 30 mins to clinical effect
- Patient must be in a monitored setting
- ***Use/overlap with oral clonidine***

α-2 Agonist Replacement for Xylazine Withdrawal Management

Clonidine **OFF LABEL USE/NOT FDA APPROVED**

- 0.1 to 0.2 mg PO
- Repeat every 45-60mins PRN for up to 4 doses until symptoms resolve
- **Maintenance Dose:** 0.1 to 0.3 every 6 to 8 hrs based on symptom severity
- **Maximum Dose:** 0.8 to 1.2 mg /day
- Stabilized, can change to clonidine transdermal patch
- **Caution hypotension/bradycardia**
- Add hold parameters (OK with & trigger notification)
- SBP<100, DBP<60, HR<60
- Contact attending service/house officer

hip.phila.gov/document/3154/PDPH-HAN Update 13 Xylazine 12.08.22.pdf **OFF LABEL USE/NOT FDA APPROVED**

α-2 Agonist Replacement for Xylazine Withdrawal Management

Clonidine **OFF LABEL USE/NOT FDA APPROVED**

- α-2 adrenergic agonist
- Antihypertensive
- 2 for 1 benefit: xylazine & opioid withdrawal coverage
- Efficacy in opioid withdrawal attributed to binding central α-2 adrenergic receptors that share K+ channels with opioids & blunts withdrawal symptoms
- Starting dose 0.1 mg po q8hours
- Recommended as standing dose/prophylaxis if BP can tolerate
- Some have standing order & prn order together
- Caution: hypotension, bradycardia, sedation
- Alternatives: tizanidine, lofexidine, guanfacine

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001 **OFF LABEL USE/NOT FDA APPROVED**

Xylazine Withdrawal Management

Anxiety/Agitation/Restlessness OFF LABEL USE/NOT FDA APPROVED

If HR/BP is normal to elevated:

Clonidine (first-line)

- Start with 0.1 mg Q4H PRN for restlessness, agitation, or anxiety, consider standing dose of 0.1 mg TID if HR >100, SBP >150, or DBP >90
- Maximum: 1.5 mg /day
- Contraindications: SBP <80, DBP <50, HR <50

- Taper by 0.1 - 0.2 mg/day by day 5
- Consider patch or IV (usually not given) if cannot tolerate PO
- Patch can take 3 days to reach steady-state
- Consider if xylazine use suspected/known or weaning/weaned off dexmedetomidine drip

α-2 Agonist Replacement for Xylazine Withdrawal Management

Clonidine **OFF LABEL USE/NOT FDA APPROVED**

- **Clonidine ICU sedation, transition from dexmedetomidine to clonidine (off-label use):**
- Consider use in patients who are hemodynamically stable & able to receive medications enterally
- Monitor BP & HR during initiation/transition (Ref)

Clonidine Oral: Immediate release

- **Initial: Note:** Decrease dexmedetomidine dose by 25% within 6hrs of each clonidine dose
  Dexmedetomidine can usually be stopped within 48 hours
- *Dexmedetomidine dose <0.7 mcg/kg/hour*: 0.1 to 0.2 mg every 6 to 8 hours (Ref).
- *Dexmedetomidine dose ≥0.7 mcg/kg/hour:* 0.3 mg every 6 to 8 hours (Ref).

Maintenance

- Titrate to achieve target sedation levels to a usual dosage range of 0.2 to 0.5 mg every 6hrs
- Gradually taper clonidine by extending dosing interval every 24 to 48 hours

Lexicomp Database. Clonidine. Accessed 2/5/25. **OFF LABEL USE/NOT FDA APPROVED**

α-2 Agonist Replacement for Xylazine Withdrawal Management

Clonidine **OFF LABEL USE/NOT FDA APPROVED**

Opioid withdrawal, medically supervised (adjunctive or alternative agent) (off-label use):

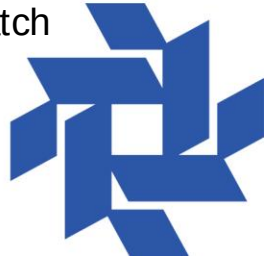
- Adjunct to opioid agonist for relief of withdrawal symptoms
- May also be used as primary treatment when opioid agonist therapy is not indicated or not available
- May be combined with other adjunctive medications prn
- To assess severity of withdrawal symptoms & adjust therapy, use of standard instrument for scoring of clinical observations (Clinical Opioid Withdrawal Scale [COWS]) is suggested (Ref)

Oral: Immediate release

- **Initial:** 0.1 to 0.2 mg (patients >90 kg may receive up to 0.3 mg)
- May repeat every 45 to 60 minutes if needed, up to total of 4 doses until symptoms resolve, provided BP & HR remain stable
- **Maximum dose:** typically, 0.8 mg/day or up to 1.2 mg/day for patients >90 kg (Ref)

- **Maintenance:** 0.1 to 0.3 mg every 6 to 8 hours determined by symptom severity
- **Maximum dose:** 1.2 mg/day in divided doses (Ref)

- After stable oral dose is established, may transition to an equivalent dose of a transdermal patch
- *According to some institutional protocols, may initiate therapy with transdermal patch in select patients*



Lexicomp Database. Clonidine. Accessed 2/5/25. **OFF LABEL USE/NOT FDA APPROVED**

α-2 Agonist Replacement for Xylazine Withdrawal Management

Clonidine **OFF LABEL USE/NOT FDA APPROVED**

Transitioning between dosage forms

Transition from oral to transdermal:

- Overlap oral regimen for 1 to 3 days
- Transdermal route takes 2 to 3 days to achieve therapeutic effect

Example Transition:

Day 1: Place transdermal patch; administer 100% of oral dose

Day 2: Patch remains; administer 50% of oral dose

Day 3: Patch remains; administer 25% of oral dose

Day 4: Patch remains; no further oral dosing

Have hold parameters established for oral dosing

If BP drops precariously: **remove the patch**

Lexicomp Database. Clonidine. Accessed 2/5/25. **OFF LABEL USE/NOT FDA APPROVED**

α-2 Agonist Replacement for Xylazine Withdrawal Management

Clonidine **OFF LABEL USE/NOT FDA APPROVED**

Transition from transdermal to oral:

After transdermal patch removal:

- Therapeutic clonidine levels persist for ~8 hours & then slowly decrease over several days
- With potential for continued effect for 24-48 hours after removal
- Persistent effect on BP should be considered when restarting oral clonidine
- Consider starting oral clonidine **no sooner than 8 hrs after patch removal**

Lexicomp Database. Clonidine. Accessed 2/5/25. **OFF LABEL USE/NOT FDA APPROVED**

α-2 Agonist Replacement for Xylazine Withdrawal Management

Clonidine

OFF LABEL USE/NOT FDA APPROVED

Discontinuation of therapy

- Do not stop oral therapy abruptly to decrease risk of acute & potentially severe rebound hypertension & withdrawal symptoms
- Nervousness, agitation, headache, tremor
- Discontinue slowly over at least 6 to 10 days
- Discontinue by reducing the dose by 33% to 50% every 2 to 3 days
- *For patients on both a beta-blocker & clonidine, withdraw beta-blocker several days before clonidine, then slowly taper clonidine*
- Rebound hypertension & withdrawal symptoms are less likely with a transdermal patch compared to oral therapy (Ref).

Note:

- Clonidine administration generally not interrupted during perioperative period (Ref).

Lexicomp Database. Clonidine. Accessed 2/5/25. **OFF LABEL USE/NOT FDA APPROVED**

α-2 Agonist Replacement for Xylazine Withdrawal Management

Clonidine **OFF LABEL USE/NOT FDA APPROVED**

Dosage adjustment for concomitant therapy

- Significant drug interactions exist, requiring dose/frequency adjustment or avoidance
- Consult drug interactions database for more information
- *Contact with your friendly neighborhood hospital pharmacist*

Lexicomp Database. Clonidine. Accessed 2/5/25. **OFF LABEL USE/NOT FDA APPROVED**

α-2 Agonist Replacement for Xylazine Withdrawal Management

Tizanidine **OFF LABEL USE/NOT FDA APPROVED**

- 2 to 4 mg PO every 8 to 12 hours prn
- Increase based on response & tolerability
- Up to max of 24 mg/day
- Better agent to use if hypotensive
- Watch for QTC prolongation

Xylazine Withdrawal Management

Anxiety/Agitation/Restlessness **OFF LABEL USE/NOT FDA APPROVED**

If HR/BP is normal to low and QTC <490 ms:

Tizanidine

- Alternative agent
- Can be given with either clonidine or guanfacine if acute pain
- Start 4 mg po TID, can titrate as needed
- **Contraindications: QTC > 500 ms**
- May be increased to augment acute pain/spasm treatment
- **Maximum**: 36 mg/day
- Taper by 4-8 mg/day by day 5 or once acute pain/spasm resolved

α-2 Agonist Replacement for Xylazine Withdrawal Management

Guanfacine **OFF LABEL USE/NOT FDA APPROVED**

- 0.5 to 1 mg PO once daily QHS
- Every 3 to 4 days, may increase to 1 mg BID, TID, QID PRN
- Up to 4 to 7 mg/day (for most adults)
- With comfort level, some increase more aggressively

Xylazine Withdrawal Management

Anxiety/Agitation/Restlessness **OFF LABEL USE/NOT FDA APPROVED**

If HR/BP is normal to elevated:

Guanfacine

- Alternative if bradycardia or hypotension exclude clonidine use
- Start with 1 mg po Q4H PRN for restlessness/agitation/anxiety
- Consider standing dose of 1 mg po BID
- **Maximum:** 9 mg/day
- **Contraindications: SBP <80, DBP <50, HR <50**
- Taper by 1-2 mg/day by day 5
- Should consider if xylazine use suspected/known or weaning/weaned off dexmedetomidine drip as an alternative to clonidine

α-2 Agonist Replacement for Xylazine Withdrawal Management

Guanfacine Discontinuation **OFF LABEL USE/NOT FDA APPROVED**

- Withdrawal syndrome including symptoms resembling nervousness and **anxiety**
- **Increased heart rate/rebound hypertension** may occur with abrupt discontinuation of guanfacine in all ages (Ref)

- **Mechanism:** Withdrawal; result of excessive plasma catecholamine levels, “catecholamine surge”

- **Onset:** Rapid
- Gradual increase back to baseline pretreatment BP after drug discontinuation
- BP readings significantly above pretreatment readings also reported (Ref).

Risk factors
- Higher doses (Ref)
- Longer duration of treatment (Ref)
- Abrupt discontinuation of guanfacine (medication nonadherence, vomiting [abrupt inability to absorb oral dosage forms]) (Ref)

Lexicomp Database. Guanfacine. Accessed 2/5/25. **OFF LABEL USE/NOT FDA APPROVED**

α-2 Agonist Replacement for Xylazine Withdrawal Management

α-2 Agonist	Typical Dosing for Withdrawal Management
Clonidine	**0.1 to 0.2 mg PO, repeat every 45-60mins PRN for up to 4 doses until symptoms resolve** **Maintenance Dose: 0.1 to 0.3 every 6 to 8 hrs based on symptom severity** **Maximum Dose: 0.8 to 1.2 mg /day**
Dexmedetomidine	**ICU Sedation dosing: 0.2 to 1.5 mcg/kg/hour** **Titrate by 0.2/kg/hour every 30 mins to clinical effect** **Patient must be in a monitored setting**
Tizanidine	**2 to 4 mg PO every 8 to 12 hours prn** **Increase based on response & tolerability** **Up to max of 24 mg/day**
Guanfacine	**0.5 to 1 mg PO once daily QHS** **Every 3 to 4 days, may increase to 1 mg BID, TID, QID PRN up to 4 to 7 mg/day (for most adults)**

hip.phila.gov/document/3154/PDPH-HAN Update 13 Xylazine 12.08.22.pdf

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Secondary Agents for Xylazine Withdrawal Management

Olanzapine

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- Atypical Antipsychotic
- Starting dose 2.5 mg
- Range: 2.5 mg to 10 mg daily
- **PO or IM**
- **IV:** alternative limited to settings to observe for respiratory depression (ED,ICU)
- **Better for QTC prolongation than haloperidol/alternatives listed**
- Alternatives: ziprasidone, risperidone, quetiapine

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001. Lexicomp Database. Olanzapine. Accessed 2/5/25

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Benzodiazepines for Xylazine Withdrawal Management

Lorazepam **OFF LABEL USE/NOT FDA APPROVED**

- Gamma-aminobutyric acid (GABA) agonists
- Starting dose 1 to 2 mg PO/IV/IM
- Titrate to effect
- Caution: sedation, lethargy, somnolence
- Alternatives: clonazepam, midazolam, diazepam

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001 **OFF LABEL USE/NOT FDA APPROVED**

Benzodiazepines for Xylazine Withdrawal Management

Lorazepam **OFF LABEL USE/NOT FDA APPROVED**

Mechanically ventilated patients in ICU, sedation (alternative agent) (off-label use)

- Used as part of multimodal strategy
- **Nonbenzodiazepine sedation preferred due to risk of prolonged sedation & delirium with continuous benzodiazepine use**
- Titrate to light level of sedation (Richmond Agitation-Sedation Scale (RASS) 0 to −2) or clinical effect (ventilator dyssynchrony)
- Intermittent PRN therapy preferred to avoid drug accumulation & prolonged sedation associated with continuous infusions (Ref)
- ***Continuous infusions not recommended for use in most ICU patients due to propylene glycol (PG) accumulation & subsequent complications (osmol gap metabolic acidosis, kidney failure)***
- **Monitor PG accumulation with osmol gap**
- **Nonbenzodiazepine or midazolam continuous infusions preferred** (Ref)

Intermittent (preferred)

- Non–weight-based dosing: **IV:** Initial dose: 1 to 4 mg; Maintenance: 1 to 4 mg every 2 to 6 hours PRN (Ref).
- Weight-based dosing: **IV:** Initial dose: 0.02 to 0.04 mg/kg (maximum single dose: 4 mg)
- Maintenance: 0.02 to 0.06 mg/kg every 2 to 6 hours PRN (maximum single dose: 4 mg) (Ref).
- *Continuous infusion:* **IV:** 0.5 to 10 mg/hour **or** 0.01 to 0.1 mg/kg/hour continuous infusion (maximum dose: 10 mg/hour) (Ref).

- Midazolam infusion vs Lorazepam Infusion (rarely needed)
- Lorazepam more lipophilic (cross BBB for CNS effect)

Lexicomp Database. Lorazepam. Accessed 2/5/25

OFF LABEL USE/NOT FDA APPROVED

Benzodiazepines for Xylazine Withdrawal Management

Lorazepam **OFF LABEL USE/NOT FDA APPROVED**

Intoxication: Cocaine, methamphetamine, other sympathomimetics (off-label use)
Based on limited data

- **IV:** 2 to 4 mg every 3 to 10 minutes as needed for agitation, sedation, seizures, hypertension, tachycardia until desired symptom control achieved
- Large cumulative doses may be required for some patients
- Monitor for respiratory depression & hypotension (Ref)
- **Note:** Initiating treatment at 1 mg may be adequate in patients who are only mildly or moderately intoxicated, but doses should be repeated or increased PRN
- Consider IM administration if IV access not possible
- Effects delayed with IM vs IV (Ref)

Lexicomp Database. Lorazepam. Accessed 2/5/25

Gabapentin for Xylazine Withdrawal Management

Gabapentin **OFF LABEL USE/NOT FDA APPROVED**

- Anticonvulsant
- Reduces transmission of voltage-gated Ca++ channels reducing excitatory neurotransmitters
- Best efficacy in neuropathic pain
- Can optimize sedation effects
- Dosing: 300 to 600 mg every 8 hours with additional 300 mg po QHS

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001 **OFF LABEL USE/NOT FDA APPROVED**

Gabapentin for Xylazine Withdrawal Management

Gabapentin **OFF LABEL USE/NOT FDA APPROVED**

Withdrawal Taper (Alcohol)

- Gabapentin 800 mg po Q6hr x 1 dose now
- Gabapentin 600 mg po q6hr x 8 doses
- Gabapentin 700 mg po q8hr x 3 doses
- Gabapentin 600 mg po q8hr x 3 doses
- Gabapentin 400 mg po q6hr x 4 doses
- Gabapentin 300 mg po q6hr x 4 doses
- Gabapentin 300 mg po q8hr x 3 doses
- Gabapentin 300 mg po q12hr x 365 days (or until discontinuation)

Alternative Agents for Xylazine Withdrawal Management

Pregabalin OFF LABEL USE/NOT FDA APPROVED

- Anticonvulsant
- Adjunct treatment for neuropathic pain & anxiety
- Dosing: 100 mg po TID/q8hours
- Up to 600 mg po TID/q8hours
- **Alternative to Gabapentin (not together!)**

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001 **OFF LABEL USE/NOT FDA APPROVED**

Phenobarbital for Xylazine Withdrawal Management

Phenobarbital

OFF LABEL USE/NOT FDA APPROVED

- Gamma Aminobutyric Acid (GABA) agonist
- Long-acting barbiturate
- Doses: 130 mg IV push (IVP) x1 dose
- Follow alcohol withdrawal protocol
- Loading dose: 130 to 260 mg IV push x1 dose now
- 130 mg IV push Q8hrs standing or prn
- IV push (IVP) preferred over IV piggy back (IVPB)
- Can give IVPB, delays care
- Caution: sedation

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001 **OFF LABEL USE/NOT FDA APPROVED**

Phenobarbital for Xylazine Withdrawal Management

Phenobarbital **OFF LABEL USE/NOT FDA APPROVED**

- Consider Phenobarbital alcohol withdrawal taper

Alcohol Withdrawal Taper

- Phenobarbital 260 mg IV Push (or 130 mg IVP) loading dose x1
- Repeat 130 mg IV Push every 15-30 minutes until desired effect or side effects prohibit additional dosing
- 130 mg IV Push q8hrs standing/prn

Alternative Agents for Xylazine Withdrawal Management

Ropinirole

OFF LABEL USE/NOT FDA APPROVED

- Non-ergoline dopamine agonist
- Used to treat motor symptoms of Parkinson's Disease/Restless Leg Syndrome
- Aid in muscle relaxation, anxiety & motor restlessness-myoclonus
- **Starting Dose:** 0.25 to 0.5 mg every 8 hours
- **Usual/Max Dose:** ≤ 4 mg per day/Max 4 mg/day (Restless Leg Syndrome)
- **Usual Dose:** 12 to16 mg/day. Max dose: 24mg/day (Parkinson's)

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001 Lexicomp Database. Ropinirole. Accessed 2.14.25.

OFF LABEL USE/NOT FDA APPROVED

Alternative Agents for Xylazine Withdrawal Management

Ketamine

OFF LABEL USE/NOT FDA APPROVED

- N-methyl-D-aspartic acid (NMDA) receptor antagonist
- Effective as opioid-sparing analgesic adjunct
- Dosing: 10 mg IV postoperatively every 6 hours
- 0.3 mg/kg IV over 15 minutes
- Short acting unless followed by continuous infusion

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001 **OFF LABEL USE/NOT FDA APPROVED**

Table. Medications for Prophylaxis and Treatment of Xylazine–Fentanyl Withdrawal

Drug	Alternatives	Description
Primary		
Clonidine	Tizanidine, lofexidine, guanfacine	α-2 Adrenergic agonist; antihypertensive; efficacy in opioid withdrawal attributed to binding to central α-2 adrenergic receptor that shares potassium channels with opioids and blunts symptoms of withdrawal; starting dose 0.1 mg every 8 h recommended as standing dose/prophylaxis if blood pressure can tolerate; caution: sedation, bradycardia, and hypotension
Secondary		
Olanzapine	Ziprasidone, risperidone, quetiapine	Atypical antipsychotic; 2.5 mg starting dose; 2.5–10 mg daily
Lorazepam	Clonazepam, midazolam, diazepam	GABA agonists; lorazepam 1–2 mg orally/intravenously/intramuscularly; titrate to effect; caution: sedation
Gabapentin	–	Anticonvulsant; reduces transmission of voltage-gated calcium channels reducing excitatory neurotransmitters; best efficacy in neuropathic pain; can optimize sedation effects; 300–600 mg every 8 h and 300 mg once daily at bedtime
Phenobarbital	–	GABA agonist; long-acting barbiturate; 130 mg intravenously; caution: sedation
Dexmedetomidine	–	α-2 agonist; sedation; antihypertensive; use in monitored settings after maximizing oral α-2 agonists: dose ≥0.2–1 mcg/kg/h
Others		
Ropinirole	–	Non-ergoline dopamine agonist used to treat motor symptoms of Parkinson disease as well as to treat restless legs syndrome; it can aid in muscle relaxation, anxiety, and motor restlessness–myoclonus; starting dose 0.25–0.5 mg every 8 h
Ketamine	–	NMDA receptor antagonist; effective as an opioid-sparing analgesic adjunct; 10 mg postoperatively every 6 h; 0.3 mg/kg intravenously over 15 min; short-acting unless followed by continuous infusion
Pregabalin	–	Anticonvulsant; adjunct treatment for neuropathic pain and anxiety; 100 mg 3 times per day up to 600 mg 3 times per day

GABA = γ-aminobutyric acid; NMDA = *N*-methyl-D-aspartic acid.

OFF LABEL USE/NOT FDA APPROVED

D'Orazio J et al. *Xylazine Adulteration of the Heroin-Fentanyl Drug Supply. A Narrative Review*. Annals of Internal Medicine. 10.10.2023 doi:10.7326/M23-2001

Xylazine Withdrawal Management

- ALL patient should receive symptom management, regardless of MOUD status
- Assess COWS/Symptoms Q3H while awake
- Consider short-term continuation of strategies used successfully in ED

Xylazine Withdrawal Management

Severe Tachycardia/Hypertension **OFF LABEL USE/NOT FDA APPROVED**

- **If severe tachycardia, HTN emergency, or evidence of new onset stress cardiomyopathy**

- Consider ICU consultation & dexmedetomidine infusion

Xylazine Withdrawal Management

Nightmare/Flashbacks **OFF LABEL USE/NOT FDA APPROVED**

If ongoing symptoms after 1 or more of the above +/- presence of PTSD-related nightmares/flashbacks:

- Prazosin 1 mg po qhs standing order
- May be titrated to maximum of 5 mg po TID
- **BP Permitting**
- Contraindications: orthostatic hypotension, HR<50, SBP <80, DBP<50
- May taper by 1mg/day if not continuing on for medical/psychiatric purposes
- Should consider if xylazine use suspected/known or weaning/weaned off dexmedetomidine infusion

Xylazine Withdrawal Management

Pain **OFF LABEL USE/NOT FDA APPROVED**

- Consider opioid-tolerant hydromorphone PCA early if acute pain
- Especially if COWS remain >8 OR
- Opioid-tolerant doses of short-acting full mu opioid agonists (oral or IV) as needed for breakthrough pain (especially if COWS remains >8)

- **Consider doses required in ED in dosage selection**

Xylazine Withdrawal Management

Pain **OFF LABEL USE/NOT FDA APPROVED**

At attending discretion, may use one or more of the following non-narcotic options:

- Acetaminophen 650 mg po TID to 1000 mg po/IV Q6H PRN or standing order
- Maximum 4000 mg/day

- Ibuprofen 600 mg po Q6H PRN (maximum 3200 mg/day)

- Ketorolac 30 mg IV Q6H PRN

- Gabapentin: start at 100 mg po TID to 300 mg po TID (maximum 3600 mg/day)
- Adjusted for renal dosing/Contraindicated in renal disease

- Tizanidine 4 mg po TID PRN for MSK pain or spasm or standing order
- **Maximum:** 36 mg/day
- Contraindications: QTC > 500 ms
- Taper by 4-8 mg/day by day 5 or once acute pain/spasm resolved

Xylazine Withdrawal Management

Pain **OFF LABEL USE/NOT FDA APPROVED**

- Consider Addiction Psychiatry Multispecialty Service (APMS) consultation +/- Ketamine and/or regional anesthesia evaluation for pain not responsive to other measures or if combining buprenorphine with full mu opioid agonists

- If using *buprenorphine concomitantly with full mu opioid agonist*, suggest *maximum dose of buprenorphine/naloxone of 4/1mg SL TID* (*total daily dose 12 mg buprenorphine*) to allow for more effective mu opioid agonist binding

Xylazine Withdrawal Management

Insomnia **OFF LABEL USE/NOT FDA APPROVED**

Melatonin

- Dosing 3 mg to 5 mg po standing Q1800
- Consider low-dose **trazodone** (25-50 mg po qhs PRN)
- If low-risk for priapism & no history of bipolar disorder
- Consider low-dose sedating antipsychotic if QTC <490ms:
- **Quetiapine** 25 to 50 mg po qhs PRN **OR**
- **Olanzapine** 2.5 to 5 mg po qhs PRN
- Consider **Prazosin** 1 mg po qhs if BP normal/elevated & presence of PTSD-related nightmares
- Attempt to avoid benzodiazepines and "**z**" drugs (**z**aleplon, **z**olpidem, es**z**opiclone)
- Unless evidence of withdrawal from GABAergic substance

Xylazine Withdrawal Management

Diarrhea **OFF LABEL USE/NOT FDA APPROVED**

Loperamide

- Loperamide 4 mg PO x1 Loading Dose
- Then 2 mg po Q3H PRN loose stool
- **Maximum:** 16 mg/day
- Standard Loperamide Dosing
- Loperamide 2 mg po q6h scheduled **+** 2 mg po q6h prn diarrhea

Xylazine Withdrawal Management

Nausea & Vomiting **OFF LABEL USE/NOT FDA APPROVED**

If QTc<490 ms:

- Ondansetron 4 mg PO/IV TID PRN

If QTc>490 ms

- Trimethobenzamide 300 mg PO Q6H PRN or
- Trimethobenzamide 200 mg IM Q6H PRN
- **Must be adjusted for renal function with CrCL ≤ 70 ml/min**
- By decreasing the dose and/or increasing the regimen
- Suppository formulation no longer available

Xylazine Withdrawal Management

Pharmacological Considerations **OFF LABEL USE/NOT FDA APPROVED**

- Attempt to **avoid concomitant use of mirtazapine** if not taking chronically while in acute stabilization phase due to central α-antagonistic effects

- Attempt to avoid benzodiazepines & "**z**" drugs (**z**aleplon, **z**olpidem, es**z**opiclone)
- Unless evidence of withdrawal from GABAergic substance
- Or active prescription for these "**z**" drugs for these patients

Appendix 2: Symptom Management Guidelines

- ALL patient should receive symptom management, regardless of MOUD status
- **Assess COWS/Symptoms Q3H while awake**
- **Consider short-term continuation of strategies used successfully in ED**

For anxiety/ agitation/ restlessness

If HR/BP is normal to elevated:

- Clonidine (first-line):
  - Start with 0.1 mg Q4H PRN for restlessness, agitation, or anxiety, consider standing dose of 0.1 mg TID if HR >100, SBP >150, or DBP >90
  - Maximum: 1.5 mg /day
  - Contraindications: SBP <80, DBP <50, HR <50
  - Taper by 0.1 -0.2 mg/day by day 5
  - Consider patch of IV if cannot tolerate PO. (Patch can take 3 days to reach steady-state)
  - Should consider if xylazine use suspected/known or weaning/weaned off dexmedetomidine gtt
- Guanfacine (alternative if bradycardia or hypotension exclude clonidine):
  - Start with 1 mg Q4H PRN for restlessness/agitation/anxiety, consider standing dose of 1 mg BID
  - Maximum: 9 mg/day
  - Contraindications: SBP <80, DBP <50, HR <50
  - Taper by 1-2 mg/day by day 5
  - Should consider if xylazine use suspected/known or weaning/weaned off dexmedetomidine gtt as an alternative to clonidine

If HR/BP is normal to low and QTc <490 ms:

- Tizanidine (alternative; can be given with either clonidine or guanfacine if acute pain):
  - Start 4 mg TID, can titrate as needed
  - Contraindications: QTC > 500 ms
  - May be increased to augment acute pain/spasm treatment
  - Maximum of 36 mg/day
  - Taper by 4-8 mg/day by day 5 or once acute pain/spasm resolved

If severe tachycardia, HTN emergency, or evidence of new onset stress cardiomyopathy:

- Consider ICU consultation and dexmedetomidine gtt

If ongoing symptoms after 1 or more of the above +/- presence of PTSD-related nightmares/flashbacks:

- Prazosin 1 mg qhs standing
  - May be titrated to maximum of 5 mg TID
  - Contraindications: orthostatic hypotension, HR<50, SBP <80, DBP<50
  - May taper by 1mg/day if not continuing on for medical/psychiatric purposes
  - Should consider if xylazine use suspected/known or weaning/weaned off dexmedetomidine gtt

For pain

Consider opioid-tolerant hydromorphone PCA early if acute pain (especially if COWS remain >8) or opioid-tolerant doses of short-acting full mu opioid agonists (oral or IV) as needed for breakthrough pain (especially if COWS remains >8). Would consider doses required in ED in dosage selection.

At attending discretion, may use one or more of the following non-narcotic options:

- Acetaminophen 650 mg TID to 1000 mg Q6H PRN or standing (maximum 4000 mg/day)
- Ibuprofen 600 mg Q6H PRN (maximum 3200 mg/day)
- Ketorolac 30 mg IV Q6H PRN
- Gabapentin: start at 100 mg TID to 300 mg TID (maximum 3600 mg/day). Contraindicated in renal disease
- Tizanidine 4 mg TID PRN for msk pain or spasm or standing (maximum 36 mg/day). Contraindications: QTC > 500 ms. Taper by 4-8 mg/day by day 5 or once acute pain/spasm resolved
- Consider APMS consultation +/- Ketamine and/or regional anesthesia evaluation for pain not responsive to other measures or if combining buprenorphine with full mu opioid agonists. If using buprenorphine concomitantly with full mu opioid agonist, suggest maximum dose of buprenorphine/naloxone of 4/1mg SL TID (total daily dose 12 mg buprenorphine) to allow for more effective mu opioid agonist binding.

Insomnia

- Melatonin 3-5 mg standing Q1800
- Can consider low-dose trazodone (25-50 mg qhs PRN) if low-risk for priapism and no history of bipolar disorder
- Can consider low-dose sedating antipsychotic if QTc <490ms: Quetiapine 25-50 mg qhs PRN or Olanzapine 2.5-5 mg qhs PRN
- Can consider Prazosin 1 mg qhs if BP normal/elevated and presence of PTSD-related nightmares
- Please attempt to avoid benzodiazepines and "z"-drugs unless evidence of withdrawal from GABAergic substance

Diarrhea

- Loperamide 4 mg PO, then 2 mg Q3H PRN loose stool (maximum 16 mg/day)

Nausea/ vomiting

- If QTc<490 ms: Ondansetron 4 mg PO/IV TID PRN
- **If QTc>490 ms: trimethobenzamine 300 mg PO Q6H PRN or 200 mg IM Q6H PRN**

Other Pharmacologic Considerations

- Please attempt to avoid concomitant use of mirtazapine if not taking chronically while in acute stabilization phase due to central alpha-antagonistic effects
- Please attempt to avoid benzodiazepines and "z" drugs such as zolpidem/eszopiclone unless concomitant GABAergic withdrawal or active prescription for these patients

Tolazoline

Reversal Agent for xylazine in animals

NOT Studied in Humans

NOT Approved for Human Use

For Veterinary Use Only

DO NOT USE!!

Atipamezole: Antisedan®

Reversal Agent for xylazine in animals

NOT Studied in Humans

NOT Approved for Human Use

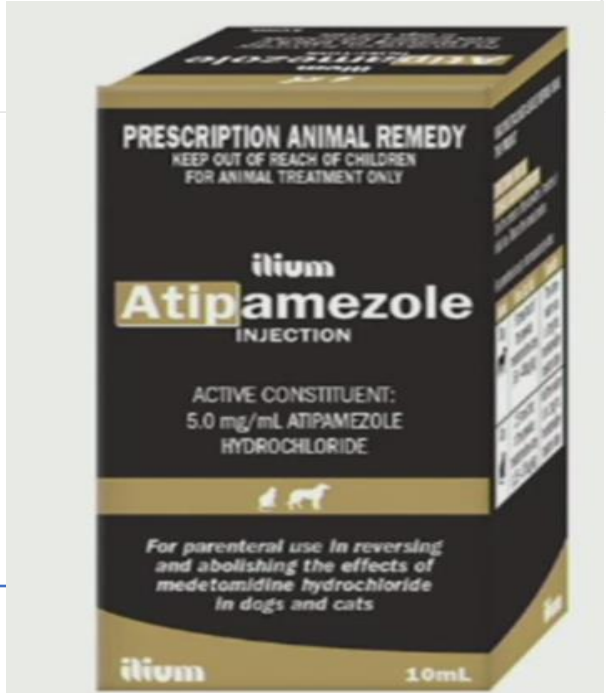
Wrong Doses severe hypotension/bradycardia

Not considered as safe as naloxone is for humans

Timing more important than with naloxone

For Xylazine's Cousin: Medetomidine

DO NOT USE!!!



Xylazine: No Documented Effective Antidote

Treatment

- No effective antidote
  - Proposed agents for withdrawal (**NOT tested in humans**)
    - α-adrenergic antagonists
      - Phentolamine, yohimbine, tolazoline
    - α-2 agonists **OFF LABEL USE**
      - Dexmedetomidine (Precedex®)
      - Clonidine (Catapres®)

Johnson J, Pizzicato L, Johnson C, Viner K. Increasing presence of xylazine in heroin and/or fentanyl deaths, Philadelphia, Pennsylvania, 2010–2019. *Inj Prev*. 2021;27(4):395-398. doi:10.1136/injuryprev-2020-043968.
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Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine

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ABSTRACT

Background: Treating opioid use disorder has reached a new level of challenge. Synthetic opioids and xylazine have joined the non-medical opioid supply, multiplying the complexities of caring for individuals in emergency departments (ED). This combination, known as 'tranq dope,' is poorly described in literature. Inadequate withdrawal treatment results in a disproportionately high rate of patient-directed discharges (also known as against medical advice dispositions, or AMA). This study aimed to describe a cohort of individuals who received a novel order set for suspected fentanyl and xylazine withdrawal in the ED.

Methods: This is a descriptive study evaluating a cohort of ED patients who received withdrawal medications from a novel protocol and electronic health record order set. Individuals being assessed in the ED while suffering from withdrawal were eligible. Individuals under age 18, on stable outpatient MOUD or who were pregnant were excluded. Treatment strategies included micro-induction buprenorphine, short acting opioids, non-opioid analgesics, and other adjunctive medications. Data collected included: demographics including zip code, urine toxicology screening, order set utilization and disposition data. Clinical Opiate Withdrawal Scale (COWS) scores were recorded, where available, before and following exposure to the medications.

Results: There were 270 patient encounters that occurred between September 14, 2022, and March 9, 2023 included in the total study cohort. Of those, 66 % were male, mean age 37 with 71 % residing within Philadelphia zip codes. 100 % of urine toxicology screenings were positive for fentanyl. Of the 177 patients with both pre- and post-exposure COWS scores documented, constituting the final cohort, patients receiving medications had their COWS score decrease from a median of 12 to a median of 4 ($p < 0.001$). The AMA rate for this cohort was 3.9 %, whereas the baseline for the population with OUD was 10.7 %. Recorded adverse effects were few and resolved without complication.

Conclusions: Fentanyl and xylazine withdrawal are challenging for patients and providers. A novel tranq dope withdrawal order set may reduce both COWS scores and rate of patient-directed discharge in this cohort of patients, though further investigation is needed to confirm findings.

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Study Methods

Study Design & Setting

- Retrospective observational study based on real world experience after implementation of novel order set to address acute fentanyl/xylazine withdrawal in ED
- Study occurred at two urban hospitals in Philadelphia, PA: 1 academic, 1 community
- Academic hospital, approximately 76,000 visits annually, level 1 academic tertiary care & trauma center
- Community hospital, approximately 34,000 visits annually, non-trauma center 2.5 miles from main hospital

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Study Methods

Participant Selection
- Study took place from 9/1/2022 to 5/5/2023

Inclusion Criteria
- ED patients who self reported non-medical opioid use disorder (OUD)
- Physicians deemed in need of withdrawal treatment, secondary to medical or surgical condition
- Final cohort for analysis consisted of all patients that presented with OUD, received at least 1 medication from 1 of 4 order pathways during study period, & had both pre- & post-exposure COWS score documented

Exclusion Criteria
- Pregnancy, children <18 yo, patients taking stable doses of outpatient medication for opioid use disorder (MOUD)

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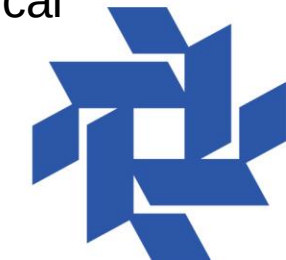
Study Methods

Participant Selection

- Currently difficult to ascertain toxicology data in assessing xylazine use
- Time relevant Philadelphia Department of Public Health data showed 98% of all non-medical opioid samples tested contained both fentanyl & xylazine [13]
- Other studies confirm high levels of correlation between fentanyl & xylazine in Philadelphia community [14]
- Xylazine use assessed by clinical suspicion & patient report of non-medical opioid use



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Study Results

Study Cohort Description

- Total: 37,101 encounters in two EDs
- 24.3% admission rate
- 1.1% rate of AMA
- 1284 patients screened positive for OUD in triage based on standardized questioning
- 24.2% admission rate
- 10.7% rate of AMA

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Study Demographics

Table 1
Demographic Data for study population.

Total Cohort with excluded patients		x	%	Final Study Cohort		x	%
Sex				Sex			
	Male	179	66.05		Male	122	68.93 %
	Female	91	33.70		Female	55	31.07
Race				Race			
	White	208	77.04		White	132	74.58
	Black	35	12.96		Black	27	15.25
	Other	23	8.52		Other	16	9.04
	Asian	2	0.74		Asian	0	
	American Indian or Alaskan Native	2	0.74		American Indian or Alaskan Native	2	1.13
Ethnicity				Ethnicity			
	Non-Hispanic/Latino	234	86.67		Non-Hispanic/Latino	150	84.75
	Hispanic/Latino	33	12.22		Hispanic/Latino	26	14.69
	N/A	3	1.11		N/A	1	00.56

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Table 2 Urine Toxicology Screening Results (N = 214)

Drug	Positive	Percentage
Fentanyl	214	100 %
Cocaine	150	70.09 %
Amphetamines	74	34.58 %
Cannabinoid	72	33.64 %
Opiates	65	30.37 %
Benzodiazepines	57	26.64 %
Methadone	38	17.76 %
Barbiturates	5	2.34 %

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Study Results

Study Cohort Description

- 177 patients met criteria for final analysis
- Male: 122 (68.93%, 95% CI 61.47–75.54)
- Median age: 37 (IQR 33–47)
- Slightly older male vs female population (38 [IQR 32–39] vs 34 [IQR 33.25–49.75], p = 0.006)
- Proportions of race & ethnicity were similar to full cohort
- White: 74.58% (95 % CI 67.39–80.68)
- Not Hispanic or Latino: 84.75% (95% CI 78.40–89.54%)

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Study Results

Study Cohort Description

- Urine Toxicology Screen Performed: 150 (84.75%, 95% CI 78.40–89.54%)
- Fentanyl Positive: 100%
- Philadelphia Zip Code: 132 (74.58%, 95% CI 67.39–80.68%)
- In **60 encounters** (33.89%, 95% CI 27.07–41.44%) patients received medications from **mild symptom pathways**
- **117** patients (66.1%, 95% CI 58.56–72.93%) received **severe symptom pathways** (Fig. 1)

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Study Results/Outcomes

Main Results

177 encounters:

- 108 admitted (61.02%, 95% CI 53.39–68.16%)
- 24 observation (13.56%, 95% CI 9.05–19.70%)
- 35 discharged (19.77%, 95% CI 14.33–26.56%)
- 4 to rehabilitation/recovery facility (2.26%, 95% CI 0.7–6.06%)
- 6 AMA/directed own discharge (3.9%, 95% CI 1.39–7.57%)

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Appendix A. Four Withdrawal Order Set Pathways

Pathway 1: Mild (or no IV) AND Normal QTc
- Buprenorphine 150 mcg Buccal
- Oxycodone 10 mg PO Liquid
- Olanzapine 5mg PO ODT
- Tizanidine 4 mg PO

Pathway 2: Mild (or no IV) AND Prolonged/Unknown QTc
- Buprenorphine 150mcg Buccal
- Oxycodone 10 mg PO Liquid
- Olanzapine 5mg PO ODT
- Guanfacine 2 mg PO

Pathway 3: Severe AND Normal QTc
- Buprenorphine 150 mcg Buccal
- Hydromorphone 2 mg IVP
- Ketamine 0.15 mg/kg up to 15 mg (rounded to nearest 5mg) via IVP over 2 minutes
- Droperidol 2.5 mg IVP
- Diphenhydramine 25 mg IVP
- Tizanidine 4 mg PO
- Lactated Ringers 1L Bolus

Pathway 4: Severe AND Prolonged/Unknown QTc
- Buprenorphine 150 mcg Buccal
- Hydromorphone 2 mg IVP
- Ketamine 0.15 mg/kg up to 15 mg (rounded to nearest 5mg) via IVP over 2 minutes
- Olanzapine 10 mg PO ODT
- Diphenhydramine 25 mg IVP
- Guanfacine 4 mg PO
- Lactated Ringers 1L Bolus

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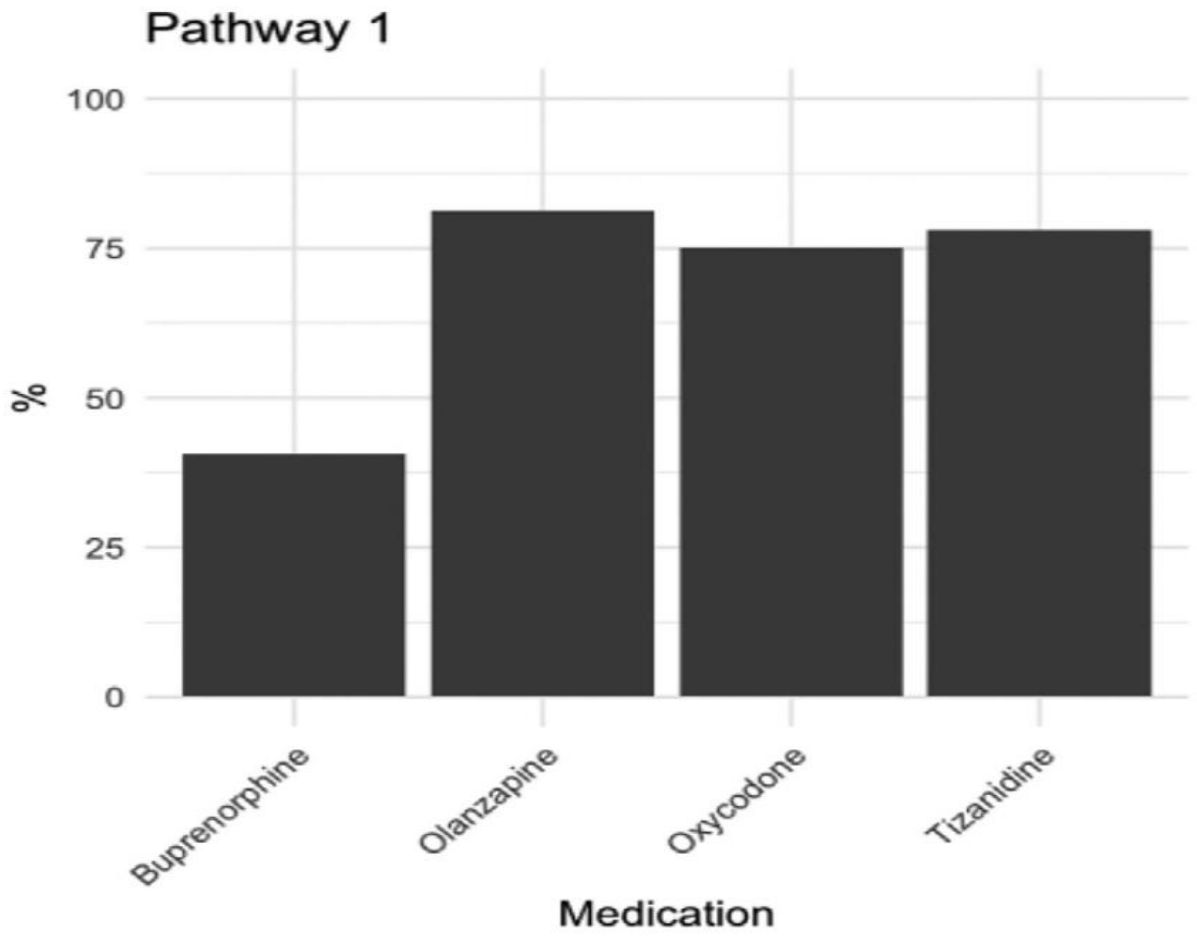

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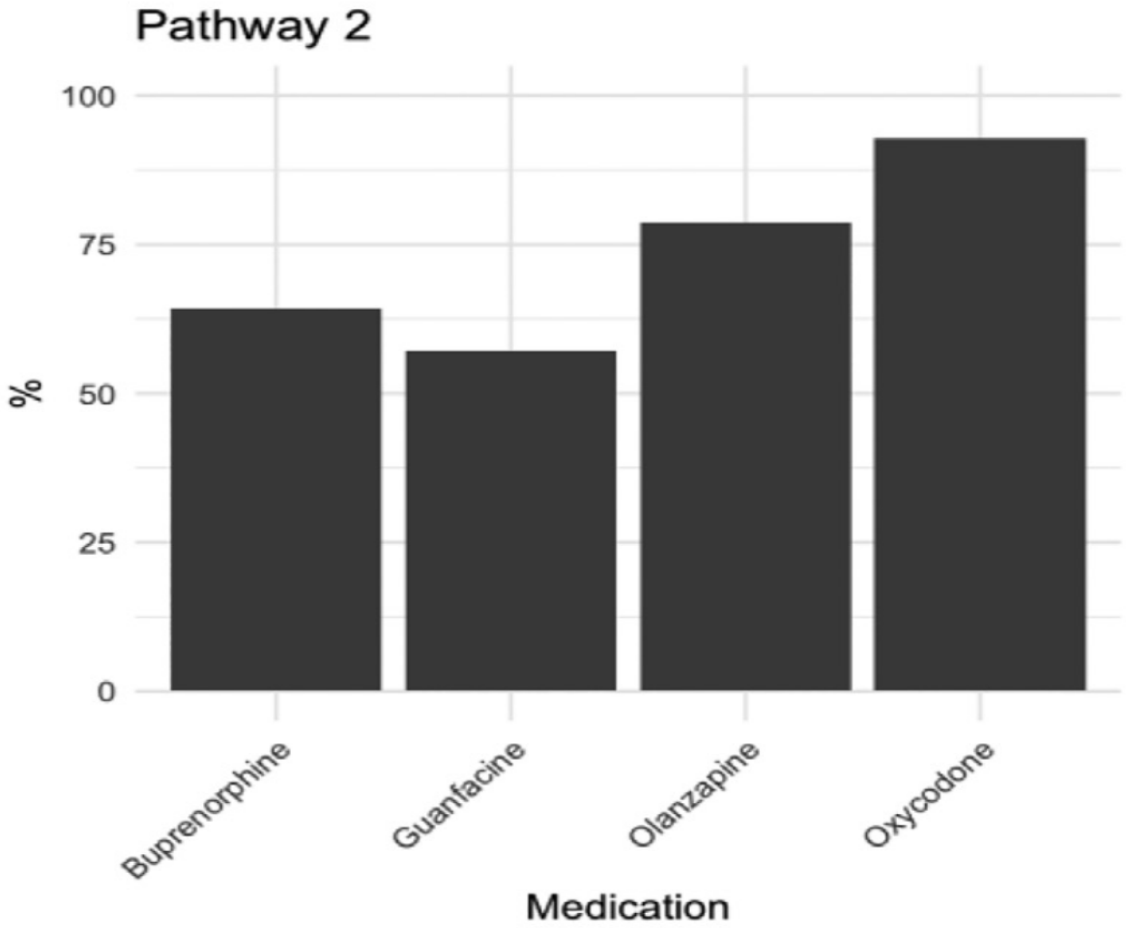

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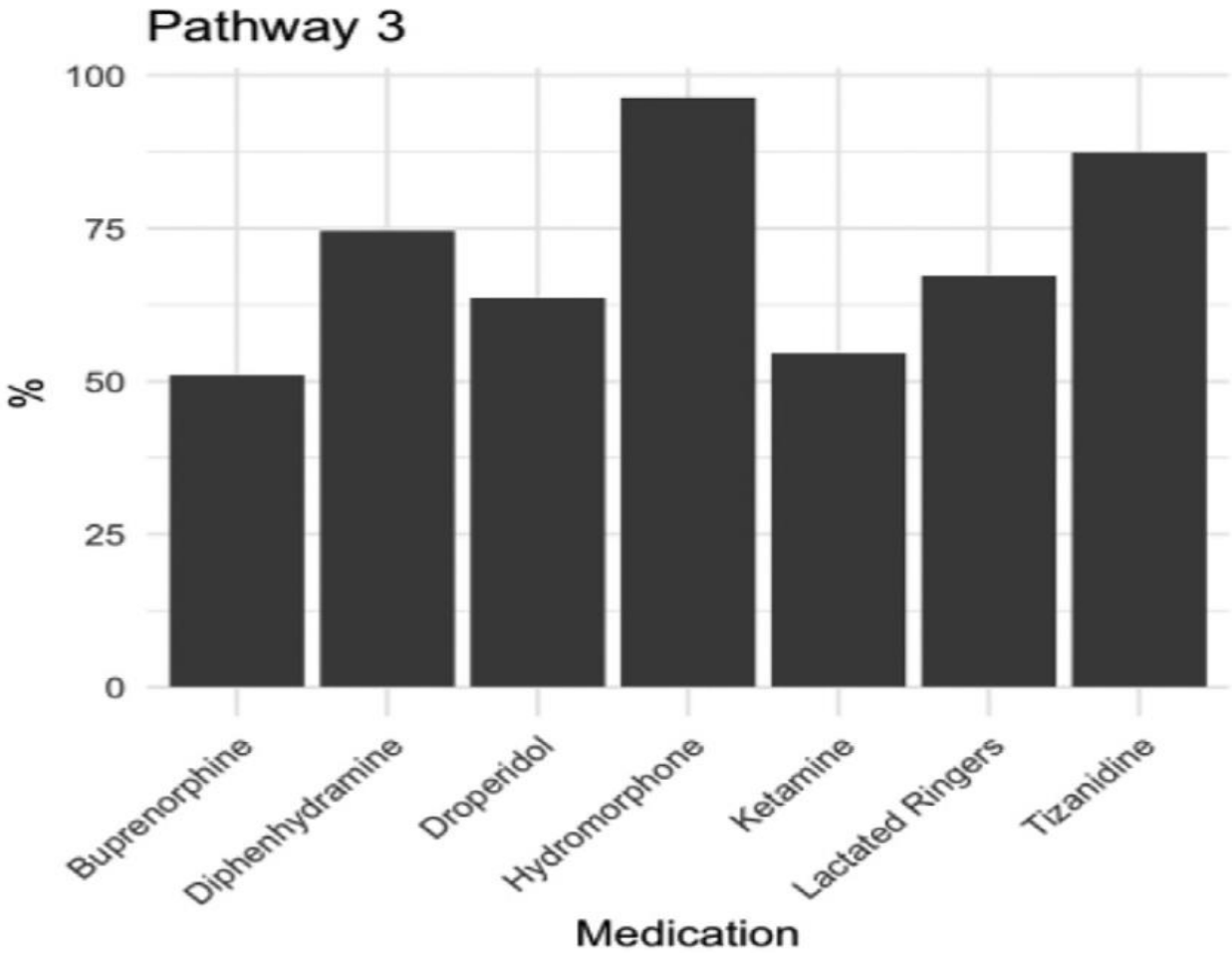

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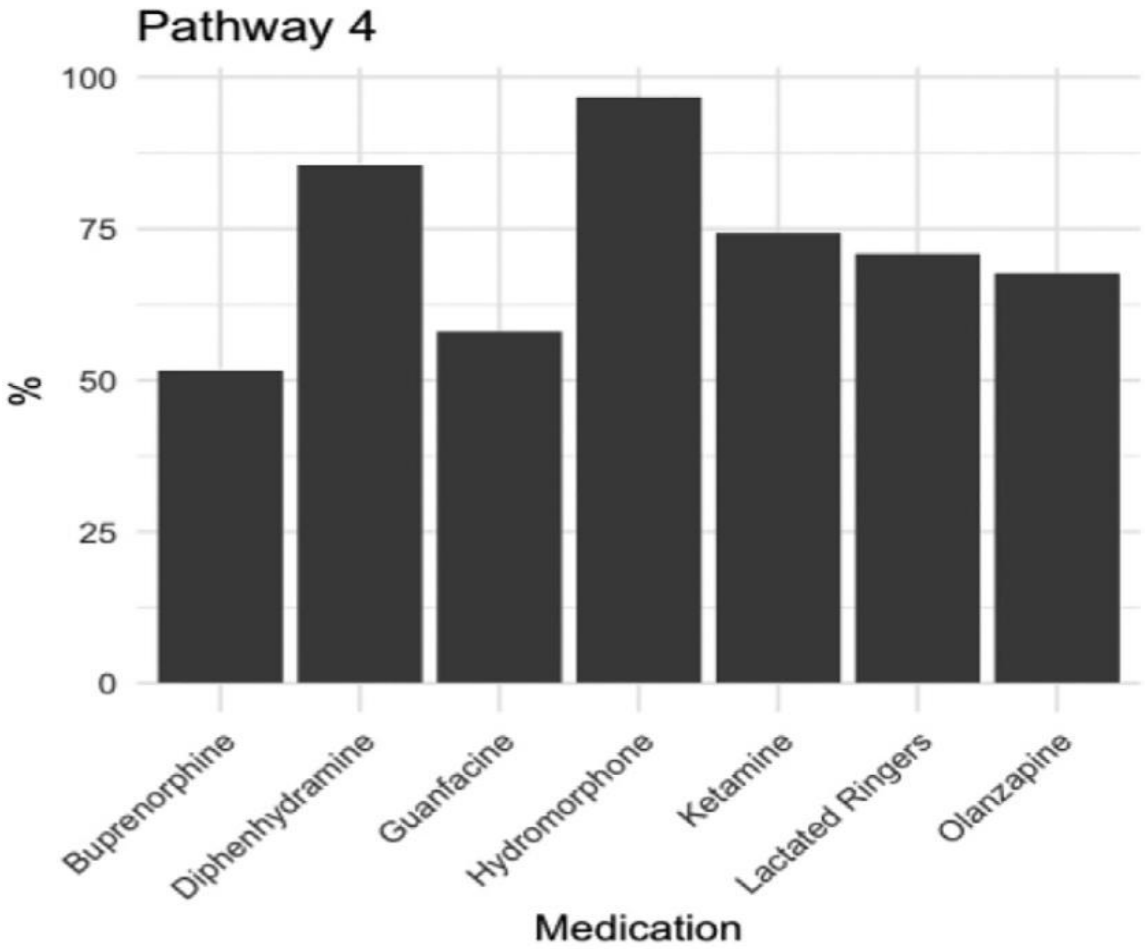

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Pathways 1 & 2
Mild Symptom
Cohort

Pathways 3 & 4
Severe Symptom
Cohort

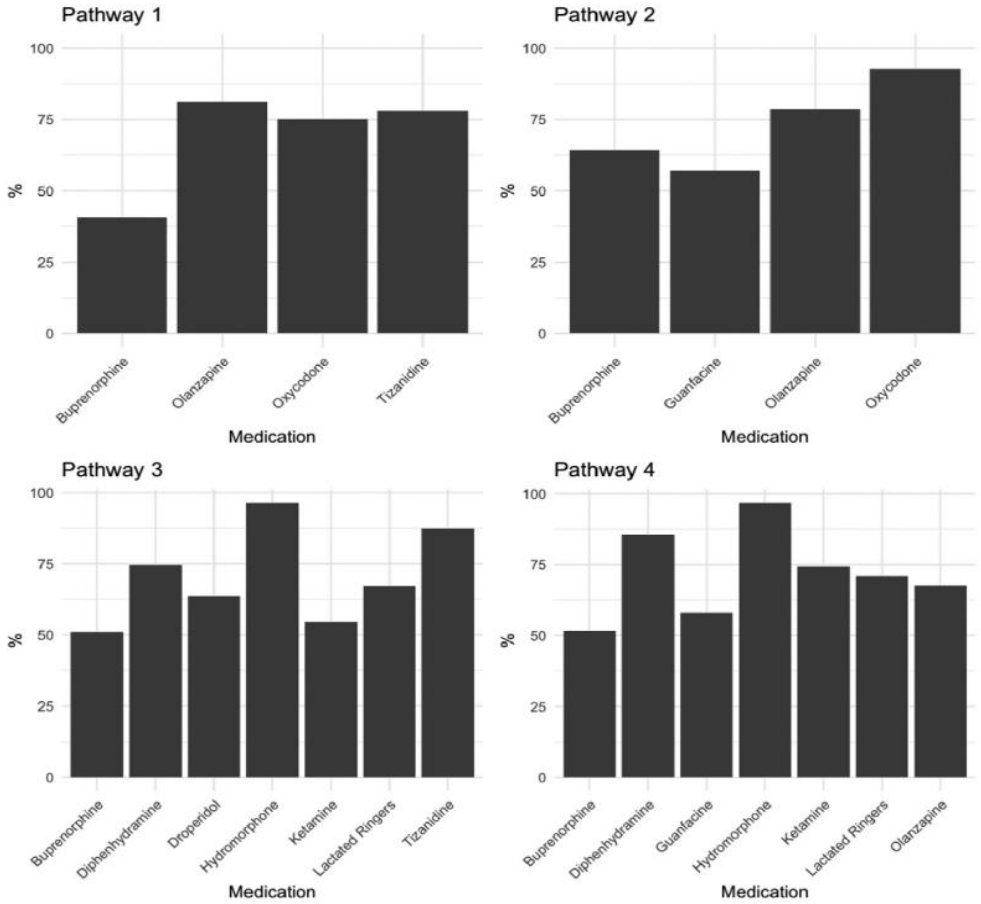

Fig. 2. Frequency of medications provided per treatment pathway.

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Adverse Event Results

Adverse Events

- Recorded adverse effects impacted 11 patients
- All resolved without complication
- 2 cases of overt dystonic reaction (1 dystonia, 1 akathisia)
- 2 cases of fluid responsive hypotension (both in patients with severe, acute illness)
- 3 cases of asymptomatic bradycardia
- 1 case of mild hypoxia requiring 2 L of oxygen via nasal cannula

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Adverse Event Results

Adverse Events

- 1 patient required non-invasive positive pressure ventilation (PPV) 8 hr after medication provision, in setting of multifocal pneumonia
- 1 patient who suffered single epileptic seizure, in setting of concomitant benzodiazepine withdrawal
- Seizure was treated with oral benzodiazepines & did not recur during their ED stay
- No cases of ventricular dysrhythmias, intubation or need for reversal medications
- No recorded instances of precipitated withdrawal
- All adverse effects were deemed, in association to treatment, as possible, or probable based on Naranjo probability algorithm

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Droperidol Use

Discussion

Droperidol

- Widely used butyrophenone neuroleptic
- Effective analgesic for those with opioid tolerance
- Can act to decrease opioid requirements in those with acute pain stimuli [40]
- Known for anxiolytic [41] & antiemetic effects [42]
- Labeled with FDA black box warning for risk of QT prolongation/ventricular dysrhythmia
- Actual risk in this population is unknown
- Other ED studies have shown reasonable safety profile [43]

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Olanzapine Use

Discussion

Olanzapine

- Given unclear risk of droperidol induced prolongation of the QT interval in this patient population

- **Olanzapine, modern atypical antipsychotic, chosen for pathways where QT prolongation was a concern**

- Olanzapine has shown efficacy in treating opioid withdrawal & can potentially have its own opioid potentiating effects [44,45]

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Clonidine or Lofexidine Use in Study

Discussion

- Given α-2 receptor agonism of xylazine, α-agonist therapies were added to pathways

- Most commonly studied α-2 agonists for opioid withdrawal have been clonidine & lofexidine [46]

- Clonidine deferred due to risk of prolonged hypotension when given with multiple other medications

- Lofexidine deferred due to cost

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Diphenhydramine & RL/LR Use

Discussion

Diphenhydramine

- Effective antihistamine/anticholinergic medication
- Treat pruritus & cholinergic symptoms of opioid withdrawal [49]

Ringer's Lactate IV fluid

- Treat common risk of hypovolemia/electrolyte derangement in patients suffering from severe withdrawal
- Prevent treatment related hypotension/mitigate risk of electrolyte mediated prolongation of QT interval

- In combination, these adjunctive interventions demonstrated significant impact

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Study Results

Discussion

- **Most patients** in cohort **received severe treatment pathway**

Treatment groups were notably different in terms of response

- **Statistically significant delta COWS of:**
- **10.03 between high dose group**
- **3.67 in low dose group**

- **Given similar safety profile, reasonable to utilize severe pathway medications when likelihood of worsening withdrawal is high**

Main concerns with using multiple adjunctive medications to synergize & potentiate opioid effects are:

- risks of oversedation
- other adverse effects related to pre-existing patient polysubstance use

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Appendix 6: Clinical Opiate Withdrawal Scale (COWS)

Resting Pulse Rate: *(Record beats per minute) measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset:** *over last ½ hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *Over past ½ hour not accounted for by room temperature or patient activity* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor:** *Observation of outstretched hands* 0 No tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness: *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	**Yawning:** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size: 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability:** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches: *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/ muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin:** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing: *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	**Score:** 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

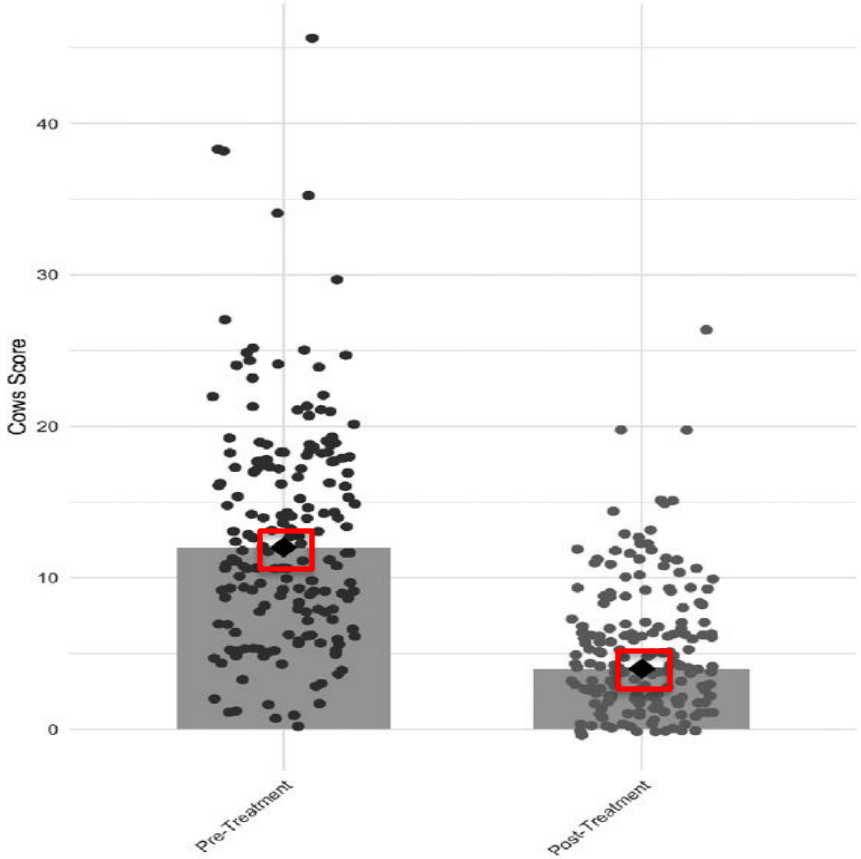

Fig. 4. Scatter plot of COWS pre and post treatment demonstrating reduction in median score.

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

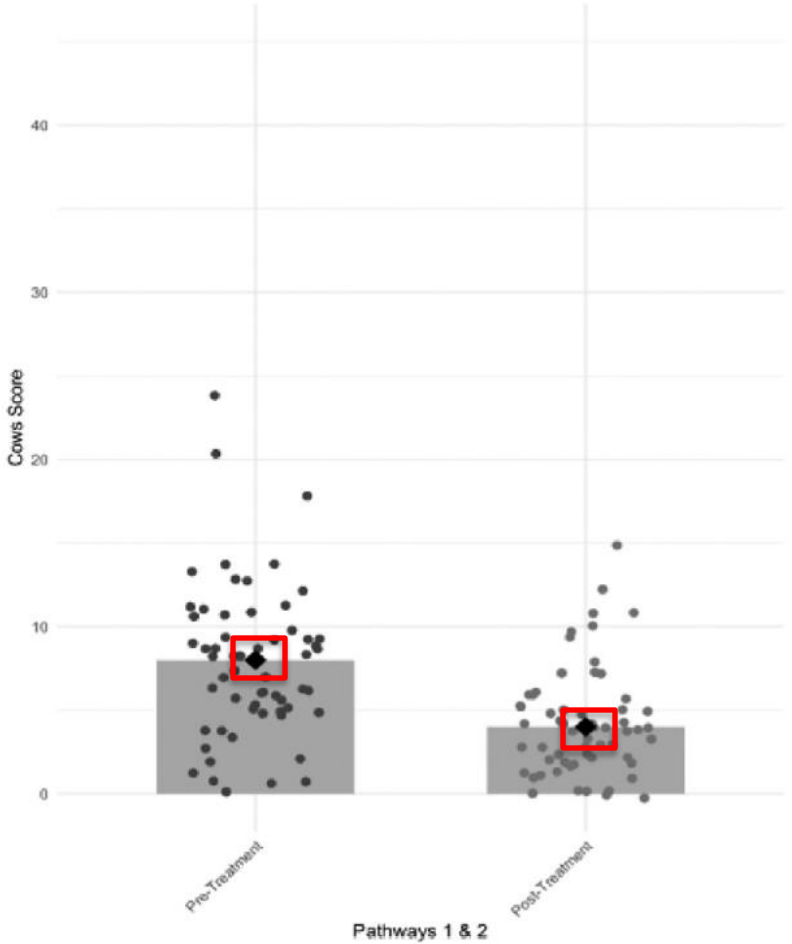

Fig. 5. Scatter plot of COWS pre- & post-treatment, separated by mild vs. severe symptom cohort, demonstrating reduction in median score

Pathways 1 & 2

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

Results

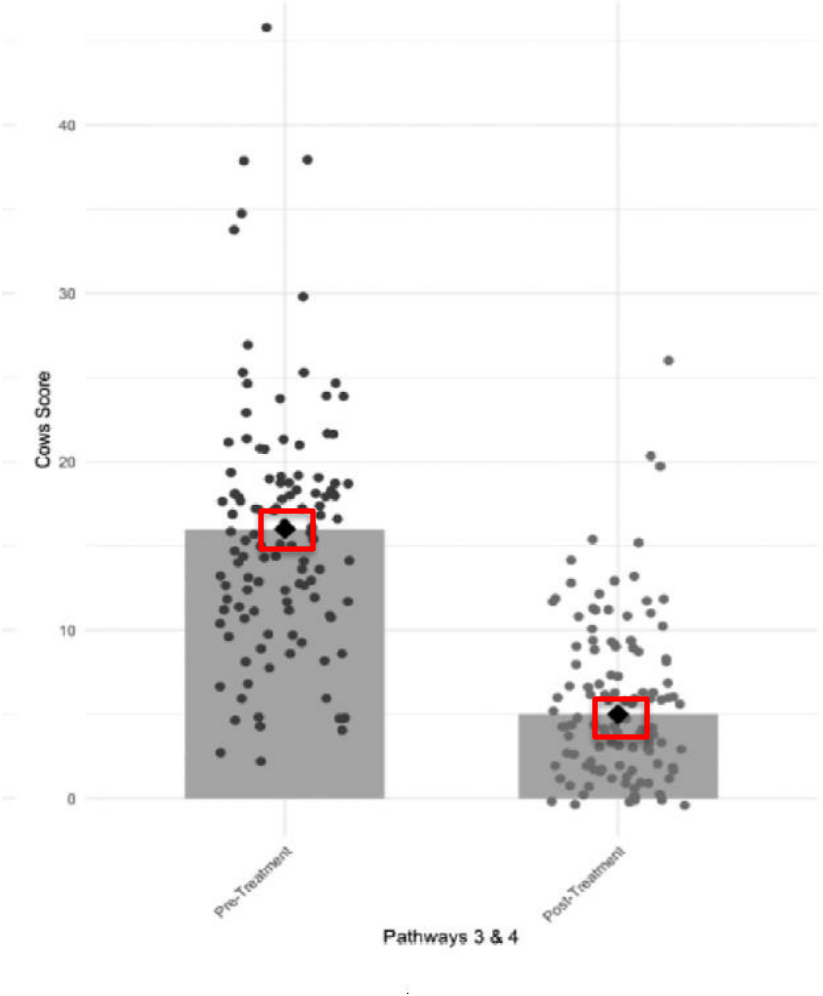

Fig. 5. Scatter plot of COWS pre- & post-treatment, separated by mild vs. severe symptom cohort, demonstrating reduction in median score

Pathways 3 & 4

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

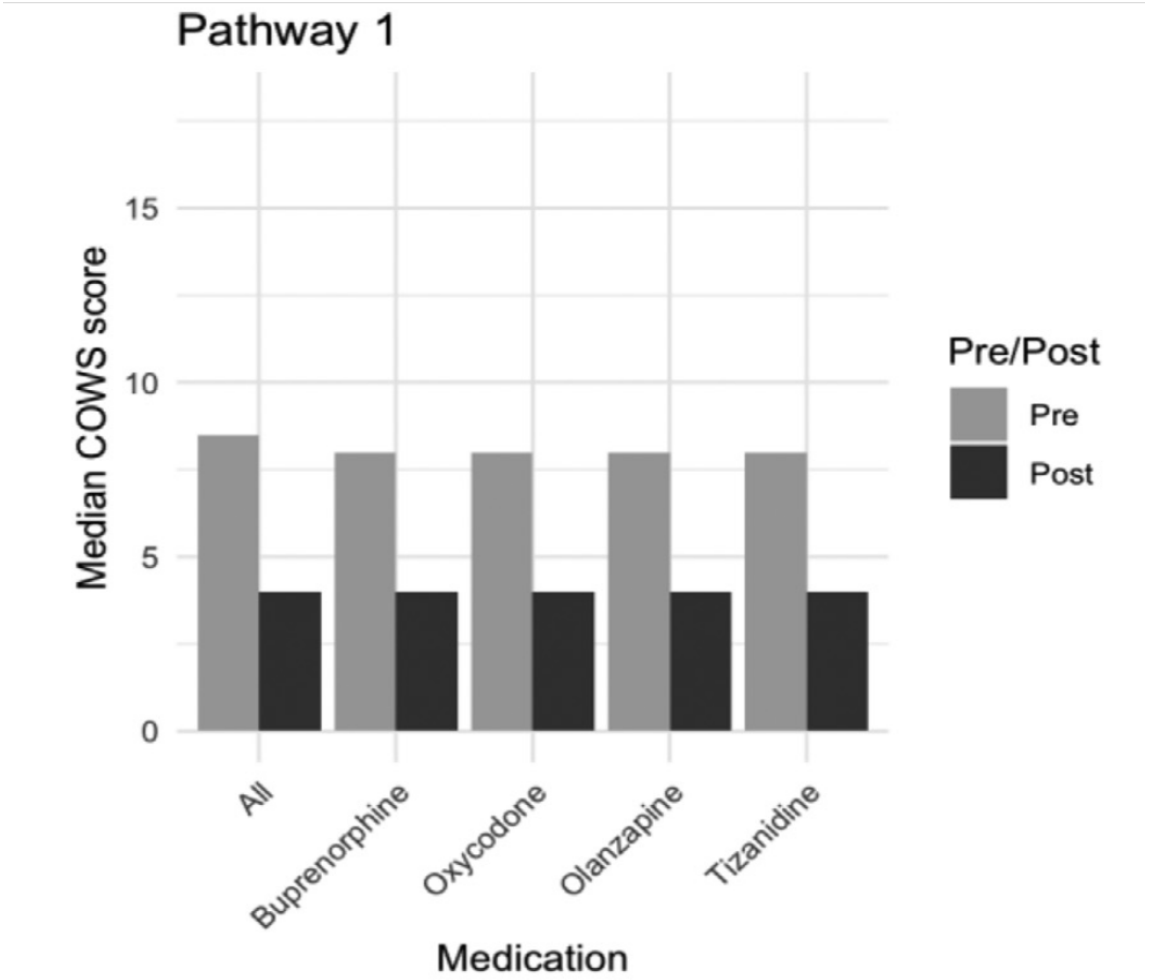

Fig. 6. Median pre & post treatment COWS scores delineated by all vs. individual medications received in each pathway

Pathway 1

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

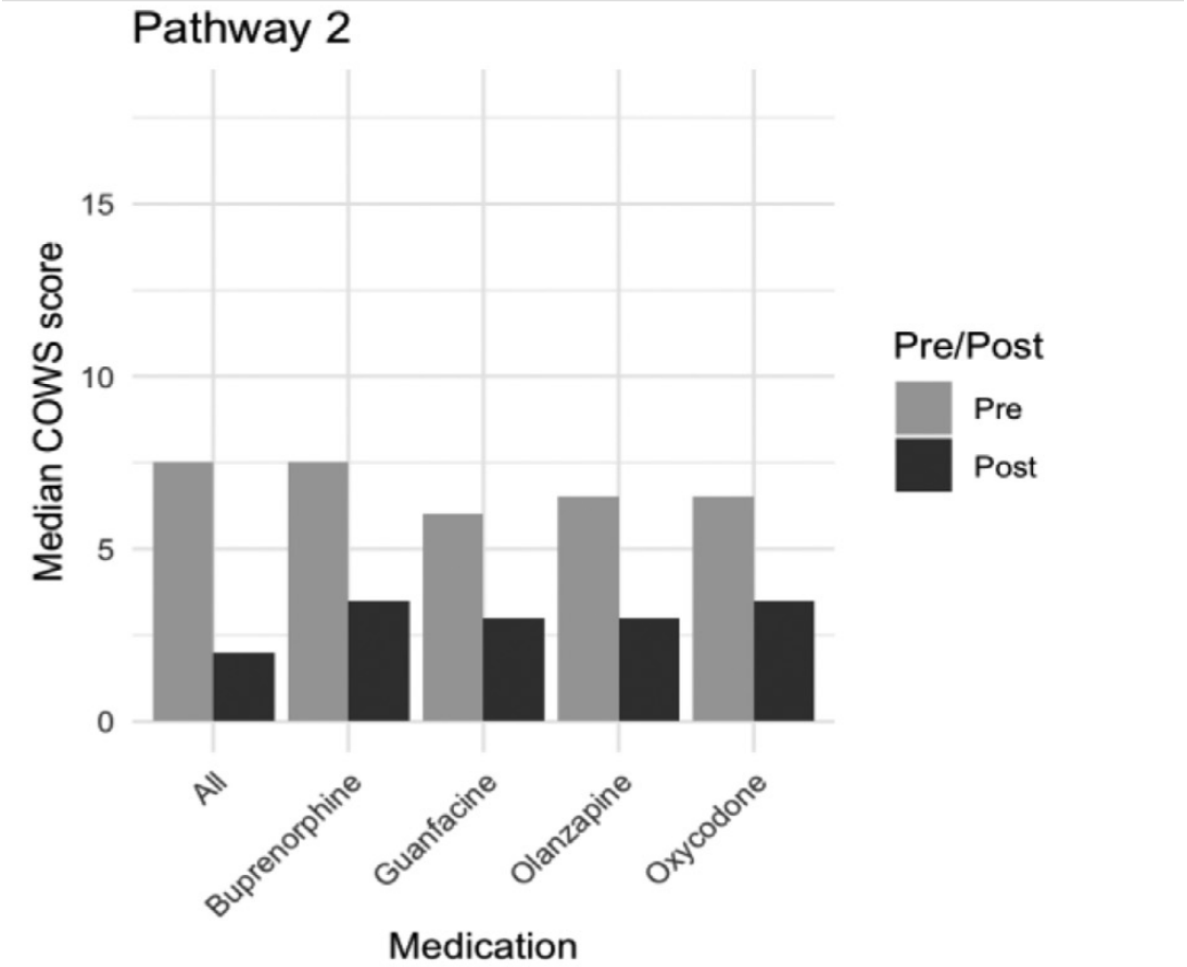

Fig. 6. Median pre & post treatment COWS scores delineated by all vs. individual medications received in each pathway

Pathway 2

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

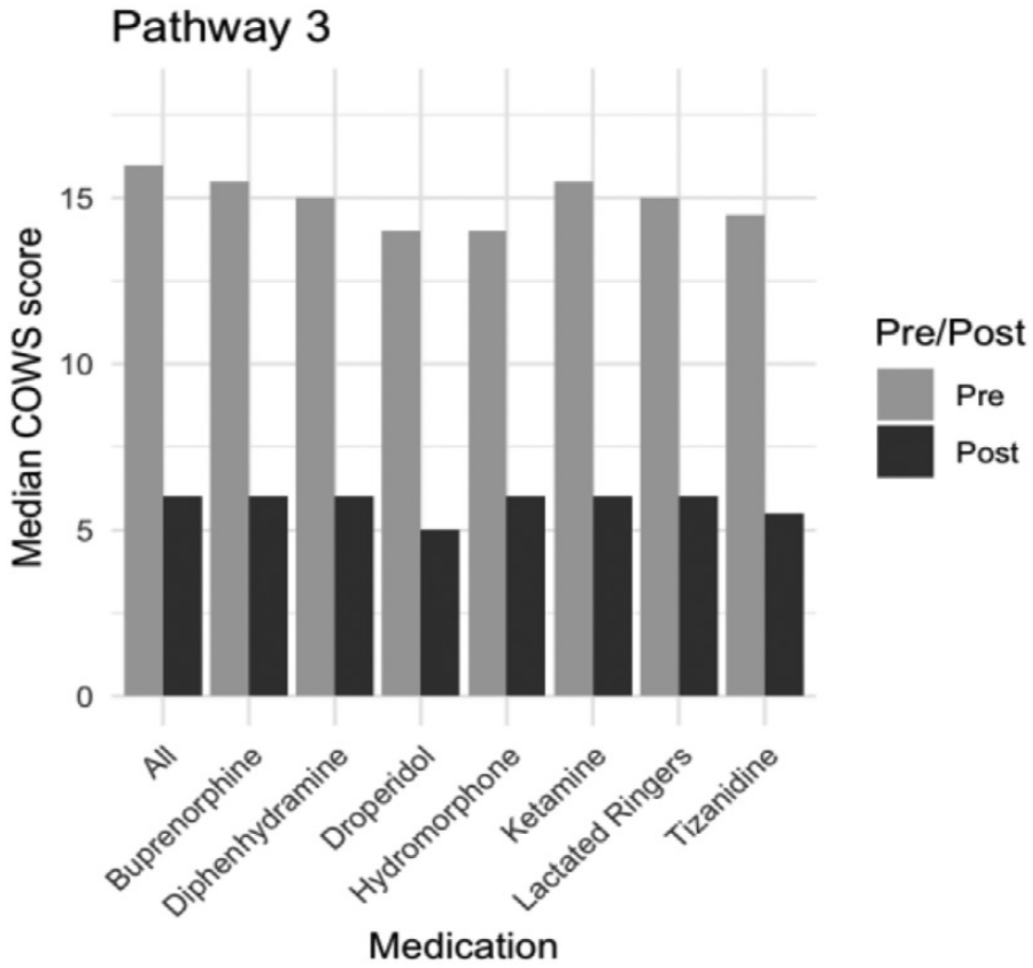

Fig. 6. Median pre & post treatment COWS scores delineated by all vs. individual medications received in each pathway

Pathway 3

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

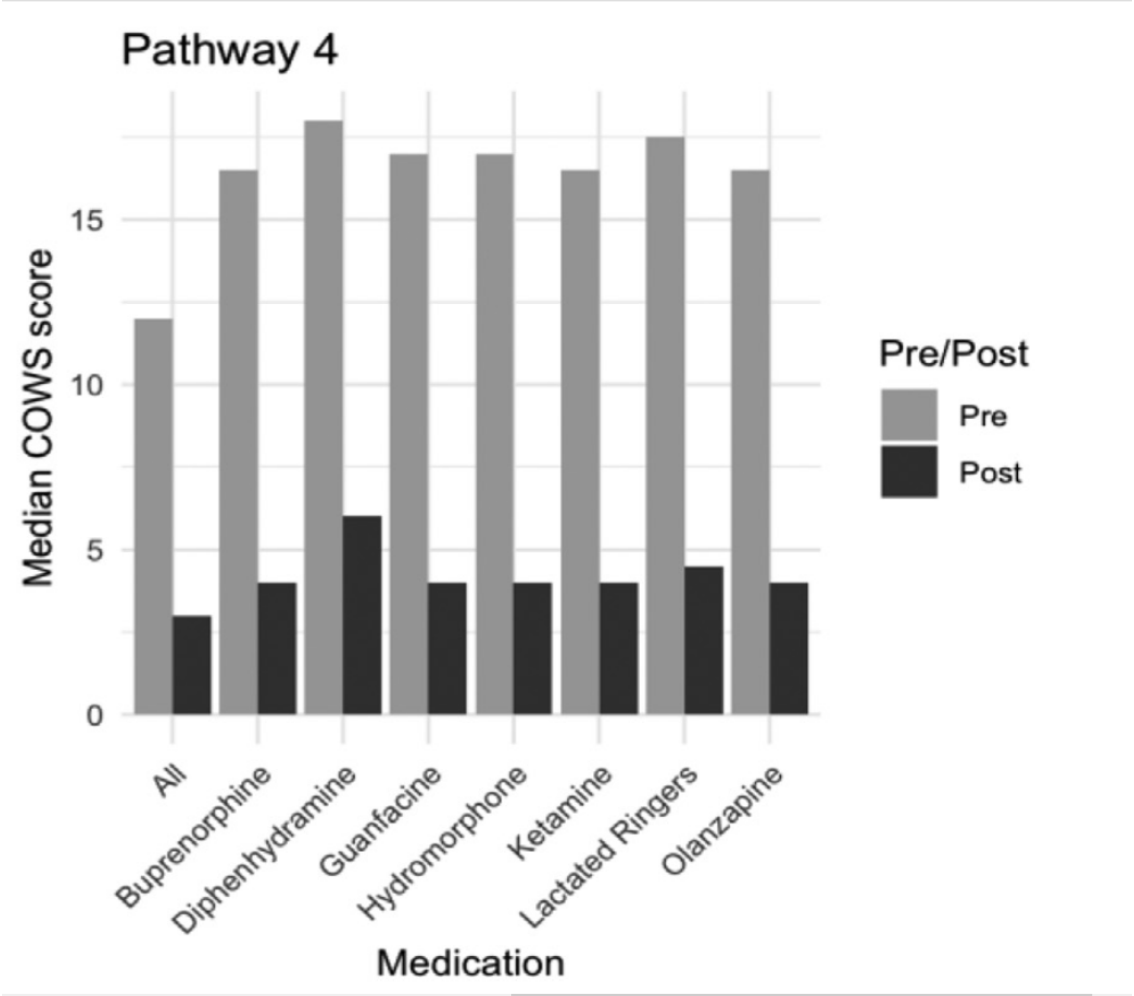

Fig. 6. Median pre & post treatment COWS scores delineated by all vs. individual medications received in each pathway

Pathway 4

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

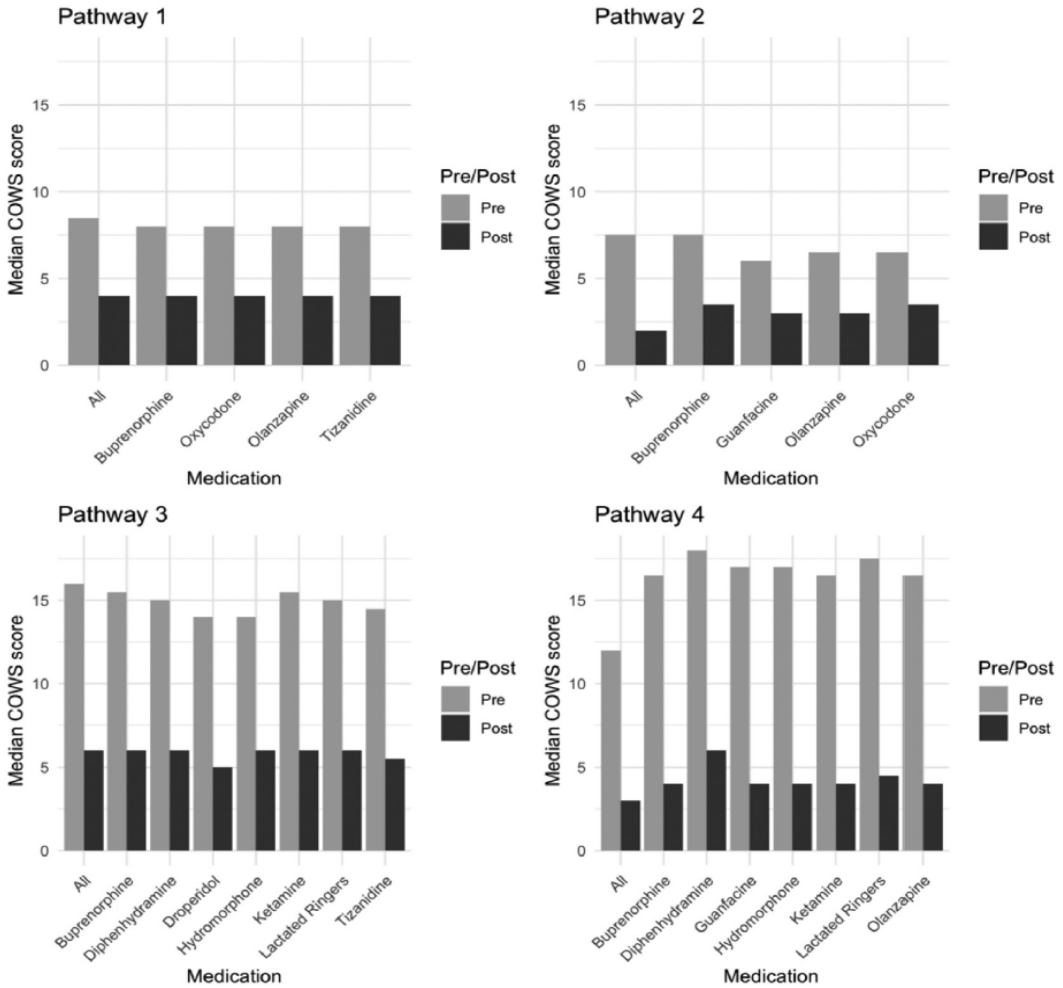

Fig. 6. Median pre & post treatment COWS scores delineated by all vs. individual medications received in each pathway

All Pathways: 1, 2, 3 & 4

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

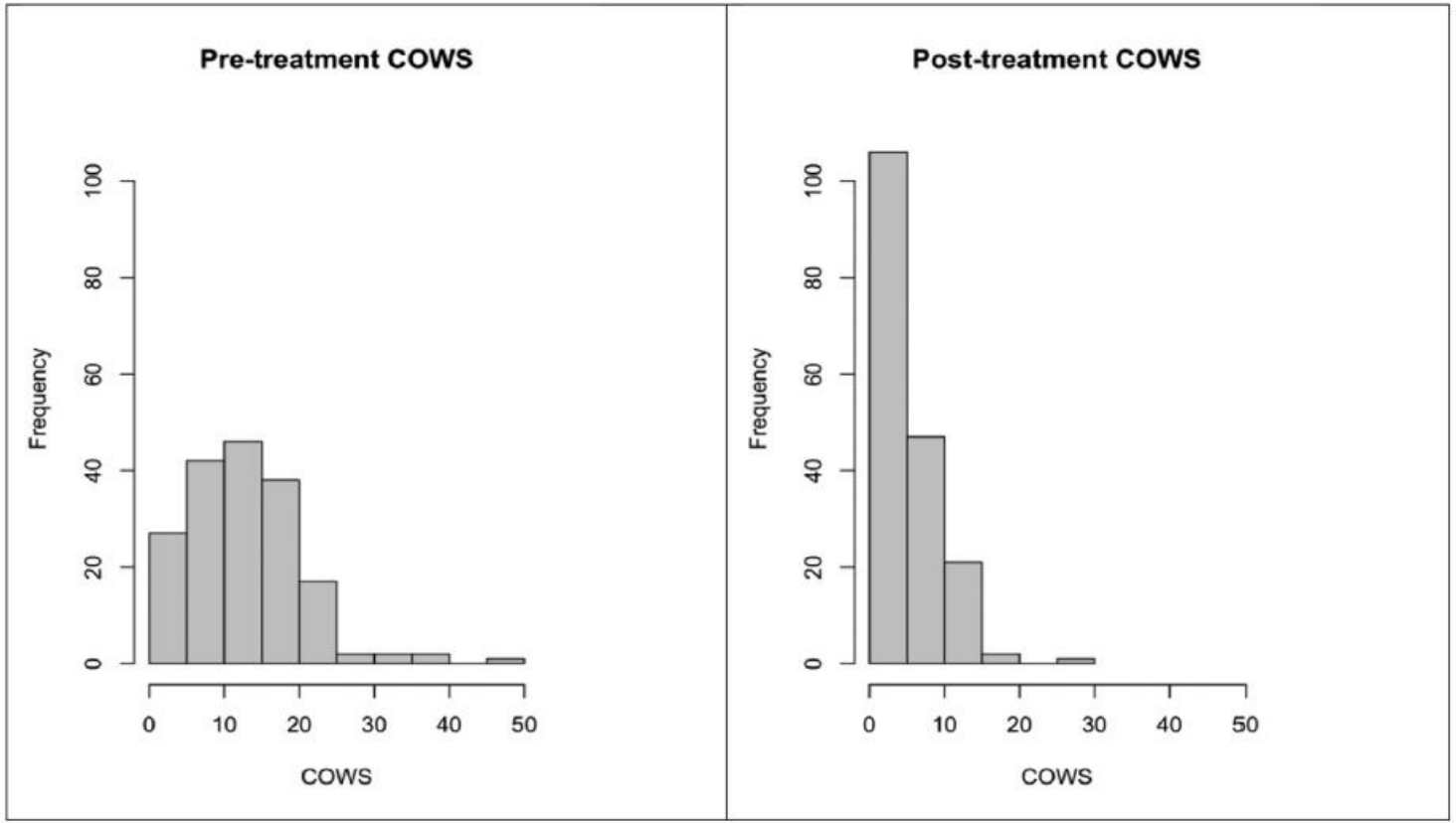

Fig. 3. Histogram of COWS pre and post treatment demonstrating reduction in score.

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

Toxicology Screening Results

Discussion

- >70 % of patients with toxicology screening positive for both fentanyl & cocaine
- >33% positive for amphetamines
- >25% positive for benzodiazepines
- Profound level of multi-substance use in group
- > 1 in 6 patients also tested positive for methadone
- Complex milieu of vulnerable substance use & recovery

London, K et al. *Tranq Dope: Characterization of an ED cohort treated with a novel opioid withdrawal protocol in the era of fentanyl/xylazine*. American Journal of Emergency Medicine 85 (2024) 130–139. August 30, 2024. https://doi.org/10.1016/j.ajem.2024.08.036

Results

Conclusions

- Novel set of withdrawal treatment pathways in EHR can be used in treatment of fentanyl withdrawal with presumed xylazine exposure
- May reduce COWS scores & rate of patient-directed discharge (AMA)
- Adverse events were few, mild & self-resolving or complicated by severe acute medical pathology or concomitant polysubstance withdrawal

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Study Summary

Results

- Patient Encounters: 270
- Timeframe: 9/14/2022 to 3/9/2023
- Male: 66 %
- Mean age: 37 years
- Residing within Philadelphia zip codes: 71%
- Urine toxicology screenings positive for fentanyl: 100%
- 177 patients pre & post-exposure COWS scores documented = final cohort
- Patients receiving medications COWS score decrease from median of 12 to 4 ($p < 0.001$)
- AMA rate for cohort: 3.9 %
- Baseline AMA rate for population with OUD: 10.7 %
- AMA rate reduction from 10.7% to 3.9%
- Few recorded adverse effects/resolved without complication

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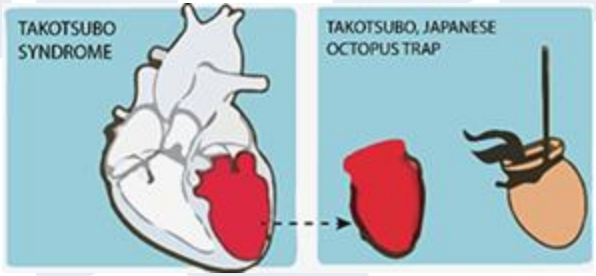
Xylazine-Related Patient Case

- 30 y.o. female with PMH of depression, endocarditis, reportedly untreated HCV, IV drug use, polysubstance abuse disorder (opioid, cocaine, heroin & benzo)
  - Reported injecting fentanyl & ketamine into right neck vein
  - Reported tapering off **30 bundles fentanyl** on her own
  - Presented to ED with 3 days of nausea/blood-streak vomiting
    - Reported vomiting > 20 times
    - Found to be agitated, had worsening hypoxia & was in shock with cold extremities
    - Temp. 103; SVT with HR in 180s; RR 30
    - Labs:
      - pH 7.47; pCO_2 30; HCO_3 21;
      - WBC 21.4; Hgb 13; Plat 181;
      - Na 140; K 3.4; Cl 105; Mg 1.4; BG 148 (A1C 5.4)
      - BUN 27; Scr 1.87 (baseline ~1.0)
      - Alb 3.5; Bilirubin (T) 4.1; Bilirubin (D) 2.8;
      - ALP 77; AST 334; ALT 110; INR 1.33
      - Lactate 2.1; Pro-BNP > 35,000; TSH 0.55
      - Troponin peak of 14,000; Troponin T 1933

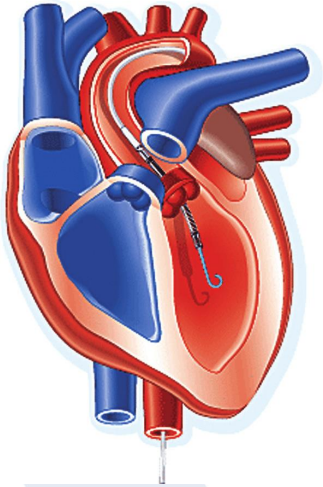
Xylazine-Related Patient Case

- ECG:
  - Sinus with atrial premature contractions (APCs), Left anterior fascicular block (LAFB), Nonspecific T-wave changes, QTC 434 ms
- Bedside Echo:
  - **Severe LV dysfunction, moderate to severe RV dysfunction with some suggestion of relative increased contractility at the base, suggestive of a stress induced cardiomyopathy (Takotsubo)**
  - **Ejection Fraction (EF): 10-15%**
- Chest X-ray:
  - Diffuse bilateral patchy opacities, **severe edema & possible pneumonia**
- HCV: **HCV(+)**, HBV(-), HAV(-)
- Covid 19 Swab (-); MRSA swab wasn't done in ED
- UA report from foley catheter grossly unremarkable
  - Glucose (+), Protein (+), Blood (+)
  - Ketones (-), Nitrite (-), Leukocyte (-)



Management

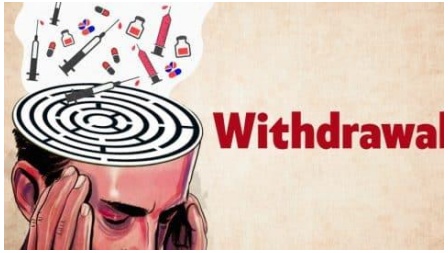
- Acute hypoxic respiratory failure:
  - Intubated (FIO_2 50%) & Sedated
    - **Fentanyl IV** (100mcg/hr)**, Midazolam IV** (4 mg/hr)
    - **Propofol infusion** (30 mcg/hr; TG 169) (Stopped Day 2)
  - **Furosemide** for pulmonary edema
- **SVT:**
  - Failed adenosine & cardioversion in ED
  - **Amiodarone IV** (Stopped on Day 3)
- **Cardiogenic shock:**
  - Impella & Pulmonary Artery Catheter placed
    - **PA 46/31** (15-28/5-16); **CVP 12** (1-10); **CI 1.3** (2.5-4)
  - **Milrinone** (0.375 mcg/kg/min) **& Norepinephrine** (0.5 mcg/kg/min)
- Sepsis:
  - No culture available; Possible pneumonia vs IV drug use
  - **Vancomycin, Piperacillin-tazobactam**
- AKI
  - On admission Scr 1.87; CrCl 74 (baseline Scr ~1.0; CrCl >130)
  - Likely due to cardiogenic shock, continue to monitor



Management

- Hypokalemia & Hypomagnesemia
  - Replenished with **KCl IV & Magnesium sulfate IV**
- DVT prophylaxis:
  - **Heparin drip**
- PUD prophylaxis:
  - **Pantoprazole IV**
- IVDU:
  - **Alcohol Withdrawal Syndrome (AWS) protocol**
  - **Clinical Opiate Withdrawal Scale (COWS) protocol**
- OG tube placed once hemodynamically stable
- Home Med per family
  - Alprazolam, Gabapentin, Citalopram
- Other inpatient medications:
  - Chlorhexidine, Senna, Polyethylene glycol

Management



- Palliative care consult:
  - Patient was at rehab in methadone maintenance program
  - Primary care team planned to wean ventilation
    - Day 3: recommend initiating methadone 10 mg daily while sedated to help with mental status
- Psychiatry consult (Day 3):
  - **“30 bundles” (likely 30 bags) fentanyl presumed to have xylazine** based on Novel Psychoactive Substances (NPS) Discovery reports from her neighborhood in Philadelphia
  - CAM-ICU (+); Opioid withdrawal (+)
  - **Presumptive xylazine use disorder & withdrawal**

Management

- **Psychiatry Recommendation based on practicing experience** (Day 3):
  - Restart **alprazolam PO 2 mg TID**
    - Alprazolam withdrawal patients often have poor response to other benzodiazepine replacements in setting of delirium
  - Strongly consider augment sedation with **dexmedetomidine** or **alternative alpha agonist**
    - **Cases of similar presentation with improved cardiac contractility after reinitiation of alpha agonist**
  - If unable to tolerate, other options Include:
    - **Clonidine** start 0.1 mg PO TID titrate as needed
      - Max 1.5 mg/day in extreme cases of withdrawal
    - Or **Guanfacine** start 1 mg PO BID titrate as needed
      - Max 9 mg/day in divided doses
    - Or **Tizanidine** start at 2 mg PO TID titrate as needed
      - Least likely to decrease BP/HR, may mildly prolong QTC
      - Max 18 mg/day in divided doses in withdrawal cases
      - Max 24 mg/day for other indications

Management

- Hospitalization Day 4:
  - **Agitated** on fentanyl 200 mcg/hr, midazolam 6 mg/hr & alprazolam 2 mg TID
- **Added Tizanidine 2 mg PO TID**
  - Least likely to decrease BP/HR, may mildly prolong QTC
  - BP 104/73 on norepinephrine; Baseline QTC 434
- Changed vancomycin & piperacillin-tazobactam to **Ampicillin/Sulbactam IV** 3g q8h for 3 more days (total 7 days)
  - Temp. 101.3; WBC 14.8; Lactate 1.6; FIO_2 30%
  - All culture (-); No clear source of infection
  - Suspected aspiration pneumonia from N/V on admission

Management

- Hospitalization Day 5
  - 12-lead ECG showed **QTC 510 → Methadone discontinued**
  - Add **olanzapine 2.5 mg PO q6h PRN** prior to weaning attempt
  - **Keep K+ ≥ 4, Mg2+ ≥ 2**
  - **Extubated on Day 5**
  - Slowly tapering fentanyl & midazolam ≤ 25% daily
- Hospitalization Day 9:
  - **Impella removed, repeat Echo showed EF ~50%, AAOx3**
  - Tizanidine discontinued
  - Patient agreed to go back to rehab & to be on methadone
  - Methadone 10 mg PO daily + 5 mg PO q6h PRN titrate up
  - Repeat ECG showed QTC 488

Management

- **Discharged** on Day 23:
  - **Methadone titrated up to 55 mg PO daily**
  - **Restarted Tizanidine 2 mg PO q8h** (last QTC 471)
  - **Gabapentin 600 mg PO TID for aid in detox**
  - **Zoloft 100 mg PO daily for anxiety**
  - **Metoprolol succinate 25 mg PO daily**
  - **Alprazolam tapered off upon discharge**
  - Melatonin 5 mg PO every evening at 8PM
  - Naloxone 4 mg/actuation spray
    - Administer 1 spray into one nostril PRN for opioid overdose
    - May repeat 2-3 min in opposite nostril if needed

"The Gestalt": Medical Services to Consult

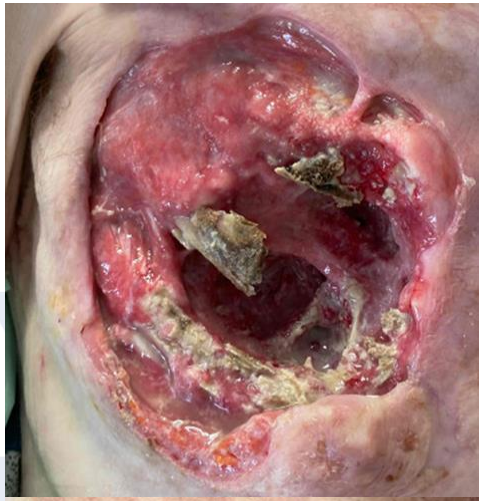
- EMS/Fire/First Responders
- Infectious Disease
- Wound Care/Mobile Team
- Surgery
- Burn Center
- Pharmacy
- Psychiatry
- Addiction Medicine
- Psychology
- Mental Health Service
- Social Services/Case Management
- Orthopedics/Orthopedic Surgery
- Cardiology
- Pulmonary
- Emergency Medicine
- Anesthesiology/Pain Management
- ENT
- Internal Medicine/Hospitalists
- Laboratory: Xylazine/Fentanyl Testing
- Project Engage/Recovery Coaches
- The Patient
- Family/Support System
- Others as Necessary/Deem Appropriate
- Surrounding Hospitals

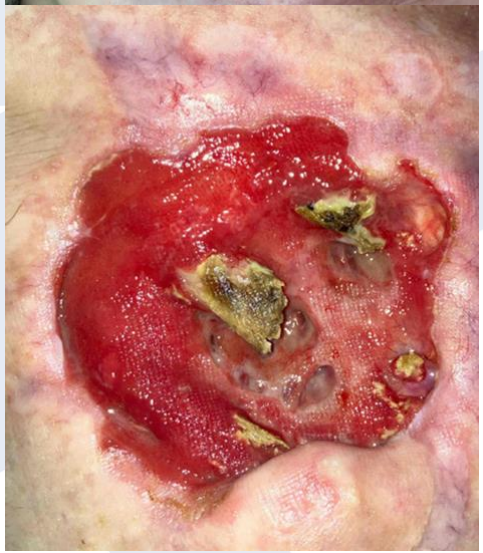
Have *"the Gestalt"* on board before the patient arrives. Plan Ahead!

Don’t Ever Give Up!

Focus of Care

- Harm reduction; stay alive
- Quality of life improvement
  - Ease of wound care
  - Pain Reduction
  - Withdrawal Management
- Improve relationship with the health system to help engage in recovery services
- Help maintain recovery or re-enter recovery at any point





Research – Educate – Prevent

For the integrity of your work,

You will be recognized,

Maybe not with praise or awards

But with the lives touched by your life!

THANK YOU FOR YOUR DEDICATION & SERVICE!!!

Individual Action Planning
(Stop – Continue – Start)

	As a result of this training, what will you **stop** doing?		As a result of this training, what will you **continue** doing?		As a result of this training, what will you **start** doing?	
Action Item **This Session**	?		?		?	

CALL TO ACTION !

Aunt

Frannie

Contact Information

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Q&A

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