



HOPEWAY

The Premier Path to Mental Wellness

The Evolving Drug Landscape in Psychiatric Practice

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Learning Objectives



Describe emerging trends in the substance use landscape, with a focus on increasingly accessible substances such as kratom, 7-OH, and synthetic opioids.



Identify the clinical effects, risks, and diagnostic challenges associated with less-regulated, easily accessed psychoactive substances.



Apply evidence-based approaches to the assessment and management of patients presenting with use of novel or legally available substances, through a case-based format.



Anticipate some of the forensic and legal issues these substances raise in psychiatric practice.

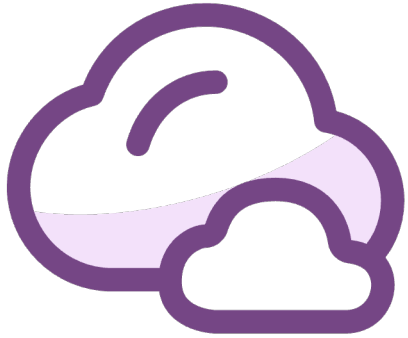


What percentage of individuals 18 and over diagnosed with a mental health diagnosis also met criteria for a substance use disorder per the 2023 National Survey on Drug Use and Health?



OBJECTIVE 1

Emerging Trends



What are the most frequent drugs of abuse that you are detecting or patients/their loved ones are reporting in your practice?

Case Example

18 y/o single, white male called 911 reporting that he was having a heart attack.

EMS: informs individual that he does not need to go to the ED because he “just used marijuana” per girlfriend who admits distribution.

Concerns over increased heart rate and chest pain. Self presented to nearby hospital.

Upon evaluation: acute agitation with HR 180, paranoia and refusal to take medications. On cardiac monitor. UDS + THC.

Medical History: None.

Let's think through the differential diagnosis...



What is the likely cause of this patient's presentation?

Why the Drug Supply Keeps Changing

The illicit and unregulated drug supply has become progressively less predictable — shaped by international regulation, enforcement pressure, economics, increased inhalation vs. injection use, and consumer demand for accessible, “legal” alternatives.

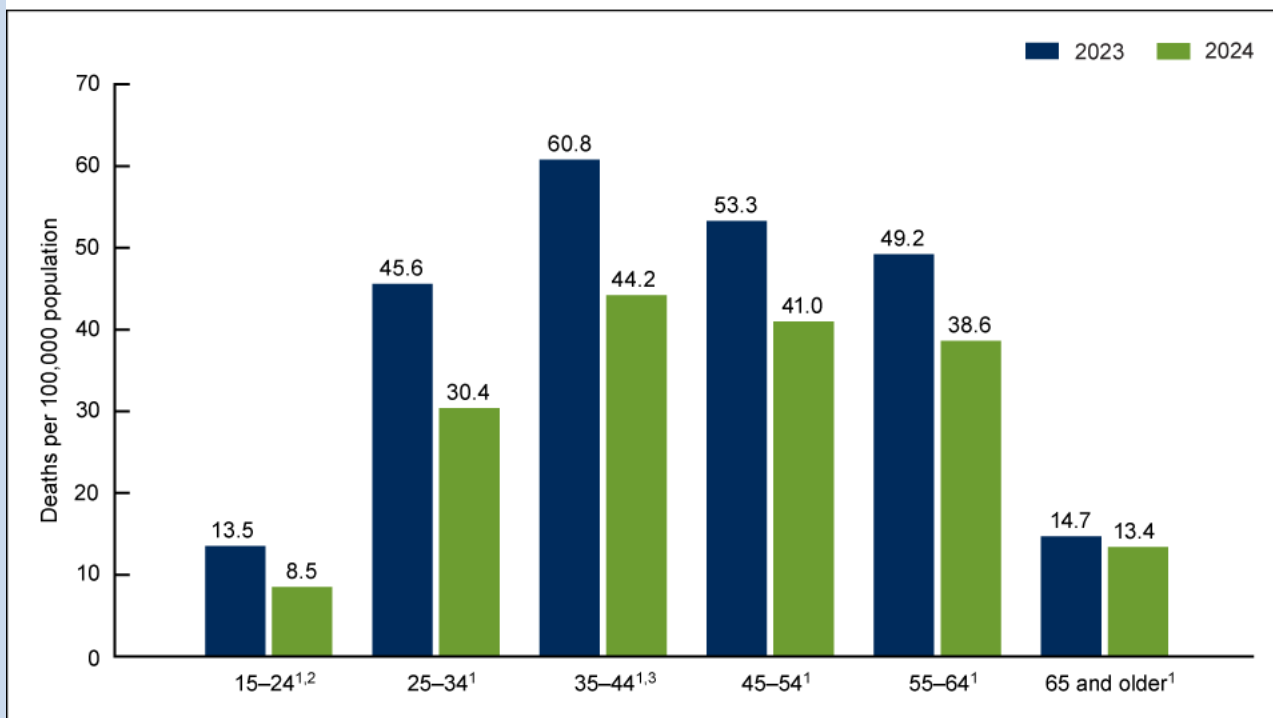


Running in parallel: an unregulated botanical and supplement market.

Good News: A Reversing National Curve

Aggregate U.S. overdose mortality rates are declining — even as new substances and adulterants have emerged within the supply.

Figure 2. Drug overdose death rate, by selected age group: United States, 2023 and 2024



¹Significant decrease between 2023 and 2024 ($p < 0.05$).

²Group with lowest rate in 2023 and 2024 ($p < 0.05$).

³Group with highest rate in 2023 and 2024 ($p < 0.05$).

NOTE: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14.

SOURCE: National Center for Health Statistics, National Vital Statistics System, mortality data file.

Possible contributing factors:

- Expanded naloxone access and community distribution
- Broader access to buprenorphine and methadone, including telehealth flexibilities
- Harm-reduction scale-up (fentanyl test strips, syringe services)
- Possible shifts within the illicit drug supply itself
- Fentanyl Cuts



Which factor do you think is doing the most to drive today's unpredictable drug supply?



Kratom

Tropical tree native to Southeast Asia

Botany & Pharmacology

- *Mitragyna speciosa*: a tree native to Southeast Asia; leaves traditionally chewed or brewed for energy and pain relief
- Primary alkaloid is mitragynine; the minor alkaloid 7-hydroxymitragynine (7-OH) is present in only trace amounts in raw leaf — but is far more potent.
- Complex, dose-dependent pharmacology: partial agonism at the mu-opioid receptor, plus $\alpha 2$ adrenergic and serotonergic activity.
- Low doses → stimulant-like effects (alertness, sociability). Higher doses → opioid-like analgesia and sedation.
- Can be ingested in the form of a tablet, capsule, or extract. Leaves may also be dried and ingested as a tea or the leaf may be chewed.



Not FDA-approved

Sold and marketed as a botanical supplement.

Clinical Use, Dependence & Regulatory Status

- **Clinical Use**

Frequently self-directed — for chronic pain, anxiety, energy, or to reduce or self-manage opioid withdrawal.

- **Systemic Impact**

Effects include nausea, itching, sweating, dry mouth, constipation, tachycardia, hepatotoxicity, seizures, vomiting, drowsiness and loss of appetite.

- **Dependence & Withdrawal**

Regular use can produce an opioid-like withdrawal syndrome

- **Psychosis**

Cases of psychotic symptoms have been documented secondary to kratom use including hallucinations, delusions, and/or confusion.



Expect More.



7-OH

7-Hydroxymitragynine

A Different Drug Wearing Kratom's Name

- In raw kratom leaf, 7-OH occurs only in trace amounts.
- Modern commercial products concentrate or synthesize 7-OH into tablets, “shots,” and vapes — sold alongside, or instead of, whole-leaf kratom.
- It is a substantially more efficacious mu-opioid receptor agonist - pharmacologically closer to a conventional opioid than to traditional kratom use.
- Marketed through gas stations, vape shops, and smoke shops as an accessible, “legal” opioid-like product.
- Growing regulatory attention (FDA communications, state-level proposals) toward regulating or scheduling concentrated 7-OH separately from kratom.



Sold as a “legal” opioid

Concentrated 7-OH tablets and vapes are marketed through ordinary retail channels.

Clinical & Forensic Considerations

Clinical

- Overdose and respiratory-depression risk more comparable to conventional opioids
- Withdrawal resembles classic opioid withdrawal
- Standard urine opioid panels do not reliably detect mitragynine or 7-OH — specific LC-MS/MS testing is required
- Consider managing suspected 7-OH use disorder within an opioid-use-disorder framework (e.g., buprenorphine & naloxone access)

Forensic

- High potency combined with inconsistent product labeling complicates dose- and causation-related opinions.
- Lack of routine detection on standard toxicology can complicate diagnostic accuracy, fitness for duty evaluations and cause-of-death determinations when 7-OH is not specifically assayed.
- Inconsistent scheduling across jurisdictions can create uncertainty in some criminal cases
- Product marketing as a “legal” or a “natural” substance may be relevant to informed-consent and product-liability questions.



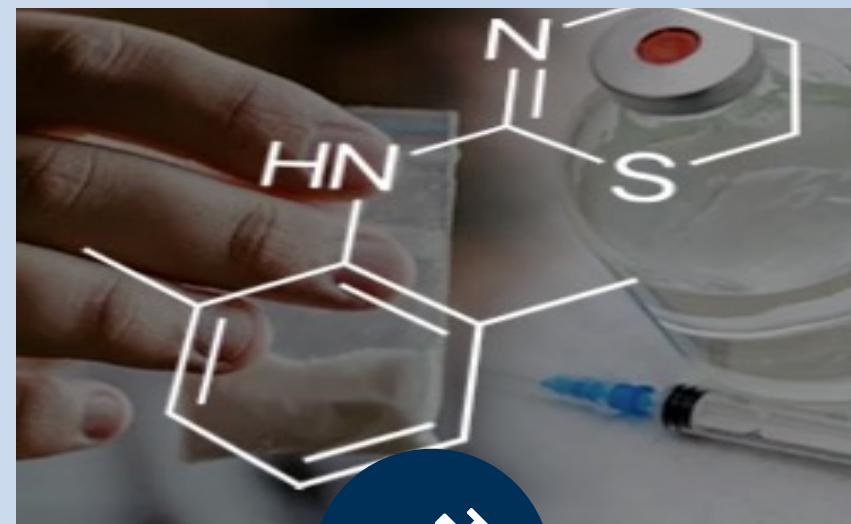
Xylazine

A veterinary sedative in the illicit opioid supply

XYLAZINE

From Barn to Street

- A veterinary alpha-2 adrenergic agonist used for sedation, analgesia, and muscle relaxation
- Added to illicit fentanyl to prolong and potentiate its effects and extend the drug supply
- First identified in Puerto Rico, then Philadelphia; now detected in the illicit opioid supply within a majority of U.S. states
- Michigan found that Xylazine was present in 4.7% of fatal overdoses on 2023
- 25% of samples in 2025 to 14% 2026



Veterinary Origin

Never approved for human use — yet increasingly present, unlabeled, and in the illicit fentanyl supply.

XYLAZINE

Clinical Management Challenges



Naloxone does not reverse xylazine's sedative or cardiovascular effects - it is not an opioid.
Still give naloxone when fentanyl co-exposure is likely or unknown.

- Profound **sedation, bradycardia, and hypotension** can prolong the overdose course and complicate resuscitation.
- **Distinctive necrotic skin and soft-tissue wounds**, which can occur even at sites remote from injection.
- Withdrawal is a distinct, harder-to-manage syndrome; adjunctive alpha-2 agonist strategies (e.g., clonidine) have been used
- Not detected on routine urine drug screens — requires specific immunoassay or LC-MS/MS testing.



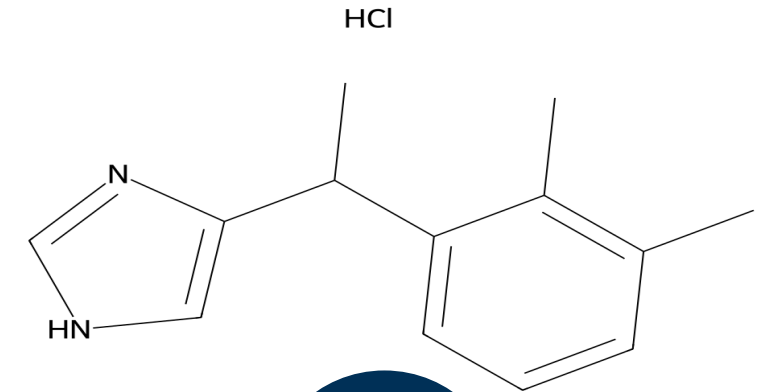
Medetomidine

The next-generation, **more potent** sedative adulterant

MEDETOMIDINE

The Next-Generation Adulterant

- A veterinary alpha-2 agonist substantially more potent than xylazine
- Structurally related to dexmedetomidine (used for human ICU sedation)
- Increasingly detected in the illicit fentanyl/opioid supply since roughly 2022, with regional outbreak clusters reported in several U.S. cities
- Appears to be displacing or supplementing xylazine as an adulterant in some local drug markets
- Street names: Dex, Rhino Tranq or Mede



More Potent than Xylazine

MEDETOMIDINE

Clinical Challenges

- Even more pronounced and prolonged **sedation**, **bradycardia**, and **hypotension** than xylazine.
- Not detected on standard toxicology; specific testing is typically available only through reference or public-health laboratories.
- Management is largely supportive: airway and ventilatory support, methadone and clonidine in Critical Care Units/ICU.
- Withdrawal s/s can include: mutism, sinus tach, HTN, N/V, tremor and myoclonic jerks.



**No Human Reversal Agent –
Naloxone Resistant**

Four Substances at a Glance

Substance	Primary Mechanism	Naloxone-Responsive?	Standard Tox Screen?	Signature Clinical Concern
Kratom (mitragynine)	Partial mu-opioid agonist + adrenergic/serotonergic activity	Partial / unclear	No — needs specific testing	Dependence; mild–moderate opioid-like withdrawal; hepatotoxicity
7-OH	High-efficacy mu-opioid agonist	Yes, opioid-like	No — needs specific testing	Opioid-like overdose and withdrawal risk
Xylazine	Alpha-2 adrenergic agonist	No	No — needs specific testing	Severe necrotic wounds; prolonged sedation
Medetomidine	Alpha-2 adrenergic agonist (high potency)	No	No — needs specific testing	Profound bradycardia/hypotension; no reversal agent

Toxicology

Standard 6-Panel: Amphetamines (including methamphetamine), Cannabinoids (THC/marijuana), Cocaine, Opiates (codeine and morphine), Oxycodone, Phencyclidine (PCP)

16-Panel: adds Barbiturates, Benzodiazepines, Buprenorphine, Carisoprodol, Fentanyl; Gabapentin, Meperidine, Methadone, Propoxyphene, & Tramadol.

Add Ons: kratom (mitragynine) screen, 7-hydroxymitraginine-specific assay, dedicated xylazine LC-MS/MS testing, and medetomidine LC-MS/MS confirmatory testing

Gold Standard: LC-MS/MS (Liquid Chromatography and Tandem Mass Spectrometry)

Fentanyl in
Transition –
Nitazenes,
Orphines &
BTMPS

DANGER:
CYCHLORPHINE
IN KENTUCKY!

10 TIMES MORE POTENT THAN FENTANYL!

EXTREME OVERDOSE RISK!



• USE PPE • REPORT IMMEDIATELY

Nitazenes

Synthetic Opioid

Can be weaker, the same or stronger than fentanyl

Longer duration of action

Often found in heroin or fentanyl mixed with xylazine, medetomidine, or designer benzodiazepines

Often multiple nitazenes in one sample

Orphines

Powerful synthetic opioids that are stronger and more powerful than fentanyl.

Created in the 1960's and returned to illegal drug labs around 2019 to bypass laws controlling fentanyl.

In 2025, China placed nitazene analogs under tighter control. After that change, they showed up less often while orphines increased in the drug supply.

Cychlorphine: 10x stronger than fentanyl (2024)

Dealers often mix orphines into counterfeit Rx pills, cocaine or methamphetamine.

BTMPS

Industrial chemical additive; added to materials, including, plastics, to protect them from breaking down due to UV heat and sunlight.

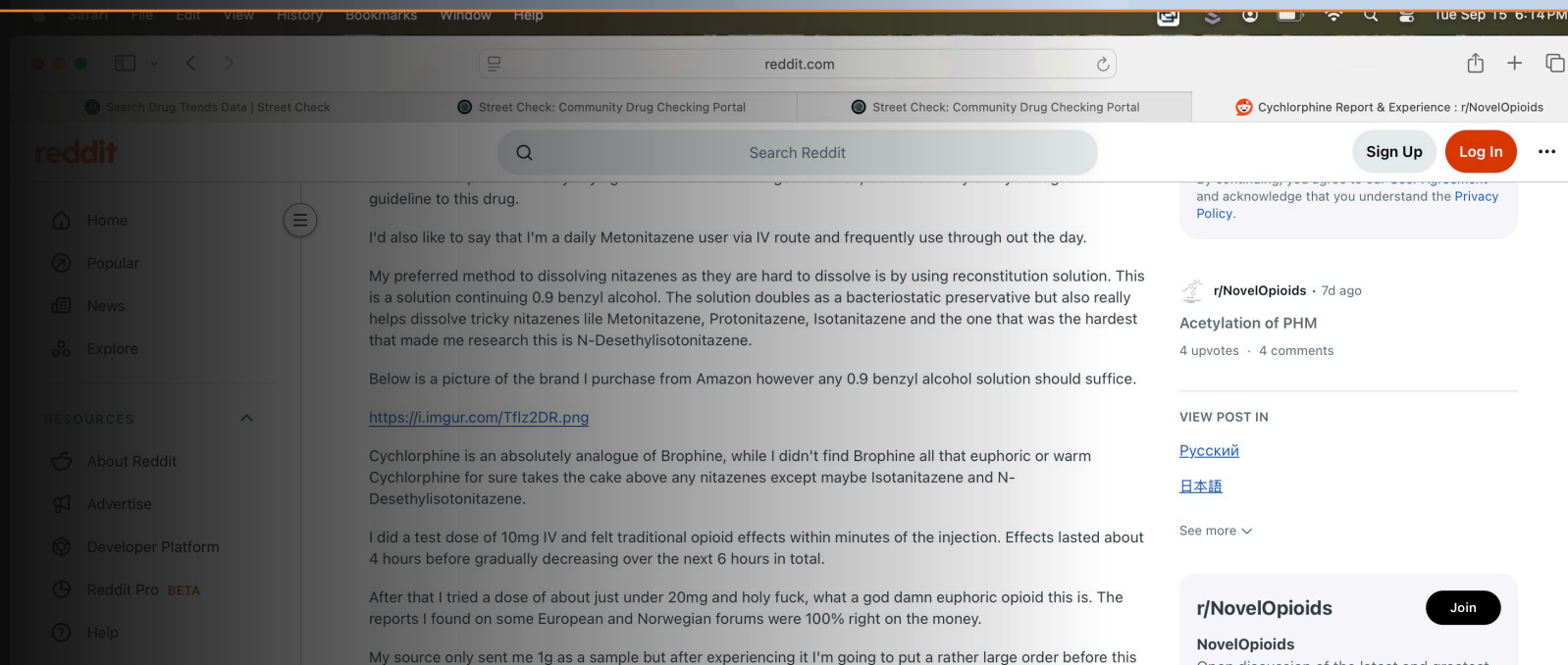
Appeared in US samples in 2024 (Philadelphia & Portland).

Use experience is negative: causes irritation at injection site and in lungs when smoked.

Continues to be found in 25-50% of fentanyl/heroin/opioid drugs and some methamphetamine and cocaine samples. Cheap bulking/cutting agent to stabilize the drug supply.

OD complications: can lead to unstable blood pressure, cardiac arrest and can make opioid reversal harder for medical professionals.

StreetCheck – Community Drug Checking





Samples with BTMPS
664
% Overall 20.0%
vs Last Month ▲ 16
% vs Last Month ▲ 200.0%

Samples with Medetomidine
752
% Overall 22.6%
vs Last Month ▲ 10
% vs Last Month ▲ 43.5%

Samples with Carfentanil
192
% Overall 5.8%
vs Last Month ▲ 1
% vs Last Month ▲ 50.0%

Samples with Orphines
40
% Overall 1.20%
vs Last Month ▼ -1
% vs Last Month ▼ -100.0%

Samples with Nitazenes
64
% Overall 1.9%
vs Last Month ▲ 2
% vs Last Month ▲ 100.0%

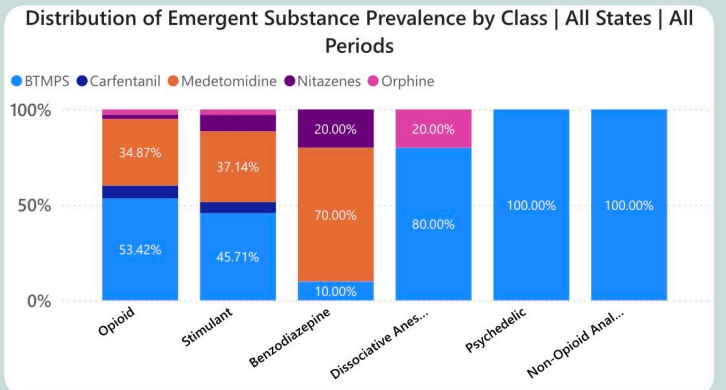
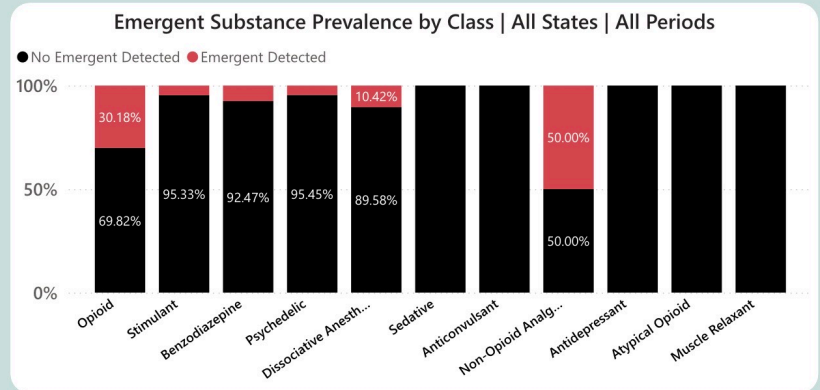
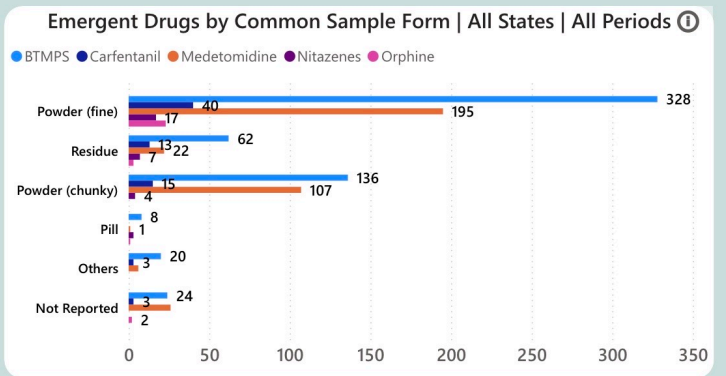
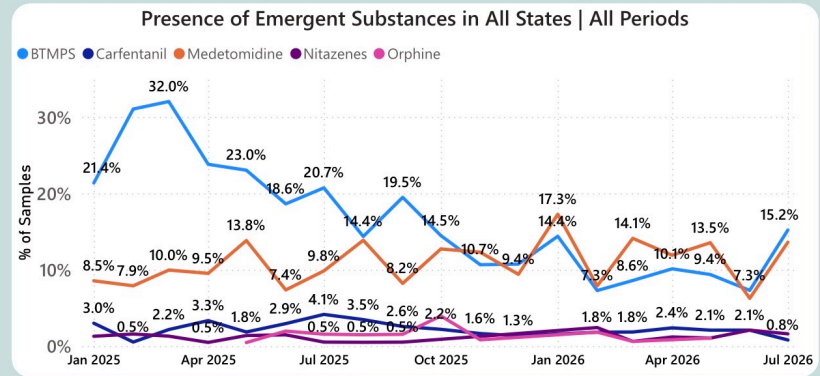
Sample Origin

All

☒ Select all
☒ Connecticut
☒ Maine
☒ Massachusetts
☒ Michigan
☒ Minnesota
☒ New York

Substance

All





Case-Based Application

Translating pharmacology into clinical assessment and management



Case Vignette:

Mr. NC, age 41, history of chronic low back pain and opioid use disorder. Has been self-managing withdrawal with over-the-counter kratom capsules and, more recently, a concentrated “7-OH” tablet product purchased at a local vape shop.

Exam & Findings

- Respiratory rate 8, heart rate 46, blood pressure 88/54.
- Pinpoint pupils; persistent sedation despite naloxone.
- Several necrotic ulcerations on both forearms, not fully explained by recent injection sites.

Presentation

- Found unresponsive by a friend; EMS gave two doses of intranasal naloxone with only partial improvement in respiratory rate.
- Sedation persists on arrival to the emergency department.
- Psychiatric consult-liaison is called given his known psychiatric and substance-use history.



**Based on the clinical presentation,
what is your leading concern for Mr.
NC?**

Assessment & Management

- Bradycardia, hypotension, and an incomplete naloxone response point to a likely alpha-2 agonist co-exposure (xylazine and/or medetomidine)
- Standard urine toxicology will miss kratom, 7-OH, xylazine, and medetomidine — request specific LC-MS/MS confirmatory testing where available.
- The necrotic wounds are a recognized xylazine signature and warrant wound care or surgical consultation
- Management is largely supportive - no reversal agent exists for the alpha-2 agonist component.
- Address the underlying opioid use disorder (e.g., buprenorphine once medically stabilized) alongside harm-reduction therapy.





OBJECTIVE 4

Forensic & Legal Considerations

Forensic & Legal Considerations

- Cause-of-death and causation opinions require specifically targeted toxicology; these substances are routinely missed by standard postmortem or clinical panels.
- Careful documentation of substance-use assessment, testing rationale, and clinical reasoning matters given how quickly the regulatory and clinical-guideline landscape is shifting.
- Relevant to competency, criminal-responsibility, and correctional-health evaluations whenever intoxication, withdrawal, or impaired capacity is at issue.
- Marketing of kratom and 7-OH as “legal” or “natural” may raise informed-consent and product-liability questions distinct from traditional controlled-substance cases.



Document everything

Clear and thorough documentation is your best protection and ideal for proper justification of diagnoses and recommended treatment plan.



Consult jurisdiction-specific statutes and confirm local toxicology-lab testing capabilities.

Fitness for Duty Case Example

38 y/o single, white male referred for evaluation by the North Carolina State Bar Association.

Concerns over unusual behavior reported at work. UDS negative via HR per P&P. Report from team includes paranoia, mood lability and decreased work performance.

Upon evaluation, self reported history of anxiety, hallucinations, and loss of appetite. Denied illicit drug use.

Medical History: chronic pain, constipation and seasonal allergies.

POC UDS - Negative.

Let's think through the differential diagnosis...



What is the most likely diagnosis?

Safety in Practice

- **52 y/o male presents to your outpatient practice intoxicated.**
- **Gait is unsteady, he is irritable and making commotion in the waiting room.**
- **UDS is positive for opiates. Breathalyzer shows BAC of 0.12 g/dL.**
- **Front desk team tells him that he will have to leave.**



What would you recommend as the physician in that practice?

Meeting Today's Objectives



We traced the trends toward more accessible, less-regulated substances that are reshaping today's drug supply.



We reviewed the pharmacology, clinical effects, and diagnostic blind spots for several substances, including kratom, 7-OH, xylazine, and medetomidine.



We applied this data to a few clinical cases using an interactive format.



We examined how causation and diagnostic challenges can intersect with forensic psychiatry practice.



Key Message

The drug supply is evolving faster than routine testing, treatment protocols, and regulation. Staying current on emerging substances is now a core clinical skill.

Where to track ongoing developments:

- FDA
- DEA
- CDC , NIDA and SAMHSA
- Info.streetcheck.org
- American Society of Addiction Medicine (ASAM)

“What questions do you have?”

LIVE Q&A