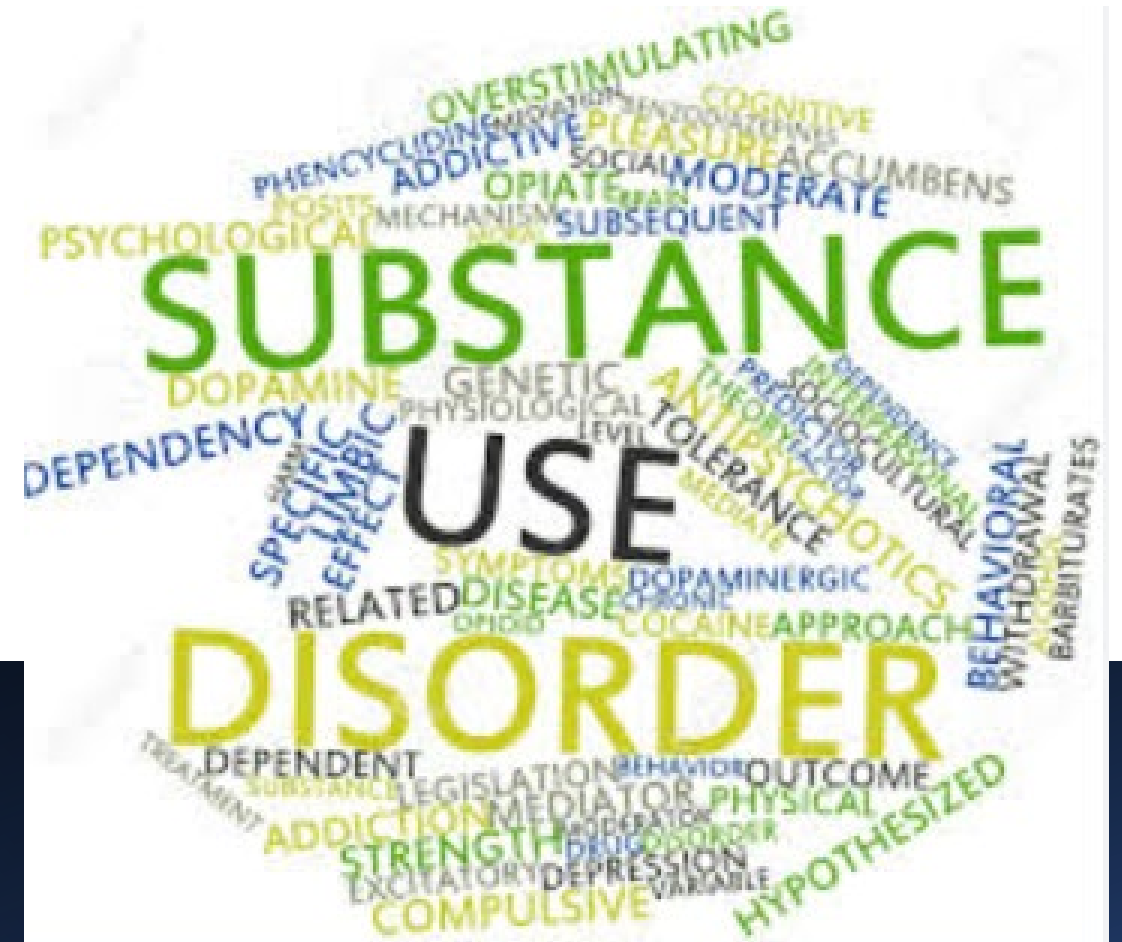


# Current trends and Treatments in SUD

Robert McMorrow, DO, FASAM



# Background

- Residency – EM / Fellowship – University At Buffalo – Addiction Medicine
- Current Director of Addiction Medicine MidMichigan Community Health Services
- MOC – University of Michigan - Consulting physician
- Stimulant Grant Medical Director - NMORC

# Objectives

- 1) Describe current Trends in OUD/Stimulant Use Disorder and overdose rates nationwide/statewide and treatment options
- 2) Understand different analogs of fentanyl and trends in Michigan
- 3) Recognize the increase of Xylazine related to OUD
- 4) Describe Kratom and potential risks



# Substance Use Disorder

	DSM-IV Abuse <sup>a</sup>		DSM-IV Dependence <sup>b</sup>		DSM-5 Substance Use Disorders <sup>c</sup>	
Hazardous use	X	} ≥1 criterion	–	} ≥3 criteria	X	} ≥2 criteria
Social/interpersonal problems related to use	X		–		X	
Neglected major roles to use	X		–		X	
Legal problems	X		–		–	
Withdrawal <sup>d</sup>	–		X		X	
Tolerance	–		X		X	
Used larger amounts/longer	–		X		X	
Repeated attempts to quit/control use	–		X		X	
Much time spent using	–		X		X	
Physical/psychological problems related to use	–		X		X	
Activities given up to use	–		X		X	
Craving	–		–		X	

# Addiction Definition

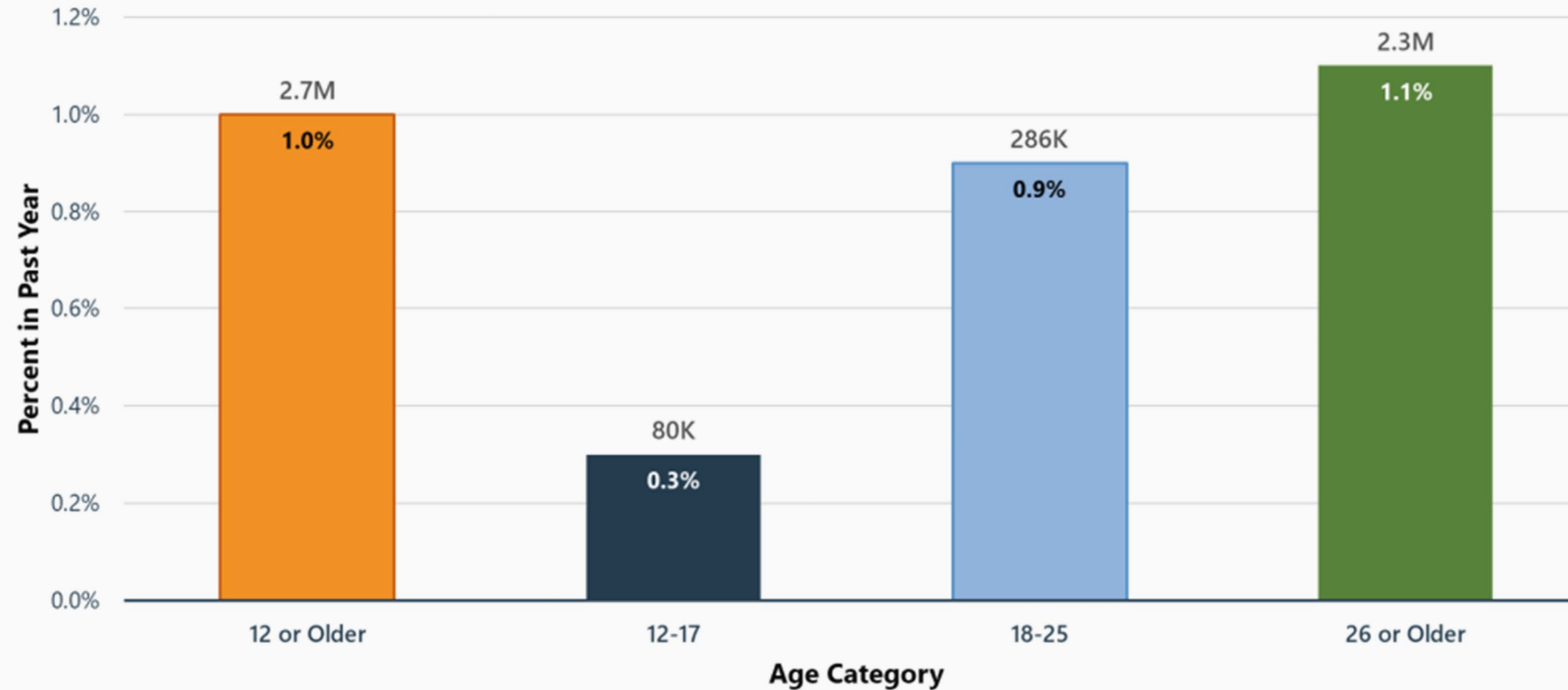
Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.

Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

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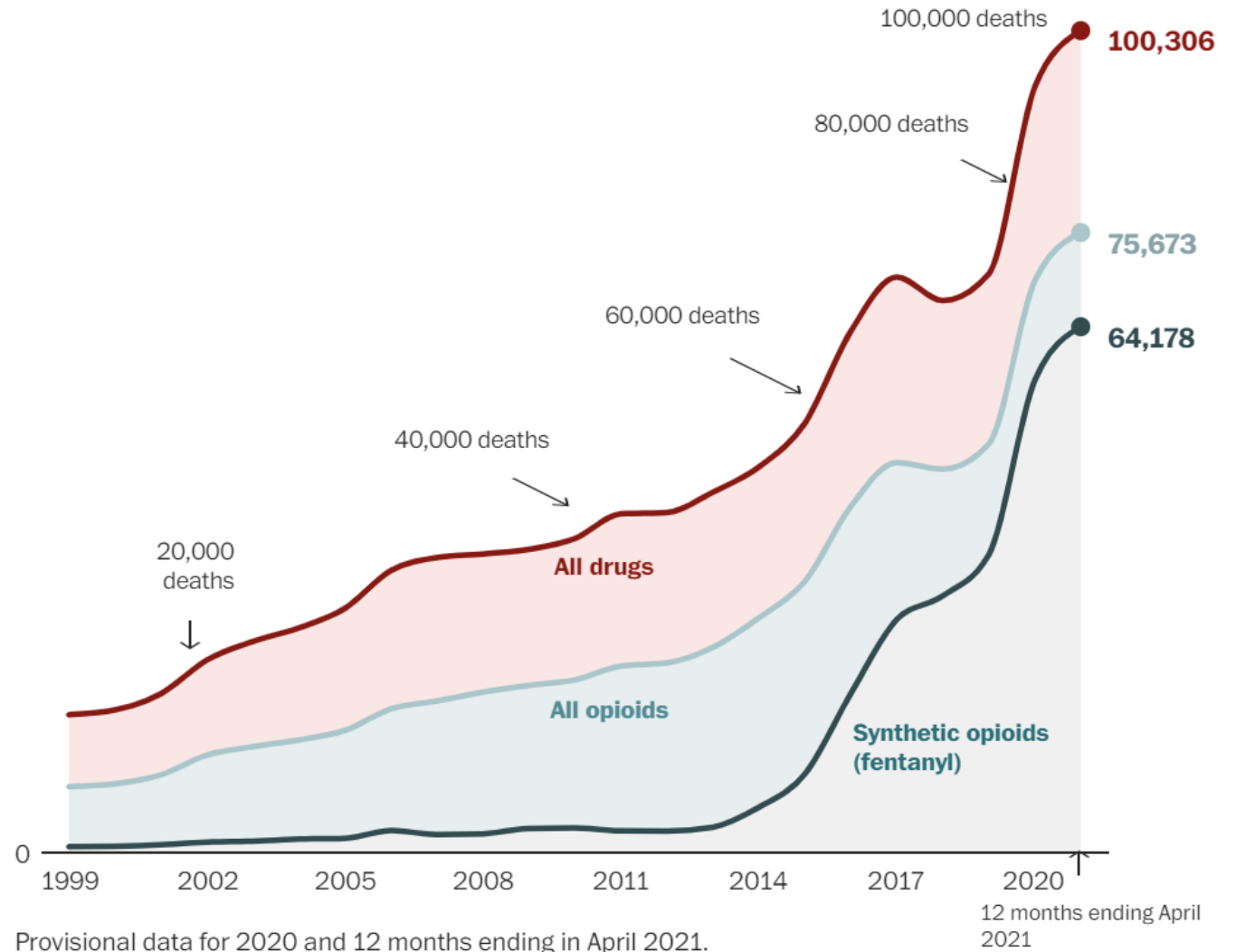
## Opioid Use Disorder in Past Year: Among People Aged 12+

PAST YEAR, 2020 NSDUH, 12+



Wrong  
direction

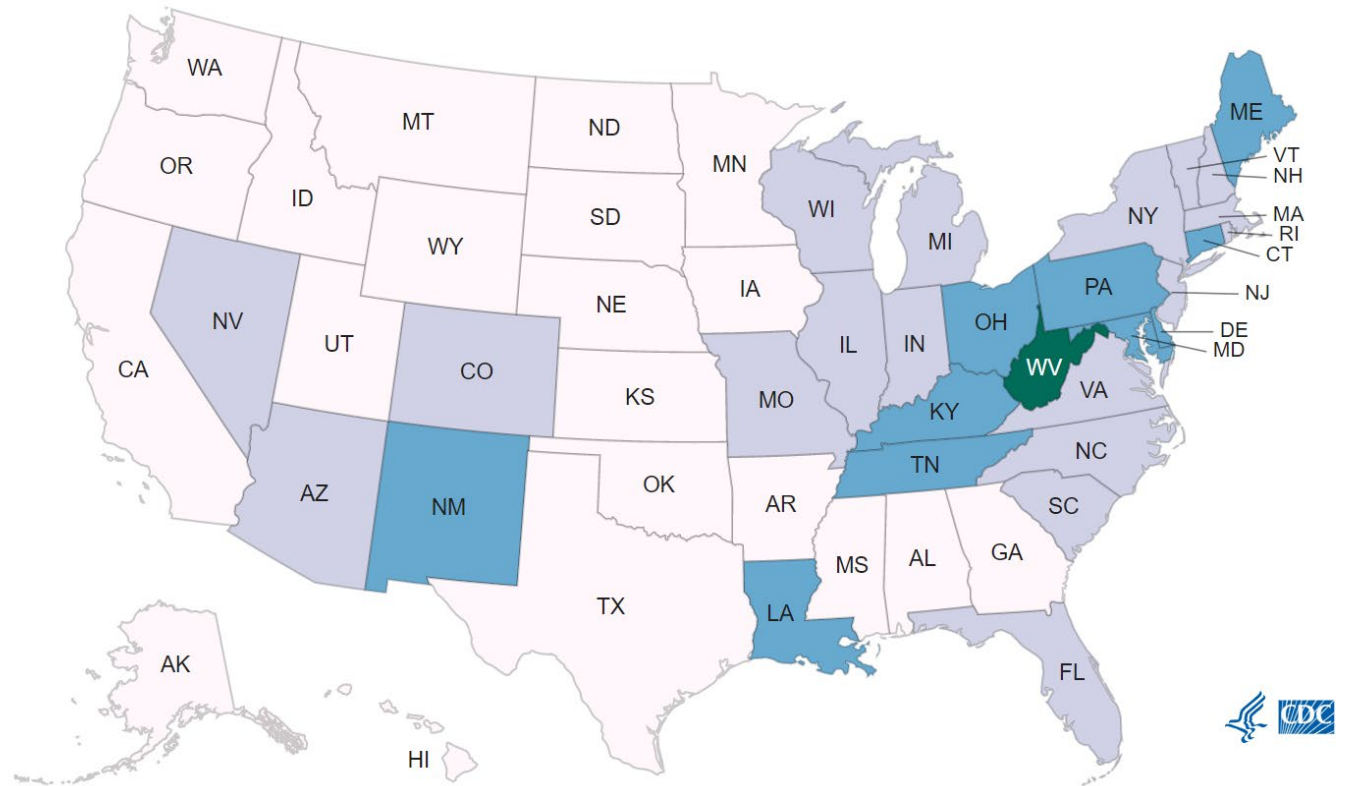
## U.S. drug overdose deaths per year



Source: [Centers for Disease Control and Prevention, National Center for Health Statistics](#) DAN KEATING / THE WASHINGTON POST



# Michigan



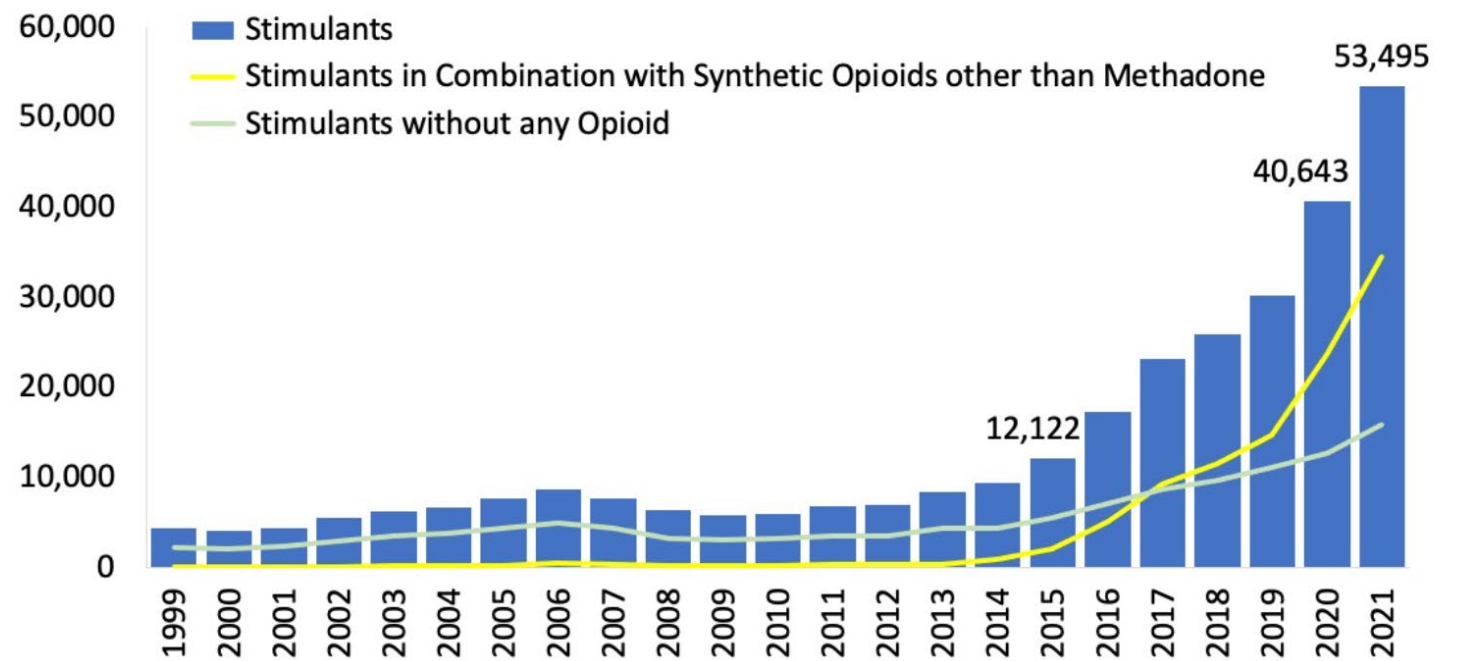
### Age-Adjusted Death Rates<sup>1</sup>





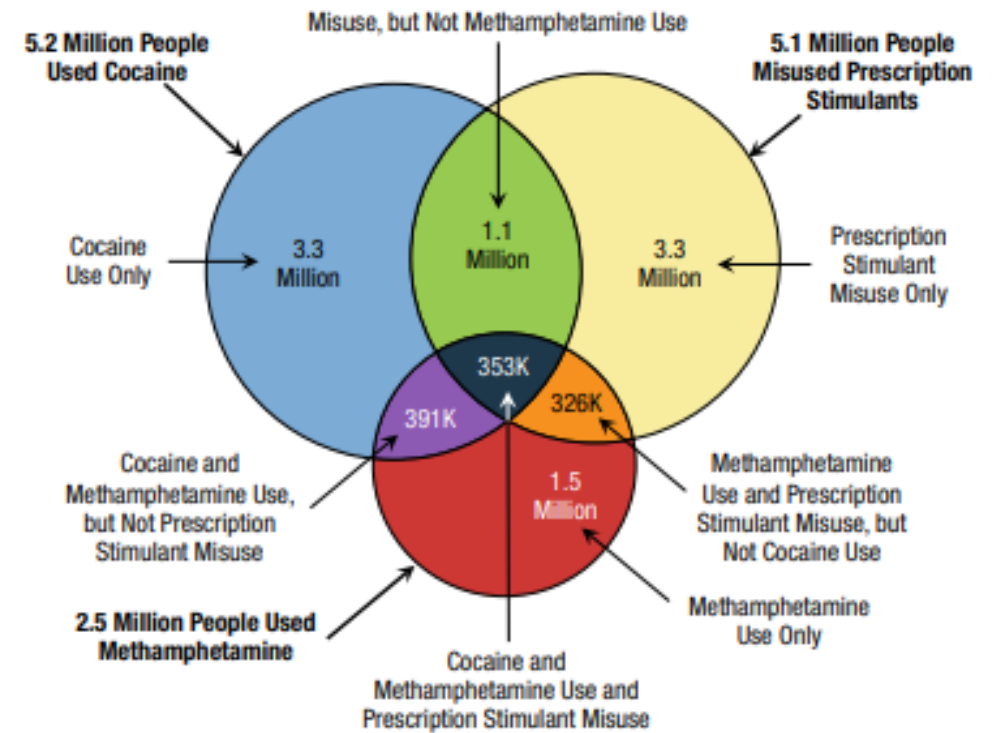
# Stimulant Overdose

Figure 6. National Overdose Deaths Involving Stimulants (Cocaine and Psychostimulants\*), by Opioid Involvement, Number Among All Ages, 1999-2021



\*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the T43.6 ICD-10 multiple cause-of-death code. Abbreviated to *psychostimulants* in the bar chart above. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

# National Prevalence



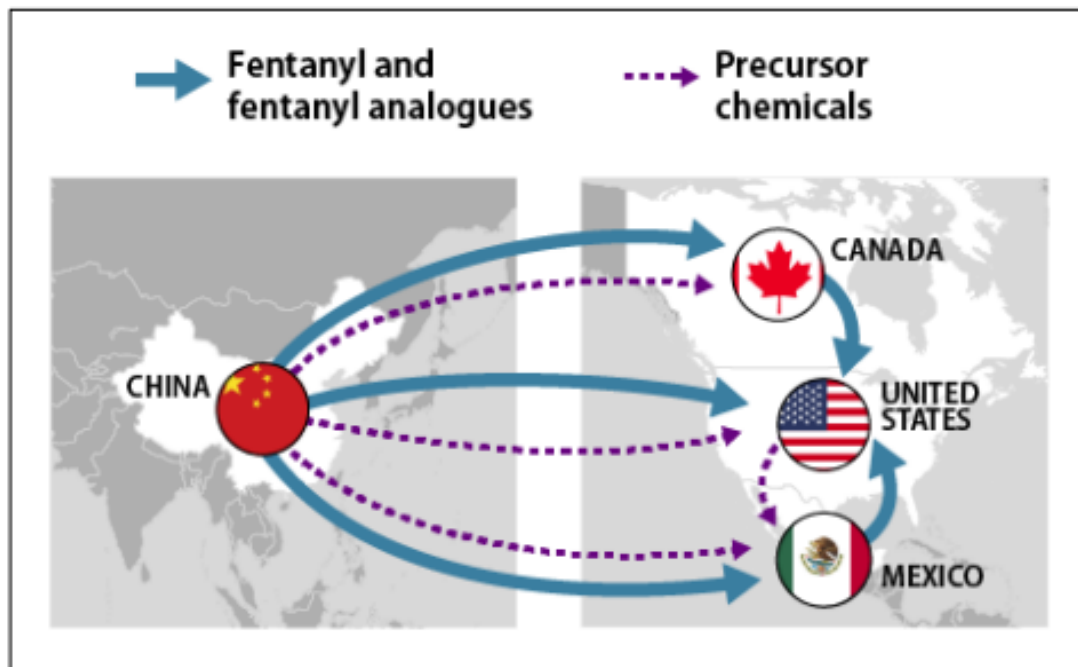
10.3 Million People Aged 12 or Older with Past Year CNS Stimulant Misuse

# Fentanyl

- Synthetic opioid first synthesized in 1960
- Relatively selective potent agonist at the MORs
  - 50x more potent than morphine and Carfentanyl  
10,000x
- Highly lipophilic (lipid soluble)
- Deaths occur quickly – within 5 minutes of injection
- Combo of factors – potency, rate of onset, muscle rigidity, lower susceptibility to naloxone reversal, lack of cross tolerance



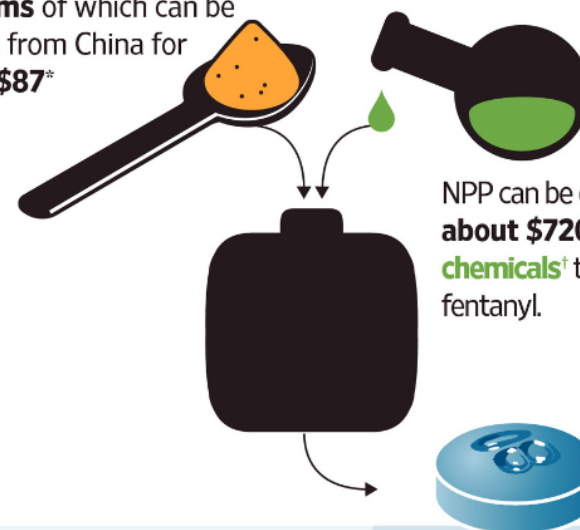
**Figure 1. Fentanyl Trafficking Flows**



## Criminal Chemistry

Traffickers manufacturing fentanyl often purchase the key ingredient from China, which doesn't regulate its sale. Here's how the chemical building blocks become a highly profitable street drug.

The key ingredient is **NPP**, 25 grams of which can be bought from China for about \$87\*



NPP can be combined with about \$720 of **other chemicals**† to produce fentanyl.

The resulting 25 grams of fentanyl cost about \$810 to produce...

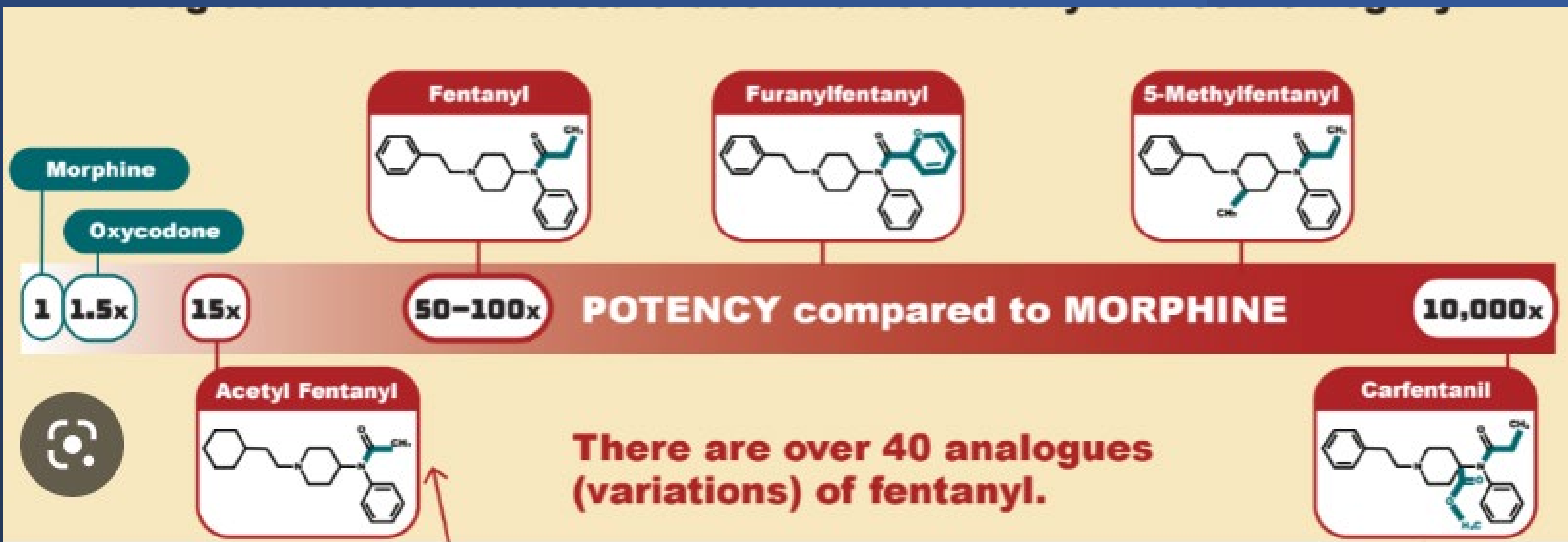
...and are equivalent to up to \$800,000 of pills on the black market.

\*Average current price from Chinese suppliers

†Prices from U.S. suppliers

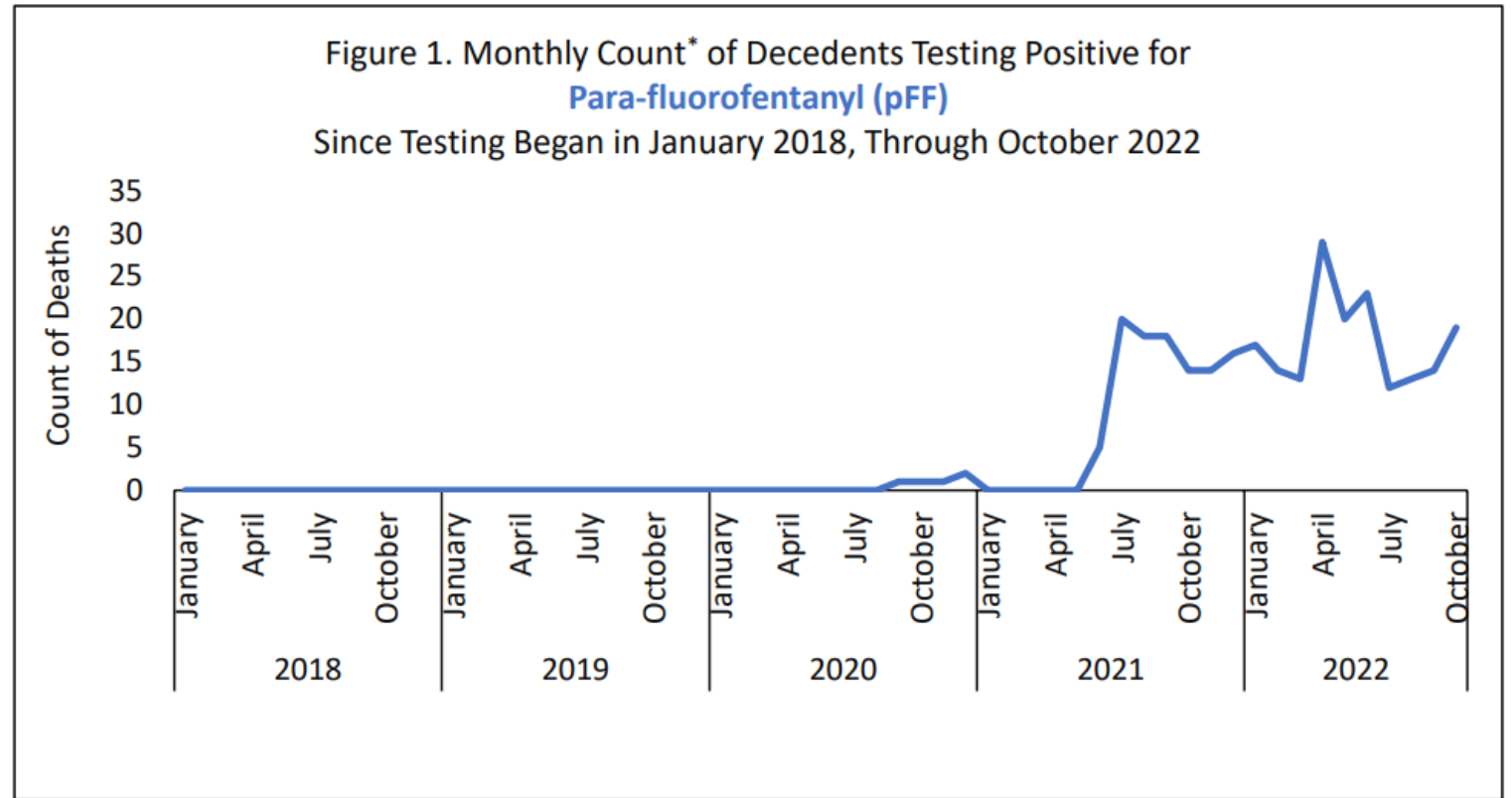
Sources: NES Inc.; Drug Enforcement Administration; Calgary Police

THE WALL STREET JOURNAL.





# Emerging trend: Para-Flourofentanyl



\*2020-2022 The Swift Toxicology of Overdose-Related Mortalities (STORM) Program at Western Michigan University Homer Stryker MD School of Medicine (WMed)

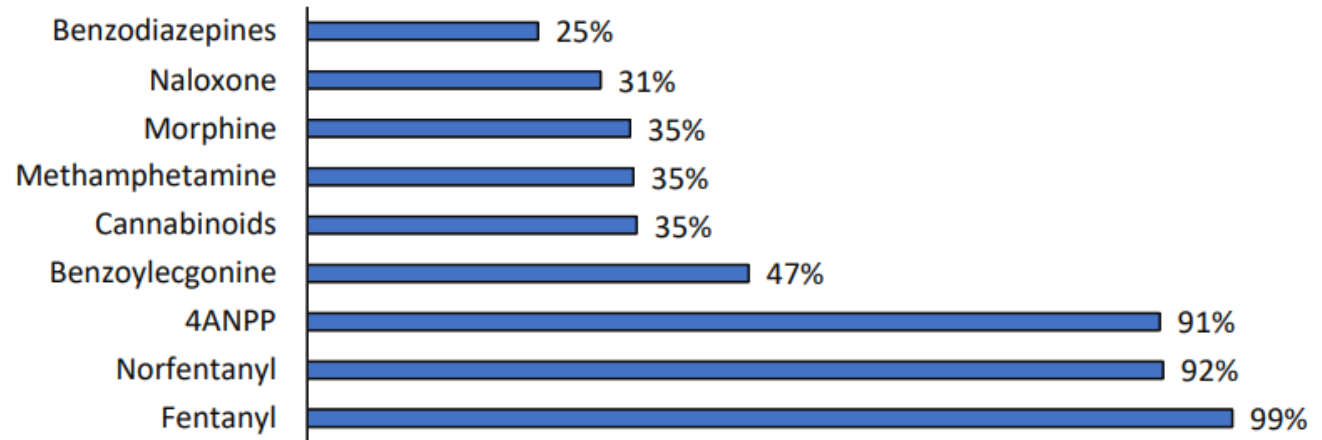


# What is Para-flourofentanyl

- Scheduled 1 synthetic opioid analgesic first synthesized for research purposes in the 1960's
- It is a Fentanyl analog with similar structure and synthesis route to fentanyl
- Clinical evidence suggests an even higher potency than fentanyl,
- Has been detected in heroin packets and counterfeit pills in the state
- Linked to multiple overdoses in other states as well
- Signs, symptoms, treatment of overdose that are associated with pFF are like other opioid analgesics

NOT JUST  
opioids !!

Figure 2. Percent of **Para-fluorofentanyl (pFF)** Positive Decedents\* (n=284)  
Testing Positive for Other Substances,  
September 2020 - October 2022



*\*2020-2022 The Swift Toxicology of Overdose-Related Mortalities (STORM) Program at Western Michigan University Homer Stryker MD School of Medicine (WMed)*

# Typical patient

Collection Date	12/1/2022	12/5/2022	12/6/2022	12/7/2022	12/8/2022	12/12/2022
Test Date	12/2/2022	12/6/2022	12/9/2022	12/9/2022	12/9/2022	12/13/2022
Analyte <sup>2</sup>						
Buprenorphine	Negative	Negative	170	187	Abnormal Specimen Validity	5
Norbuprenorphine	Negative	Negative	233	216	Abnormal Specimen Validity	26
Fentanyl	31	29	10	24	Abnormal Specimen Validity	> 161 <sup>3</sup>
Norfentanyl	> 1,356 <sup>3</sup>	873	401	253	Abnormal Specimen Validity	> 642 <sup>3</sup>
Lorazepam	Negative	Negative	933	364	Abnormal Specimen Validity	160
Hydroxybupropion	Not Ordered	Not Ordered	Not Ordered	Not Ordered	Abnormal Specimen Validity	1,129
Quetiapine	Negative	Negative	205	269	Abnormal Specimen Validity	Negative
Norquetiapine	Negative	Negative	80	179	Abnormal Specimen Validity	Negative
Naloxone	Negative	Negative	435	430	Abnormal Specimen Validity	Negative
Cocaine metabolite	> 8,477 <sup>3</sup>	> 11,268 <sup>3</sup>	3,012	1,357	Abnormal Specimen Validity	> 4,015 <sup>3</sup>
4-ANPP	5	Negative	Negative	Negative	Abnormal Specimen Validity	54
Acetyl norfentanyl	Negative	Negative	Negative	Negative	Abnormal Specimen Validity	4
Para-fluorofentanyl	Negative	Negative	Negative	3	Abnormal Specimen Validity	7

# Emerging Trend: Xylazine in Michigan

## 2019-2022 Year-to-Date

≡ **CNN** health Life, But Better Fitness Food Sleep Mindfulness Relationships

## How xylazine, a veterinary tranquilizer, is making overdoses even riskier

By Nadia Kounang, CNN

Published 6:30 AM EDT, Thu March 17, 2022



An animal tranquilizer is making street drugs even more dangerous

August 5, 2022 · 5:00 AM ET

MARTHA BEBINGER

FROM **wbur**

 4-Minute Listen

+ PLAYLIST <>



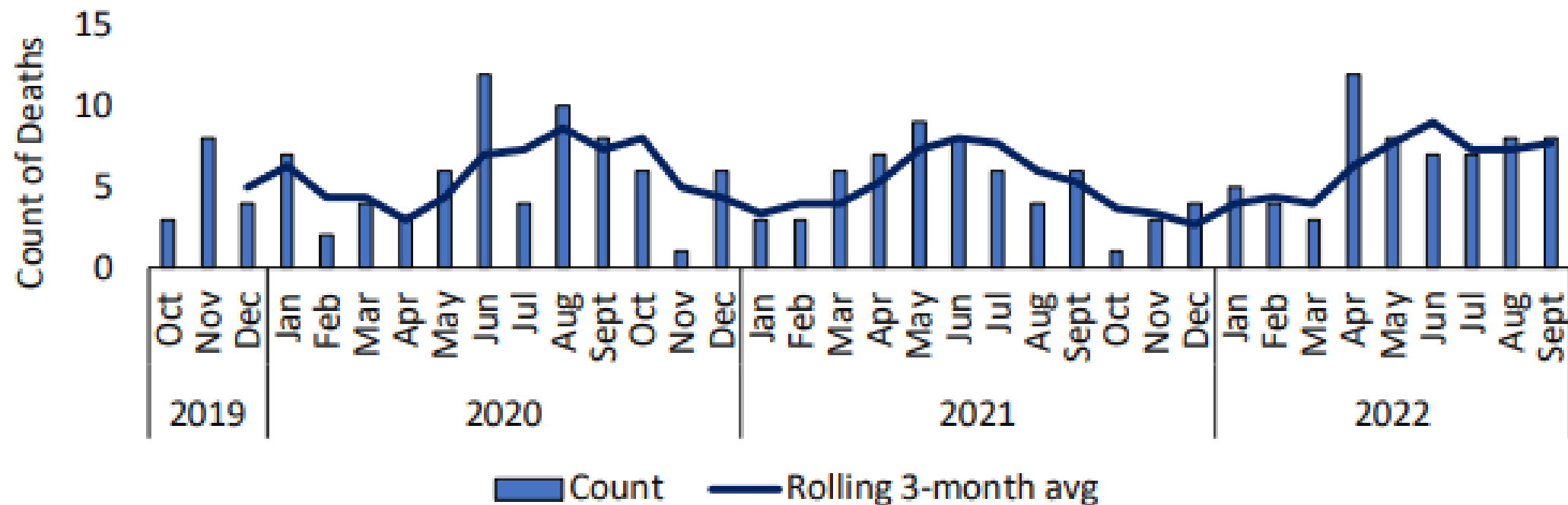


# Xylazine

- FDA warns about risk of xylazine exposure in humans – November 8, 2022
- Called “Tranq-dope”
- Seen uptick in Philadelphia and northeast US
- Non- opioid agent the FDA originally approved in 1972 as sedative for use in veterinary medicine,
- Structurally similar to clonidine, and tizanidine and may share clinical effects
  - Doesn’t seem to have affect on the imidazoline receptor – hypotension and bradycardia

# Michigan Xylazine- involved fatalities

Figure 1. Monthly Count and Rolling 3-Month Average of Decedents Testing Positive for **Xylazine** Since Testing Began, October 2019 - September 2022\*



\*2019-2022 The Swift Toxicology of Overdose-Related Mortalities (STORM) Program at Western Michigan University Homer Struiker MD School of Medicine (WMed)

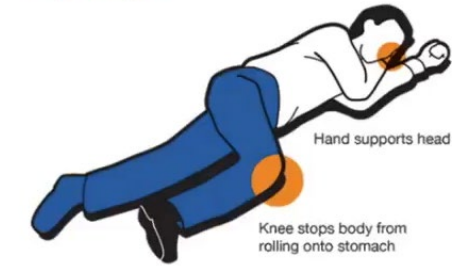


# Harms

- Combined effect may increase overdose potential
- May worsen withdrawal symptoms
- Has been associated with severe, necrotic skin lesions that differ from other soft-tissue infections – may develop in sites away from the site of injection
- NOT currently known to be reversed by naloxone – wont hurt
- NOT detected by routine toxicology screens
  - Hard to diagnose with a half life of 23-50 minutes

## The Recovery Position

Keep the Airway Clear



Stay with person. If you must leave them alone at any point, or if they are unconscious, put them in this position to keep airway clear and prevent choking.

**WCEB News**

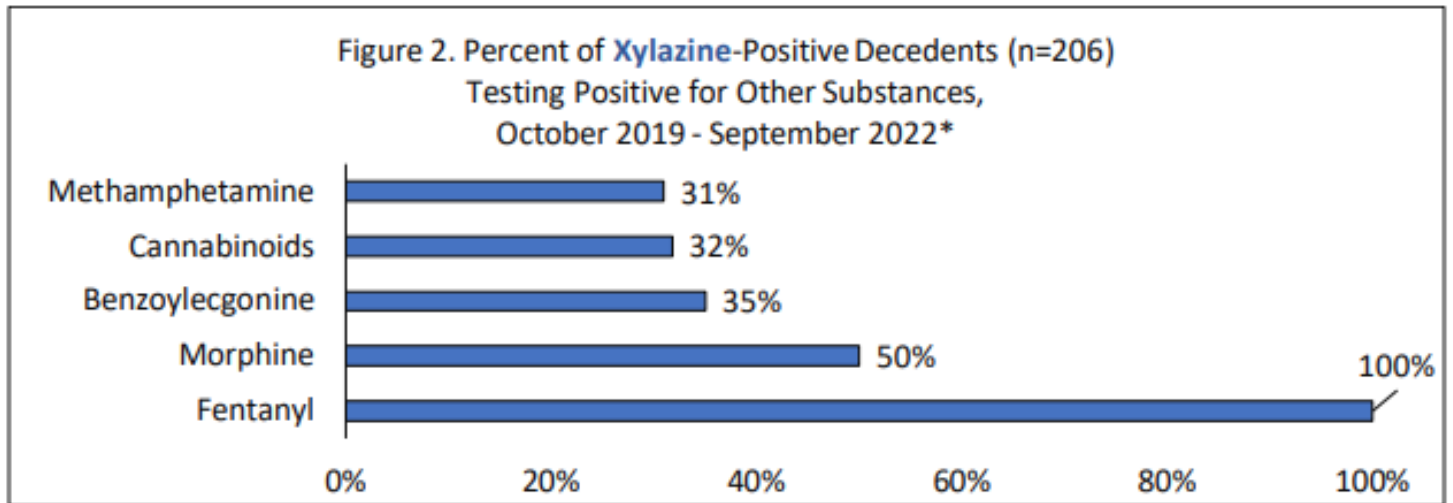
## Drug Users Are Losing Their Fingers and Toes After Shooting 'Tranq Dope'

In Philadelphia, the animal tranquilizer xylazine has infiltrated the opioid supply, and it's been linked to horrific wounds and amputations.

By Marissa Koshovec  
TORONTO, CA

March 22, 2022, 7:00am [Share](#) [Tweet](#) [Save](#)

# Drug Combinations



\*2019-2022 The Swift Toxicology of Overdose-Related Mortalities (STORM) Program at Western Michigan University Homer Stryker MD School of Medicine (WMed)

# Xylazine withdrawal

- Major symptom is Anxiety
- Duration few days to weeks
- Overlap with opioid withdrawal syndrome
- Anxiety irritability, restlessness
- Some corollary to clonidine withdrawal
  - Hypertension, tachycardia, diaphoresis, anxiety and agitation
  - Manage with sedative/ hypnotic withdrawal
    - First line – benzo, phenobarbital
    - Adjunct – Clonidine, Tizanidine, lofexidine, gabapentin, antipsychotics – not great anecdotal effect

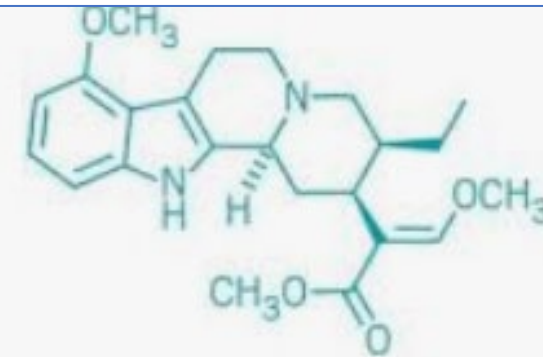
# Kratom

- *Mitragyna Speciosa* - tropical evergreen tree native to Southeast Asia - in the coffee family
- Traditional folk medicine to treat a number of conditions, most notably musculoskeletal pain, anxiety and depression.
- May be chewed, smoked, or transformed to powder that can be used as a tea. Largely obtained from internet and “legal high” shops
- marketed as cheaper alternative to opioid replacement therapy without need for Rx or medical supervision. Opioid dependence treatment

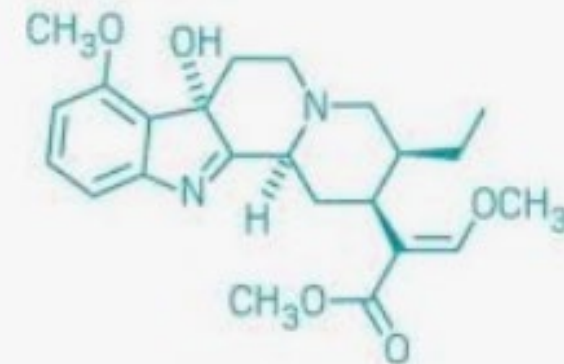


# Kratom

- Contains over 40 structurally related alkaloids, most common is mitragynine which acts a weak mu-opioid agonist (partial) and a second key component is 7-hydroxymitragynine (2% kratom by weight),
- Both act as weak antagonists at the kappa and delta- opioid receptors in vitro.
- Has a broad affinity for receptors including serotonergic, adrenergic, and GABAnergic pathways
- An estimated 10 -16 million people in the US take Kratom, though current prevalence ranges of 1.3 % - 6.1 % from surveys may underestimate regular Kratom users
- Persons who use Kratom report beneficial effects of relaxation, pain relief, increased energy and decreased depression



**(-)-Mitragynine**



**7-Hydroxymitragynine**

# Kratom

- Reaches peak concentration at around 1 hour and half life of 23 hours
- Exhibits dose - dependent effects
  - Stimulant at low doses (<5g)
  - Opioid - like effects at 5 to 15 g
  - Sedation at doses >15 g





# Key points

- Common side effects reported by users include stomach upset, vomiting, tachycardia, agitation, drowsiness, nausea and hypertension
- Case series of 12 patients from poison control main clinical effects are seizure, AMS, agitation, CNS depression and tachycardia.
- Not detected by conventional drug screening tests; requires advanced test like liquid chromatography-tandem or mass spectrometry
- Unsure how long detectable in urine - cases showed in urine 2-4 days - may be very lipophilic and stored in lipid tissue longer
- Given the increased use for self - treatment and lack of regulation, much needed safety studies and evidence on addictive potential
- No systematic human studies on the addictive potential of Kratom

# Kratom Metabolism/clearance

Collection Date	5/17/2022	5/18/2022	5/19/2022	5/26/2022	6/2/2022	6/9/2022
Test Date	5/18/2022	5/19/2022	5/20/2022	5/27/2022	6/3/2022	6/10/2022
Analyte <sup>2</sup>						
Buprenorphine	Negative	98	295	134	283	190
Norbuprenorphine	Negative	80	299	799	1,576	2,117
7-Amino-Clonazepam	207	241	215	184	312	378
Hydroxybupropion	5,059	6,165	5,894	Not Ordered	Not Ordered	Not Ordered
Trazodone	414	212	268	153	578	Negative
Naloxone	Negative	425	1,061	305	533	631
Mitragynine (Kratom alkaloid)	734	158	58	6	1	Negative
7-OH-Mitragynine (Kratom alkaloid)	> 749 <sup>3</sup>	371	120	6	1	Negative

# Key points

- OUD and Stimulant use disorder are increasing in prevalence and see co-occurring often
- Educate patient on dangers of Xylazine and Fentanyl
- Ask about Kratom use
- Don't forget Narcan – practice Harm Reduction



Don't Forget



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