



# Potent Poisoning:

WHEN SLEEPING BEAUTY GETS A BAD  
APPLE

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# Disclosure Slide



Do not have a vested interest in or affiliation with any corporate organization offering financial support.

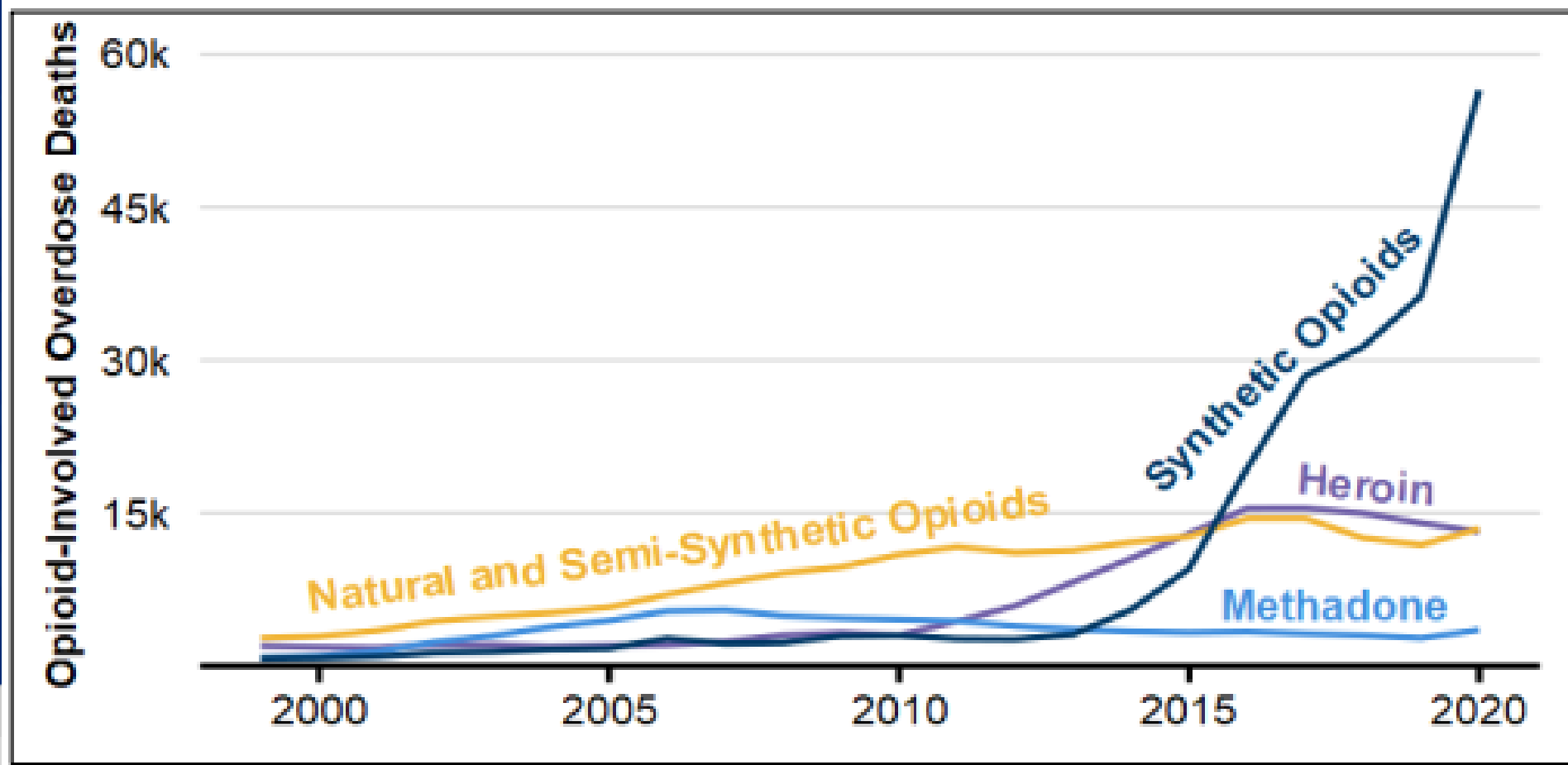


# Objectives

- Discuss the use of adulterants in illicit drugs, including common substances encountered in polypharmacy overdoses such as acetaminophen, cocaine, methamphetamines, kratom, xylazine, and metamizole
- Identify the challenges posed by adulterants in the acute management of polypharmacy fentanyl overdose, including the unpredictable nature of adulterant interactions and their impact on diagnostic and therapeutic approaches
- Develop evidence-based strategies and best practices for navigating the complexities of polypharmacy overdose to optimize patient care and treatment outcomes

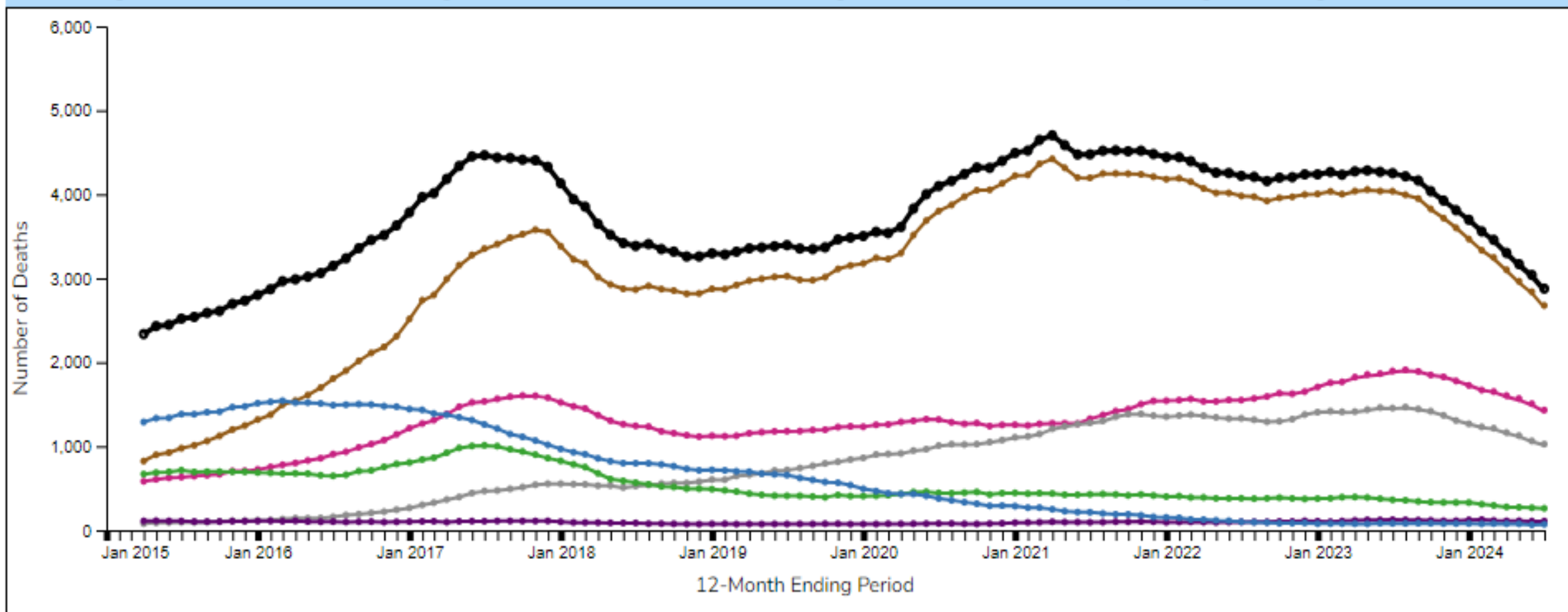
# Background

**Figure 2. Opioid-Involved Overdose Deaths in the United States, by Opioid Type, 1999-2020**



# Background

Figure 2. 12 Month-ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class: Ohio



- Based on data from December 1, 2024

# NFLIS

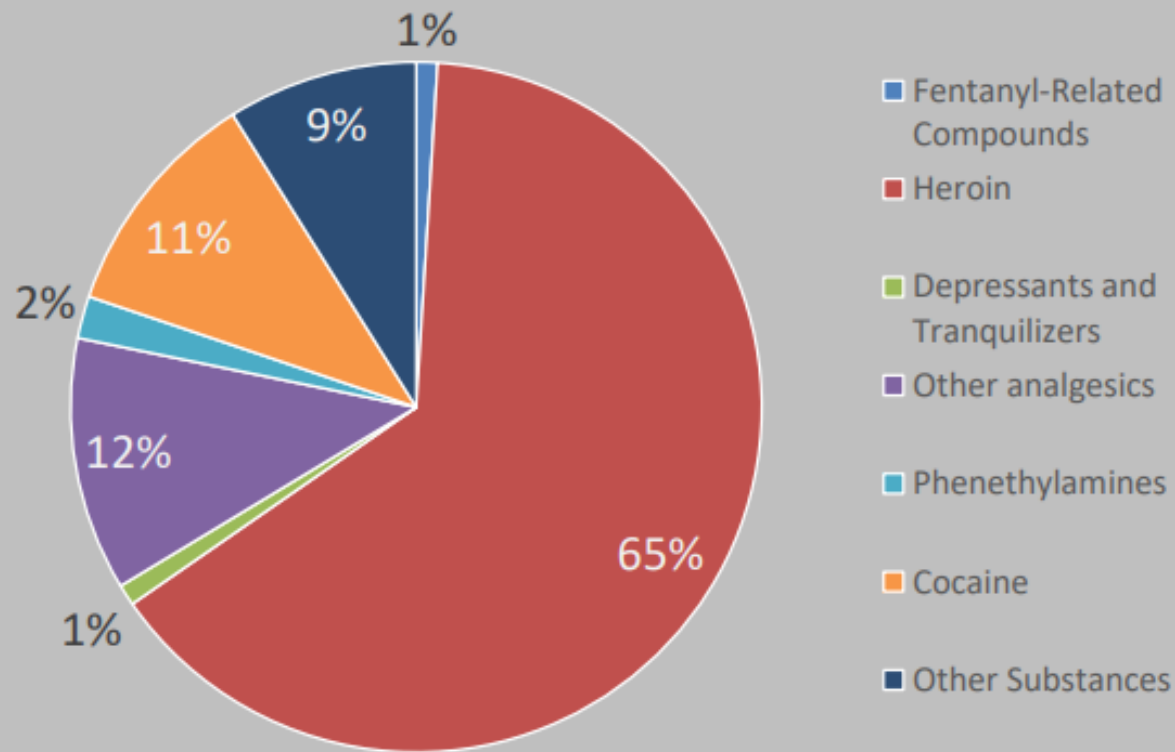
- National Forensic Laboratory Information System
- Systematically collects drug identification results from drug cases submitted to and analyzed by Federal, State, and local forensic laboratories
- Fentanyl has been in the top 5 drugs identified nationally since 2017



# NFLIS

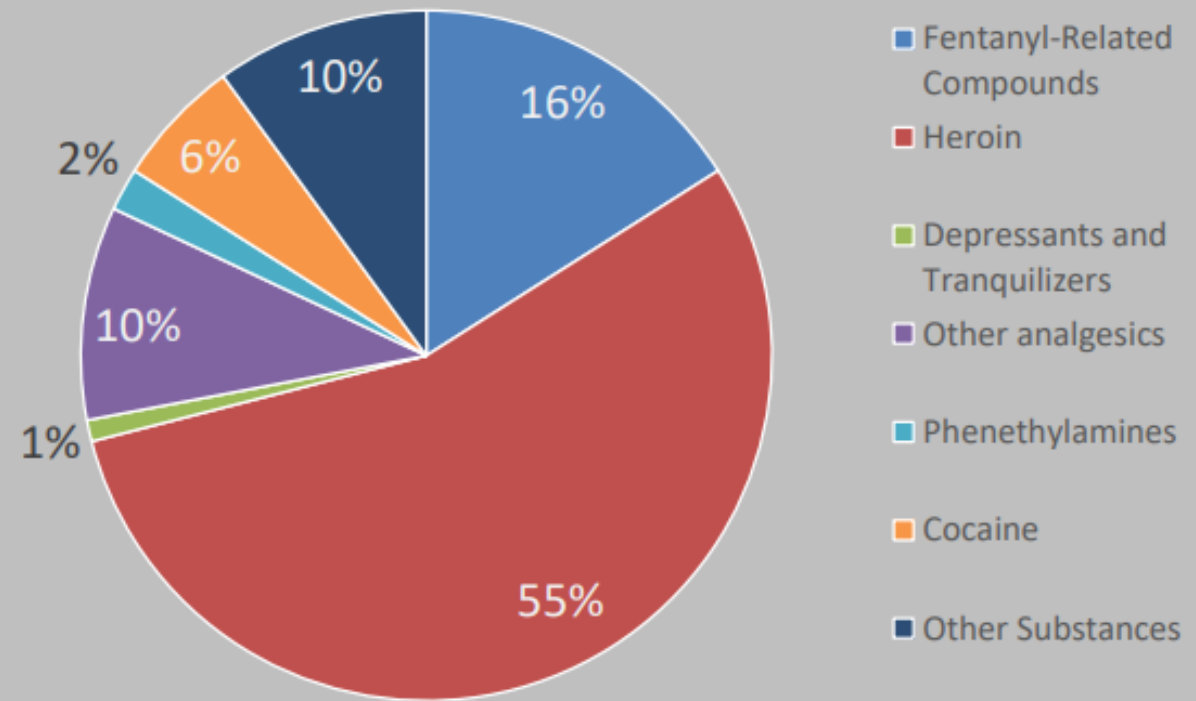
Percentage of all substances co-reported with fentanyl in NFLIS-Drug, **2013**

(n=881)



Percentage of all substances co-reported with fentanyl in NFLIS-Drug, **2018**

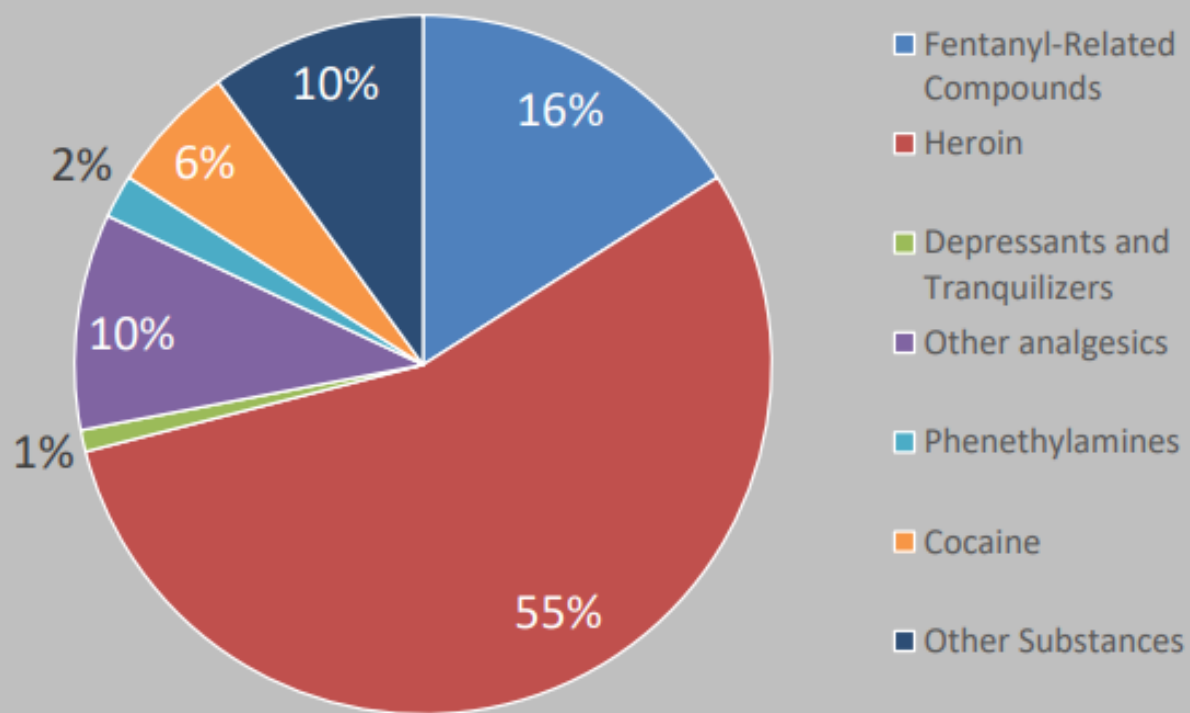
(n=38,141)



# NFLIS

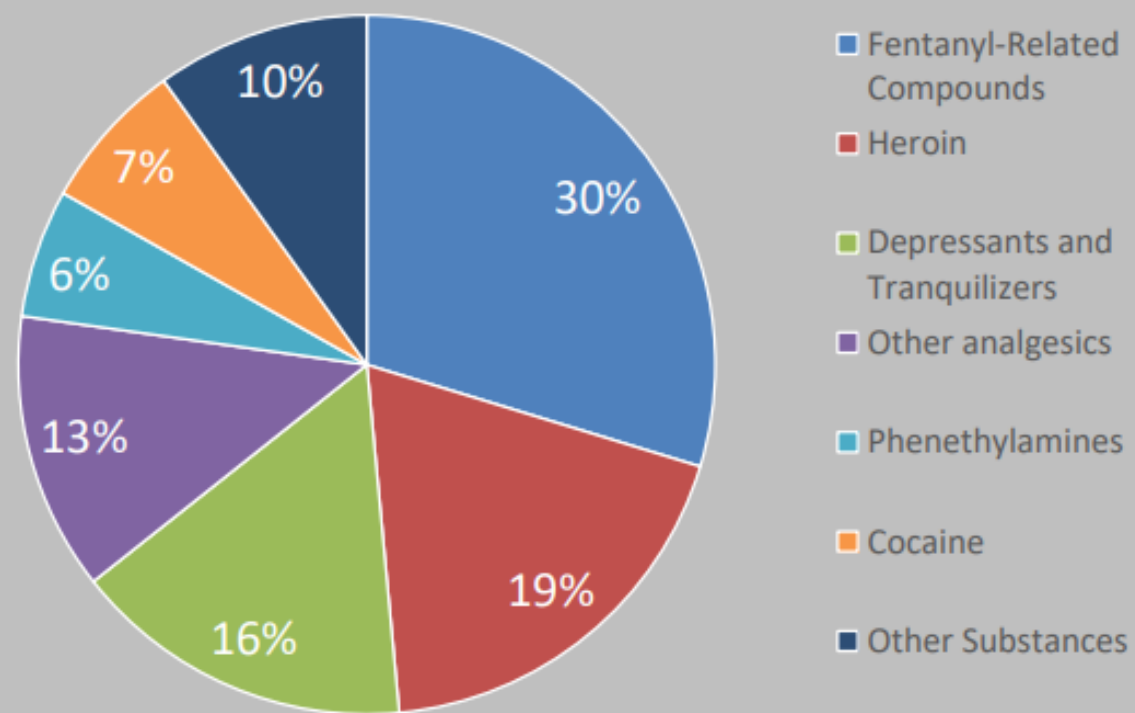
Percentage of all substances co-reported with fentanyl in NFLIS-Drug, **2018**

(n=38,141)



Percentage of all substances co-reported with fentanyl in NFLIS-Drug, January–June **2023**

(n=10,730)





# DEA TOX

- Surveillance program to detect new psychoactive substances in the United States
- Mass Spectrometry testing for cases where traditional drug screen has produced little or no options to explain patient symptomology
  - Also, Mass Spectrometry testing for drug seizures
- Email: [DEATOX@DEA.GOV](mailto:DEATOX@DEA.GOV)
  - Include brief description of the case (initial toxicology screen and history) and a request for testing
- The DEA will cover the full cost of testing the patient samples received



**DEA TOX**  
DRUG ENFORCEMENT ADMINISTRATION  
TOXICOLOGY TESTING PROGRAM

# Fentanyl still #1 Concern

- 2023 Drug Seizures analyzed by DEA Tox (n=45)
  - Fentanyl found in 62.2%
- 2023 Overdose Cases analyzed by DEA TOX (n=582)
  - Fentanyl found in 50.5%
  - Norfentanyl found in 38%
  - Fentanyl precursor 4-ANPP found in 28.5%
- Of the 505 fentanyl samples analyzed between Jan 2020 and June 6<sup>th</sup>, 2023, only 2 contained fentanyl alone



# Fentanyl still #1 Concern

- Blood levels of overdoses in both living and deceased is rising
  - Therapeutic range for analgesia = 0.6–3.0 ng/mL
  - Illicit ranges
    - 2006: 5-152ng/mL (n=23 all deceased)
    - 2016: 7.9-162ng/mL (n=18, 1 deceased)

# Treating Fentanyl Overdose

- Opioid antagonist e.g. naloxone, naltrexone, nalmeffene
- $T_{1/2}$  naloxone:
  - IM, IV, SUBQ: 30-90 minutes
  - Intranasal: ~1.1-2 hours
- Opioid Reversal Initial doses
  - 0.04-2mg IV q 2-3 minutes prn
- One study investigating high dose ( $>0.15\text{mg}$ ) naloxone, found 17.4% of patients did not have adequate reversal after 3 doses of naloxone
  - Continuous Infusion: administer 2/3 of initial effective naloxone bolus per hour (usual dose 0.25-6.25mg/hr)
- Higher doses of naloxone can result in cardiac arrhythmias and pulmonary edema due to release of catecholamines



# Adulterated Fentanyl

- Sent through the mail from various countries (China, Netherlands, Hungary)
- Cut at the local level
  - Alter pharmacologic effects
  - Enhance potency
  - Bulk up drug quantity
- Fun fact: Some dealers are color-coding with plant food/fertilizer to *brand* their product



## Representations of Fentanyl Forms in Ohio

**Powder**



**Tablets**



**Chalk**



**Rocks**



**Black Tar**



**Gum**



## Fentanyl Forms Encountered Throughout North America

**Alaska: Pellets**



*Image Credit: Anchorage Police Department*

**Halton, Canada: Popcorn**



*Image Credit: Halton Regional Police Twitter Photo*

**Calgary, Canada: Lego Blocks and Puzzle Pieces**



*Image Credit: Calgary Police*

**Arizona: Confetti Tablets**



*Image Credit: Arizona Department of Public Safety*



# Adulterants



# Opioids not named Fentanyl

- Fentanyl analogues
  - E.g Beta-Hydroxy Fentanyl 9.3%
  - Clinical Presentation: same as any opioid

Vital Signs	Consciousness/neuropsychiatric symptoms	Other symptoms
Miosis Bradycardia Hypotension Bradypnea/Respiratory arrest Pulmonary edema Hypothermia	Coma CNS depression	Decreased gastric tract motility

- Nitazenes
  - E.g. Metonitazene 3.4%
  - Tenfold more potent than fentanyl
  - Clinical Presentation: Deceased





# Kratom

- Active ingredients: Mitragynine – stimulant, 7-hydroxymitragynine – sedative
- Low Dose (1-5g)
  - Stimulatory
  - Antidepressant-like effect associated with serotonin, norepinephrine and dopamine
- High Dose (>5g)
  - Sedative and analgesic due to activating opiate receptors
  - Can also counteract opioid withdrawal
- Clinical Presentation:

Vital Signs	Consciousness/neuropsychiatric symptoms	Other symptoms
Brady/tachycardia	Coma	Decreased gastric tract motility
Hypo/hypertension	CNS depression	Face flushing
Bradypnea/Respiratory arrest	Insomnia	Nausea/Vomiting
Pulmonary edema	Extreme fatigue	Diaphoresis
Hypo/hyperthermia	Psychosis	

Suhaimi FW, et al. Brain research bulletin. 2016 Sep 1;126:29-40.; Saingam D, et al. International Journal of Drug Policy. 2013 Jul 1;24(4):351-358  
Yates, C. Novel Psychoactive Substances. Academic Press, 2022. 181-202.

# Stimulants

- Cocaine
  - Directly inhibits the reuptake of DA, 5-HT, and NE
    - ↑ NE stimulates  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$  and  $\beta_2$  with preferential  $\alpha$  activity on the cardiac and peripheral vasculature
  - Sodium channel blockade (local anesthetic)
  - Increases glutamate and aspartate
- Amphetamines
  - Binds to DAT, NET, SERT transporters
  - Inhibits reuptake of neurotransmitters
  - Triggers efflux of intracellular neurotransmitters
- Clinical Presentation:



Vital Signs	Consciousness and neuropsychiatric symptoms	Other symptoms
Mydriasis	Agitation	Diaphoresis
Tachycardia	Anorexia	Tremor
Hypertension	Paranoia, psychosis, violent behavior (AMP>cocaine)	Hyperreflexia
Tachypnea		Hypertonia
Hyperthermia		Clonus
		Seizures

<b>Current Street Names</b>		
	<b>Crack Cocaine</b>	<b>Powdered Cocaine</b>
<b>Most Common</b>	crack, hard, rock, work	coke, girl/white girl, powder, snow, soft
<b>Other</b>	butter, crackle, dope, hardball, hardware, ready rock, stones, straight drop	Becky, blow, booger sugar, Brittany, Christina Aguilera, fast, fish scales, fluff, nose candy, rich man's drug, ski slopes, snowball, Snow White, white, Whitney Houston, yay, yayo

<b>Current Street Names for Methamphetamine</b>	
<b>General</b>	breakfast/fast, chicken feed, crank, full throttle, go/go-go/go-fast, gorilla, green light, juice, King Kong, jib, meth, poor man's cocaine, slick, speed, tweak, zoom/zoom-zoom
<b>Crystal</b>	clear, Christina/Tina, crystal, glass, ice/ice cream/cream, Ice Boulevard, ice cubes/cubes, ice skating/skating, icicles, shards, shatter, window
<b>Powdered</b>	bathtub crank, shake/shake-and-bake

# Cathinones

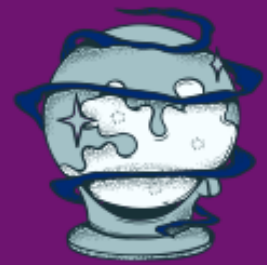
- AKA Bath Salts
- Can have a sympathomimetic effect and/or serotonin syndrome
  - Generally, has less ability to cross blood brain barrier
  - Water soluble
- Clinical Presentation:



Vital Signs	Consciousness and neuropsychiatric symptoms	Other symptoms
Mydriasis	Agitation	Diaphoresis
Tachycardia	Anorexia	Tremor
Hypertension	Confusion	Hyperreflexia
Tachypnea	Coma	Hypertonia
Hyperthermia	Euphoria	Clonus
	Increased concentration	Induced myoclonus
		Seizures
		Muscle rigidity
		Diarrhea



# Benzodiazepines



- Designer
  - Bromazolam 17.4%
    - Brominated version of alprazolam
- Prescription
  - Midazolam 9.1%
  - Alprazolam 7.7%
  - Lorazepam 6.7%

- Clinical Presentation:

## Consciousness and neuropsychiatric symptoms

Sedation  
Hypnosis  
CNS depression  
Euphoria  
Amnesia  
Seizures when discontinued

## Other symptoms

Anxiolysis  
Muscle relaxation  
Ataxia

## Current Street Names for Sedative-Hypnotics

General	beans, benzos, forget-me-nots
Xanax®	<p><i>General:</i> X, xannie/xannies, xans</p> <p><i>0.5 milligram:</i> peach/peaches</p> <p><i>1 milligram:</i> blues, footballs/footies</p> <p><i>2 milligrams:</i> bars/four bars/xan bars/xannie bars, buses/school bus/yellow school bus, green hulks/hulks, ladders, purple, sticks, wagon wheels, white, yellow</p>
Klonopin®	forget-a-pins, Ks, K-cuts, K-pins/pins
Valium®	Vs, vacuums, V-cuts



# Alpha 2 Agonists

- Xylazine 14.6%
- Inhibit the release of norepinephrine and epinephrine centrally
- Xylazine has been shown to impair the anticonvulsant properties of phenobarbital, phenytoin and diazepam in rats
  - Xylazine was abandoned as an antihypertensive due to excessive sedation compared to clonidine
- Clinical Presentation:



Vital Signs	Consciousness and neuropsychiatric symptoms	Other symptoms
Bradycardia Hypotension Decreased peripheral vascular resistance Bradypnea	Sedation Euphoria Amnesia	Severe necrotic skin ulcerations Abscesses Lesions Myocardial necrosis and fibrosis Muscle Relaxation Hyperglycemia

# Evaluation





# Case

A middle-aged female is rolled out of a car in front of the ED entrance which then drives off. She is pale, tachycardic, agitated and confused. The patient is brought into the ED where upon she seizes, loses consciousness and stops breathing.

## FIRST

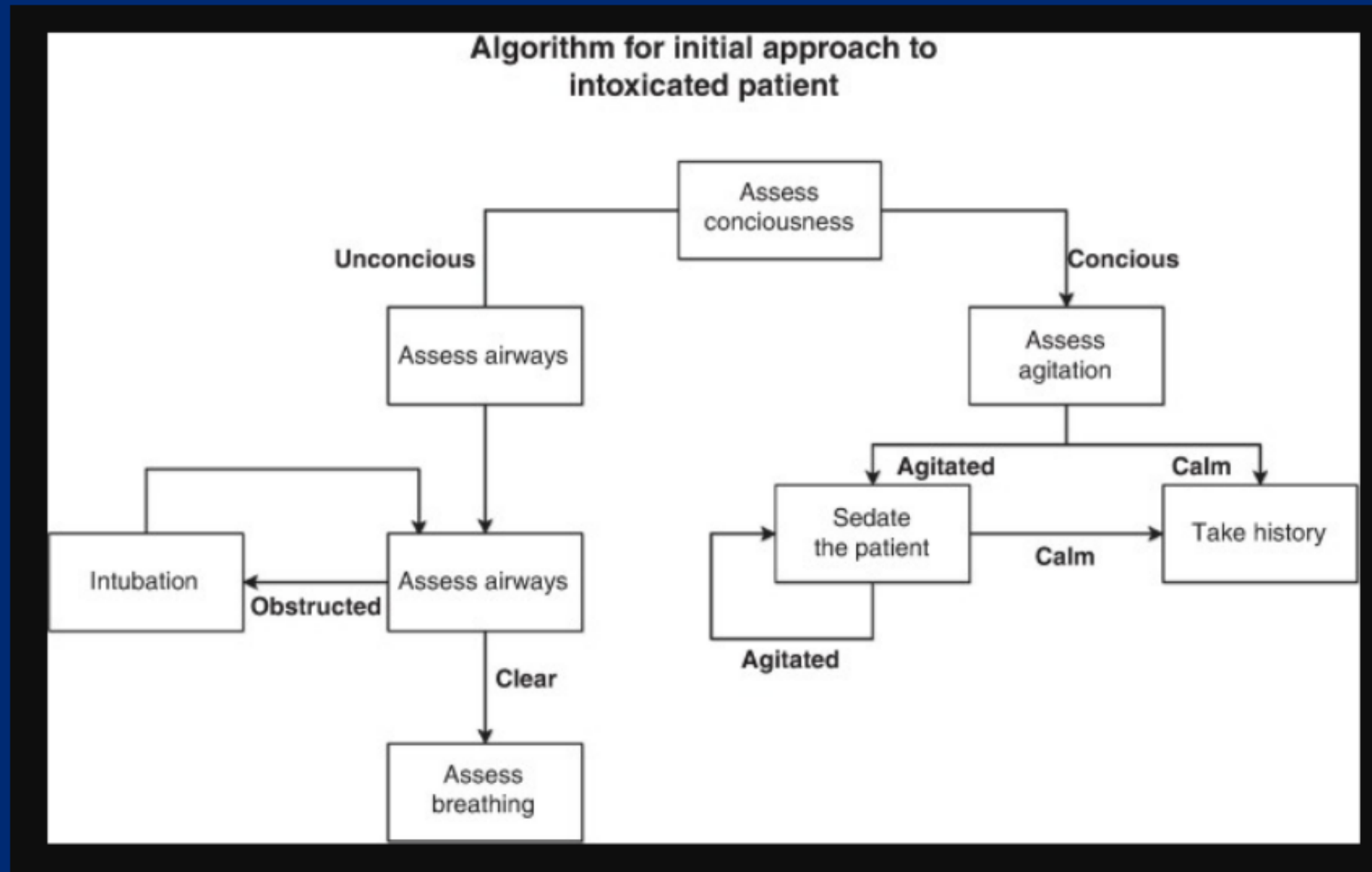
- Manage the airway and stabilize the patient

## THEN

- Figure out what is going on



# Initial Approach



# Taking a Recreational Drug History

- Record any information provided on the substances and circumstances of use by friends, co-users, witnesses, etc
  - Social media contents can provide details like time of use
- Who?
- What was the substance?
  - Was the effect similar to previous uses?
  - Was supplier the same?
  - Were the effects expected?
- How was substance used?
- When?
- Where?
- What is happening?
  - Symptoms reported and/or observed pre-hospital and at/after presentation to the Emergency Department
  - If “seizures” were witnessed, documentation of their characteristics
- Why?

# Evaluation Considerations

- Airway obstruction is a leading cause of death after toxic exposure
- Toxic effects of psychoactive substances may abruptly end resulting in sudden patient awakening
- Inadequate ventilation, oxygenation, and clinical deterioration are considered strong markers for intubation
- If a presentation “looks like” a known drug class, it is reasonable to treat it in the same way
- Airway patency should be confirmed if not secured
- Respiratory rate and breathing pattern assessed
- Lung auscultation for aspiration pneumonia, bronchospasm etc
- Circulatory status
- Vital signs



# Laboratory Values

- Blood glucose
- Arterial Blood Gases
- Complete Blood Count (Hg, Ht, PLT, WBC)
- Liver and kidney function tests (transaminases ALT/AST, GGT, alkaline phosphatase, total and unbound bilirubin, creatinine, and urea)
  - Serum osmolality if hyponatremia is present
  - Myoglobin (in urine) if signs of rhabdomyolysis
- Biochemical markers of muscular damage (creatine kinase)
- Electrolytes (sodium and potassium)
- Coagulation studies (activated partial thromboplastin time, prothrombin time, platelet count, D-dimer)
- ECG and cardiac markers (troponins and creatine kinase MB)

# Cardiac and EKG Abnormalities

	Abnormalities	Substances
Rhythm	Tachycardia Bradycardia Supraventricular tachycardia Atrial fibrillation Ventricular tachycardia A-V Blockade Sinus tachycardia	Stimulants, Synthetic Cannabinoids, Antihistamines Synthetic Cannabinoids Stimulants, Synthetic Cannabinoids Stimulants, Synthetic Cannabinoids Stimulants, Synthetic Cannabinoids, Antihistamines Stimulants, Synthetic Cannabinoids Antihistamines
QRS	Wide QRS, R in aVR, S in I and aVL (sodium channel blockade)	not common in NPS, Antihistamines, Quinine
T wave	T wave inversion T wave decreased	Synthetic Cannabinoids Quinine
ST	ST segment depression, ST elevation	Stimulants, Synthetic Cannabinoids
QT	Prolonged QT interval and related dysrhythmia	Phenethylamines, Synthetic Cannabinoids, antihistamines, Quinine, Xylazine

# Urinalysis Example

Drug Screen	Analyte	Detection Limit	Detection Times
Benzodiazepine	oxazepam	200 ng/mL	Diazepam: 3-12 days Alprazolam: 1-3 days Flunitrazepam: 1-2 days Clonazepam: 3-8 days
Cocaine	benzoylecgonine	300 ng/mL	0.5-3 days
Amphetamine	amphetamine, methamphetamine	1000 ng/mL	48 hours
Cannabis	$\Delta$ -9-THC	50 ng/mL	Casual user: 1-2 days Moderate user: 5-10 days Chronic user: 10-28 days
Opiate	morphine	2000 ng/mL	1-3 days
Barbiturate	secobarbital	200 ng/mL	Secobarbital: 1-2 days Pentobarbital: 2-4 days Phenobarbital: 10-20 days
Ethanol	Only 1% to 2% is excreted unchanged in the urine	< 10 mg/dL	7-12 hours



# Opioid Screening

Type	Examples	Positive on standard UDS for opiates?
Opiates	Morphine	Yes
	Codeine	Yes
Semisynthetic Opioids	Heroin	Yes
	Hydrocodone	Maybe
	Oxycodone	Maybe
	Buprenorphine	Unlikely
Fully Synthetic Opioids	Tramadol	No
	Fentanyl	No
	Methadone	No

# Treatment



# Opioids

## Peri-Stabilization

- Manage airway (Intubation)
- Naloxone boluses
  - May consider continuous infusion
- Cardiovascular Stabilization
- Manage other clinical presentation
  - Seizures
  - Clonidine for anxiety, tachycardia
  - Analgesics
  - Nausea/Vomiting/Diarrhea

## Post-Stabilization

- 80%-90% relapse without medications for Opioid Use Disorder (MOUD)
  - Methadone
  - Buprenorphine
  - MOUD should always be paired with cognitive behavioral therapy and counseling
- 50% reduction in death rate with MOUD
- All studies of tapering and discontinuation demonstrate very high rates of relapse
- Novel Regimens
  - IV buprenorphine protocol
  - Buprenorphine Long-acting Injectable SUBQ



# Ohio Automated Prescription Reporting System Updates

- State indicator
  - Patient participating in Opioid treatment program (OTP)
  - Patient consent
  - OTP program name, city and contact information
  - Medication not displayed
- Non-fatal overdose indicator
  - Reported from Ohio emergency departments on or after April 8th, 2024
  - Not reflected in the overdose risk score
  - Goal: providing information to improve and promote access to medication for MOUD

**State Indicators (2)**

- ! Patient is participating in an opioid treatment program to address a diagnosed opioid use disorder at
- !  $\geq 5$  opioid or sedative providers in any year in the last 2 years

**Other Health Information**

**Non-Fatal Drug Overdose Events** ⓘ

No history of overdose reported.

# Stimulants + Cathinones

## Life-Threatening Complications

- Airway, breathing, and circulation management
  - Benzodiazepines
  - Phentolamine 5-10 mg IV q 5-15 minutes PRN
  - Oxygen
  - Nitroglycerin for patients w/ HTN
- Fluid resuscitation
- Vigorous cooling measures
- Activated charcoal (oral amphetamines)
- Avoid physical restraints as they may cause aggressive behavior, heighten risk of hyperthermia and asphyxia

## No life-threatening signs or symptoms

- Sedation and observation
- Benzos ± antipsychotics

# Benzodiazepines

- Monitor for seizures and protect airway
- Flumazenil will likely reverse illicit and prescription benzodiazepines
  - Increases risk for agitation
  - Increases risk for seizures
  - Increases adverse cardiovascular events



# Alpha-2 Agonists

- Hypotension and diuresis may respond to just IV fluids
- Hypotension, bradycardia – vasopressors
  - Atropine has been used in case reports (xylazine)
- Skin Ulcers: wound care including debridement, silver sulfadiazine or antibacterial ointments
  - Skin grafts and/or amputation in severe cases
- Monitor for somnolence, lethargy
- Naloxone may help reverse respiratory depression



# Harm Reduction



# Harm Reduction

- Naloxone
  - Opioid antagonist
  - Safe and effective
  - Available prescription and over the counter
- Test Strips: Fentanyl and Xylazine
  - Not 100% accurate and will not detect non-fentanyl or non-xylazine drugs
  - Fentanyl
    - Detects the presence of about 12 analogues
- Syringe Service Program (SSP)
  - Offer comprehensive care and facilitate safer methods of drug use

# Case

- Acute Management
- Pulmonary
- Cardiovascular
- Neurological
- Renal
- Hepatic
- Evaluation of Labs, EKG, Radiology
- Disposition





# Summary/ Pearls

- Follow the Clinical Trail
- Patients may frequently have concomitant psychostimulants and depressants in the presence of respiratory suppressants and proconvulsant agents
- Duration of action of supportive interventions need to be balanced against duration of action of offending agents in order to not precipitate a later iatrogenic adverse effect
- If possible, use medications with short duration of action and repeat dosing
- Evaluate electrolytes in all patients
- Just because urine does not test positive, it doesn't mean a class of drug is not present

**ABCs have not changed!**

## Drug Category: General Drug Reference

Oxycodone, Hydrocodone,  
Xanax™, Adderall™, Fentanyl,  
Ecstasy



Fentanyl, Heroin,  
Cocaine



Drug Dealer  
("Plug")



Drug Price  
("Ticket")



Potency:



Drug Effects:



## Drug Category: Pills, Counterfeit Tablets

Oxycodone/Percocet™



Hydrocodone/Vicodin™



Alprazolam/Xanax™



## Drug Images:



Example of  
Oxycodone 30mg



Example of  
Vicodin™



Example of  
Xanax™ 2mg



Example of  
Xanax™ 0.5mg



Example of  
Percocet™ 10mg

**Drug Category: Opioids** (Fentanyl/Fentanyl Analogs/Fentanyl-Related Compounds, Heroin, Codeine)

Fentanyl / Fentanyl Analogs /  
Fentanyl-Related Compounds



Heroin



Codeine



**Drug Images:**



Example of  
Fentanyl



Example of  
Brown Powder Heroin,  
White Powder Heroin, and  
Black Tar Heroin



Example of  
Codeine

**Drug Category: Methamphetamine, Crystal Methamphetamine**

Methamphetamine



Crystal Methamphetamine



**Drug Images:**



Example of Methamphetamine

**Drug Category: Cocaine, Crack Cocaine**

Cocaine



Crack Cocaine



**Drug Images:**



Example of Powdered Cocaine



Example of Crack Cocaine

**Drug Category: Marijuana**

Marijuana



**Drug Images:**



Example of Marijuana



### Drug Category: THC Products

THC Extract/Concentrate



THC Edibles



THC Vape Cartridges



### Drug Images:



Example of  
THC Extract/Concentrate



Example of  
THC Edibles



Example of  
THC Vape Cartridges

### Drug Category: Hallucinogens

Psilocybin Mushrooms



Ecstasy/MDMA



LSD/Acid



### Drug Images:



Example of  
Psilocybin Mushrooms



Example of  
Ecstasy/MDMA



Example of  
LSD



# Potent Poisoning:

WHEN SLEEPING BEAUTY GETS A BAD  
APPLE

Amy Durell PharmD, BCPS