



Pacific Southwest

RURAL OPIOID TECHNICAL

ASSISTANCE REGIONAL CENTER

Emerging Drug Trends in Rural Settings

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Learning Objectives

1. Describe the current information on the availability and at least three (3) patterns of emerging drug trends in non-metropolitan rural communities across United States.
2. Identify at least three (3) key characteristics and acute and chronic effects of synthetic drugs, most notably synthetic opioids (fentanyl), xylazine, synthetic cannabinoids (spice) and synthetic cathinones (bath salts).
3. Explain at least two (2) strategies for communicating the dangers involved with the use of emerging drugs.

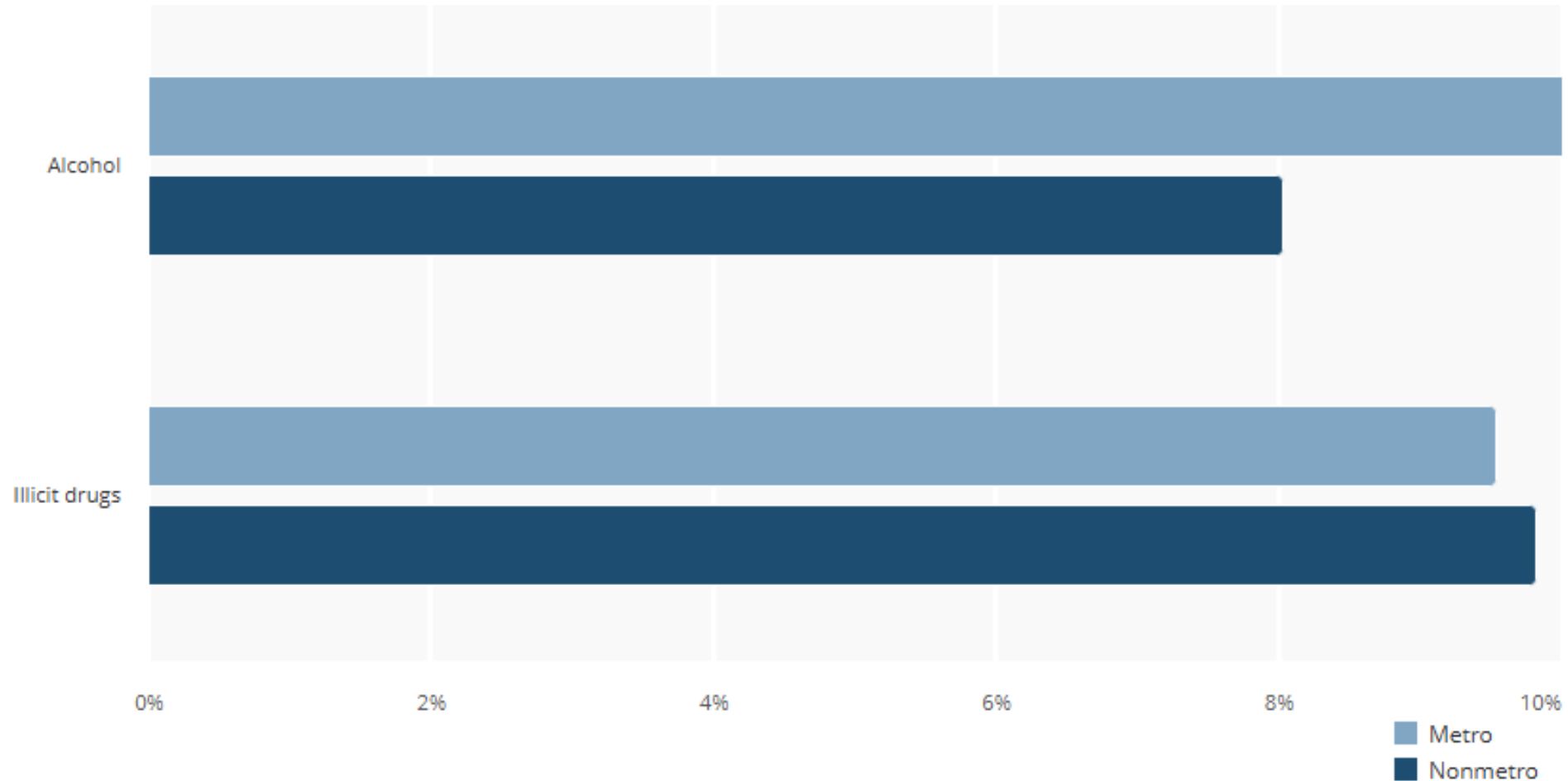
Rural Settings as Drivers of Substance Use



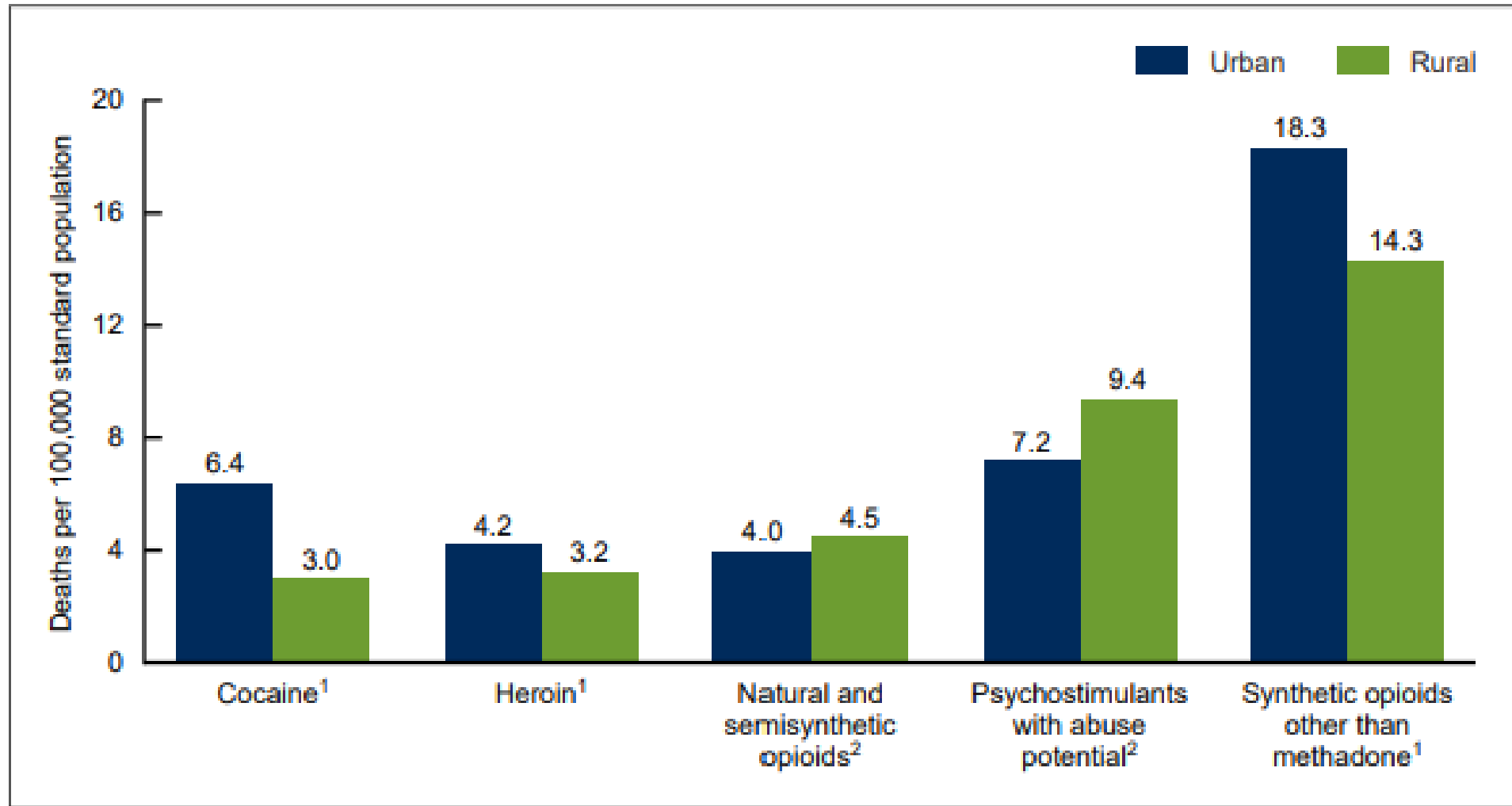
Barriers to Effective SUD Treatment Experienced by People Living in Rural Areas

- Fewer treatment options
- Lack of educational resources
- Limited continuing education opportunities
- Lack of good facilities
- Challenges with transportation
- Distance of home from treatment facilities
- Reliance on friends or family for transportation
- Challenges in meeting housing/other ancillary needs
- Need for mental health, medical and dental services

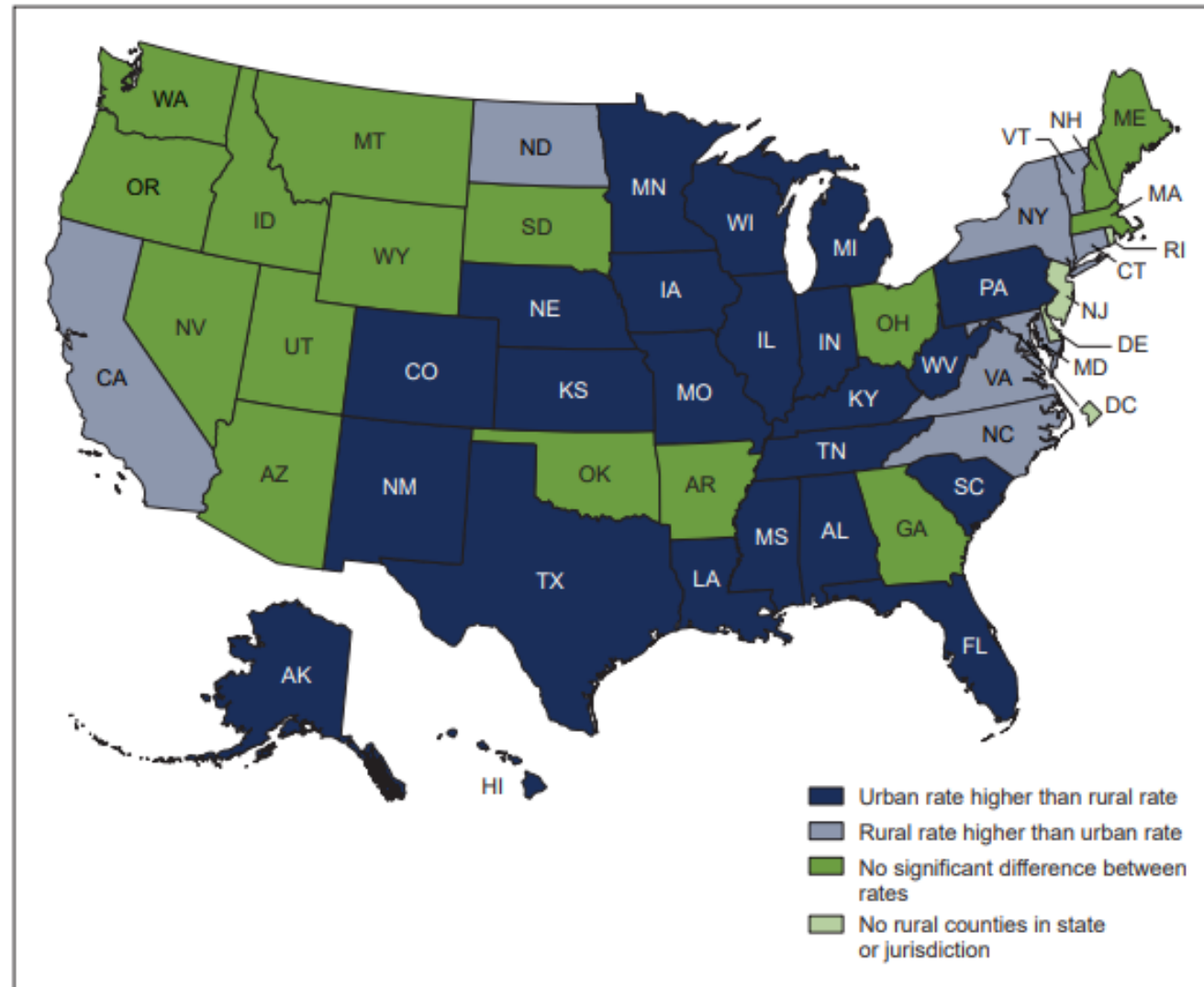
Past Year SUD in Metro and Nonmetro Counties, 2023



Drug Poisoning Death Rates by Drug Vary by Urbanicity



Location Matters



SOURCE: Spencer et al., 2022

What questions do you have,
before we move on to a deep-
dive into emerging drugs?

Commonly Used Psychoactive Substances

SUBSTANCE	EFFECTS
Alcohol (liquor, beer, wine)	euphoria, stimulation, relaxation, lower inhibitions, drowsiness
Cannabinoids (cannabis, hashish)	euphoria, relaxations, slowed reaction time, distorted perception
Opioids (heroin, opium, many pain meds)	euphoria, drowsiness, sedation
Stimulants (cocaine, methamphetamine)	exhilaration, energy
Club Drugs (MDMA/Ecstasy, GHB)	hallucinations, tactile sensitivity, lowered inhibition
Dissociative Drugs (Ketamine, PCP, DXM)	feel separated from body, delirium, impaired motor function
Hallucinogens (LSD, mushrooms, Mescaline)	hallucinations, altered perception

What are New Psychoactive Substances (NPS)?

- Chemically diverse emergent substances in the global drug market
- Rapid evolution/emergence and limited data about health effects poses large challenges related to prevention and treatment
- Analysis, identification, information sharing and monitoring are demanding given how rapidly new substances emerge

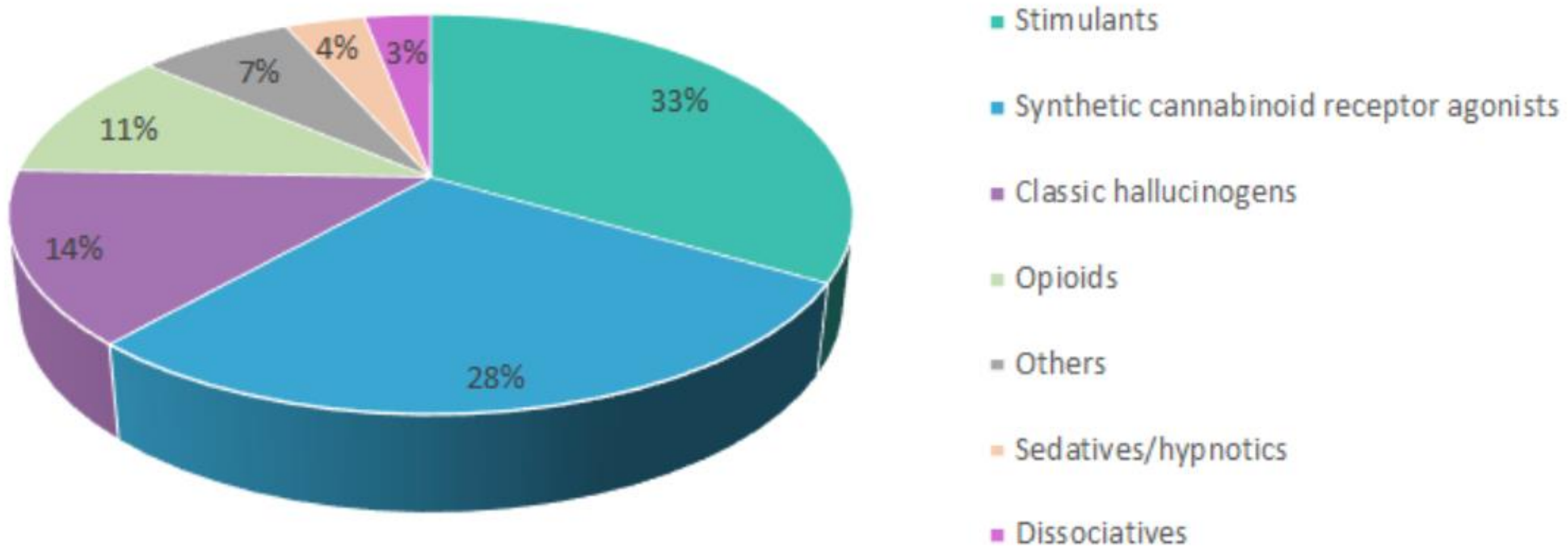
NPS Categories

- Aminoindanes
- Benzodiazepines
- Fentanyl analogues
- Lysergamides
- Nitazenes
- Phencyclidine-type substances
- Phenethylamines
- Phenidates
- Phenmetrazines
- Piperazines
- Plant-based substances
- Synthetic cannabinoids
- Synthetic cathinones
- Tryptamines

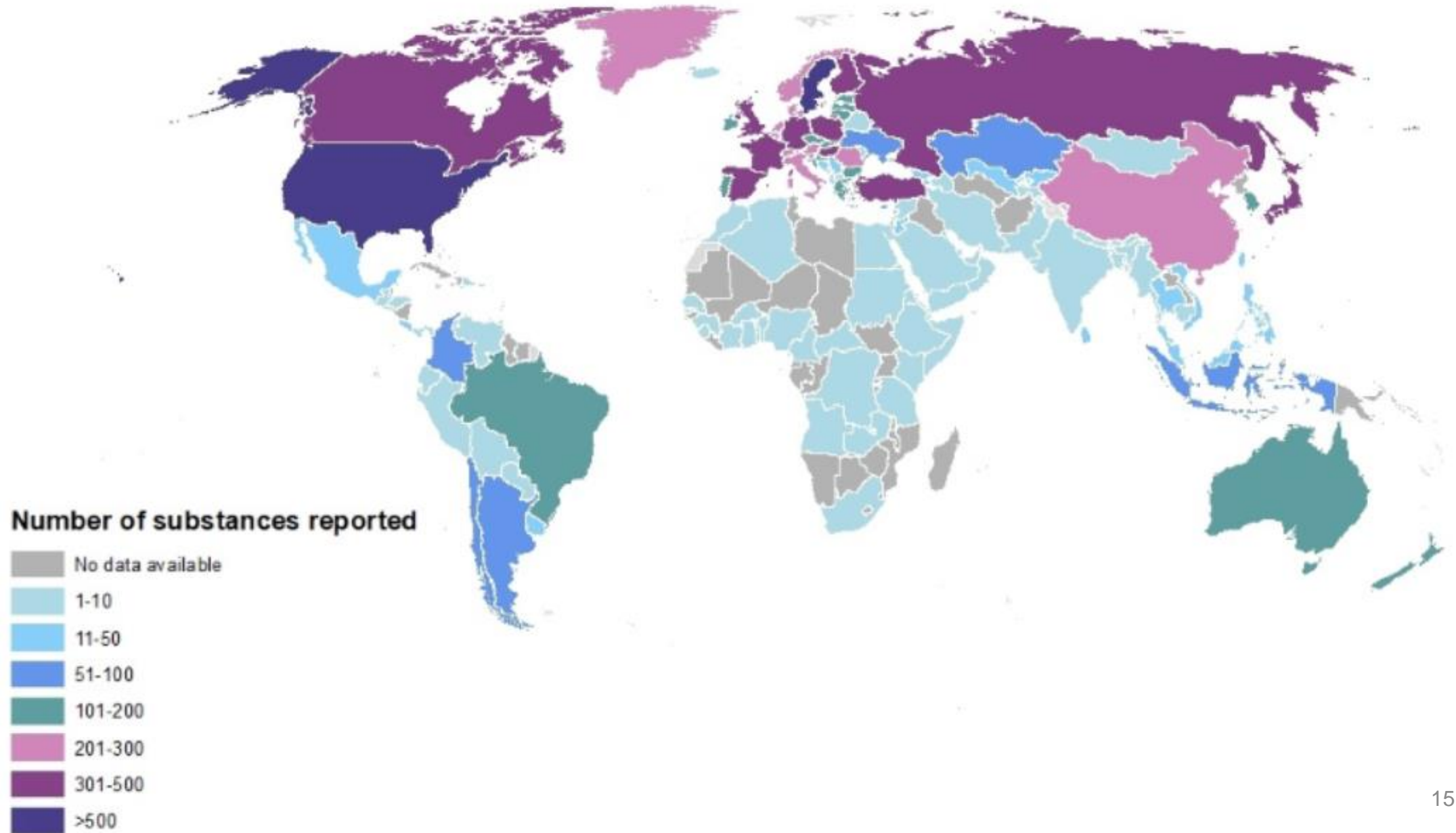
Risks Associated with NPS

- Linked to health problems such as seizures and agitation, aggression, acute psychosis
- Severe intoxication or dependence can result
- Safety data and long-term risks are often unknown
- Purity and composition are often not known
- Polysubstance use can increase risk of hospital admission and death

Synthetic NPS by Drug Category (aka Effect Group)



Global Emergence of New Psychoactive Substances



Ecstasy pills sold today often contain more than double

Methamphetamine prices in North America and South

The decrease in prices and increase in availability has

Synthetic drugs are often cheaper than an alcoholic drink in night club settings, which increases their attraction for young people with limited financial resources

to a life-threatening overdose.

\$7-\$12

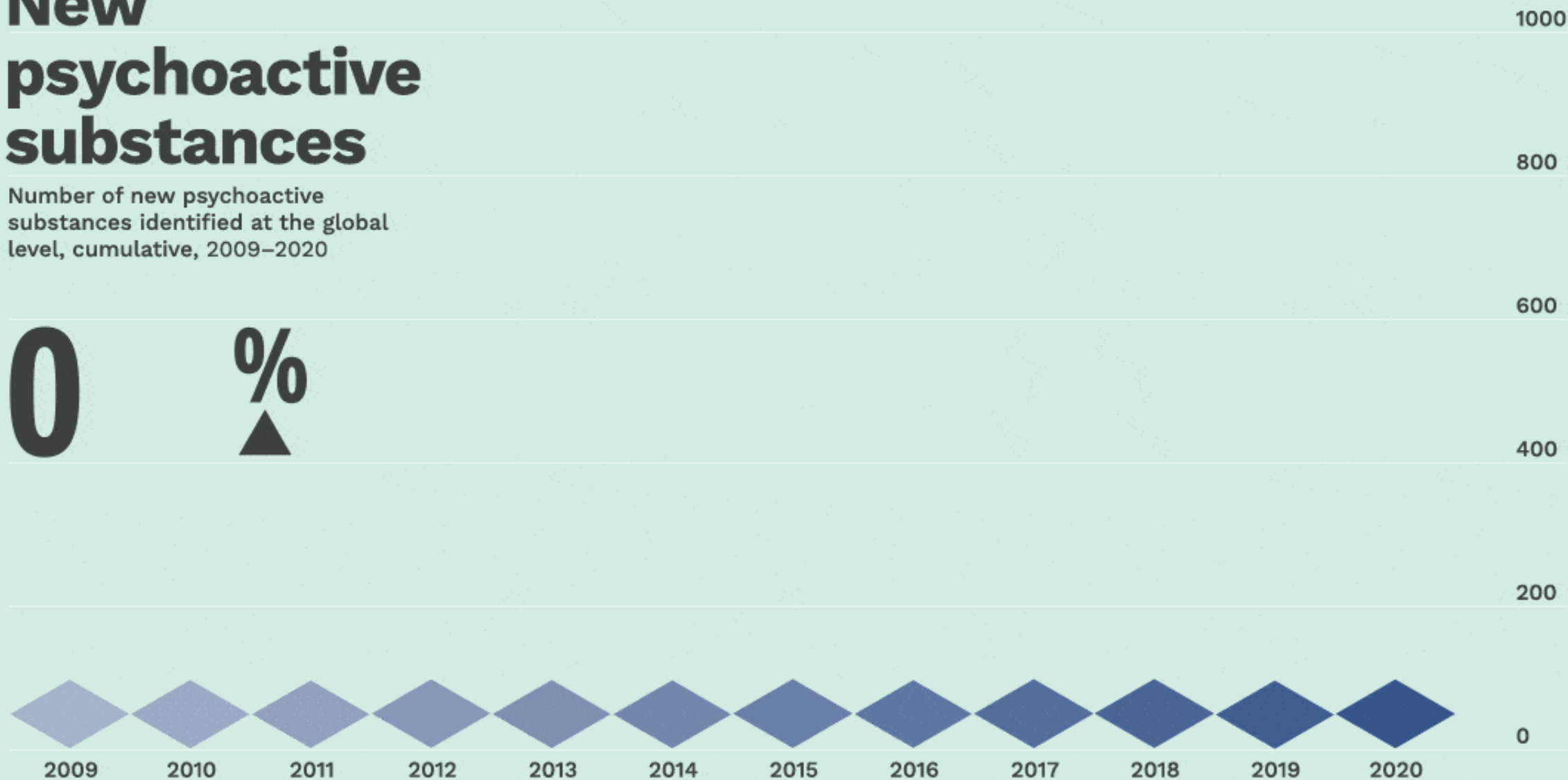
~~\$115~~
/gram
Methamphetamine

/tablet
Ecstasy

New psychoactive substances

Number of new psychoactive substances identified at the global level, cumulative, 2009–2020

0 %
▲



UNODC

United Nations Office on Drugs and Crime

Adulterants and Health Effects




Adulterant and health effects

Found in

Mood changes  Anxiety  **Caffeine**  Psychostimulant action
(potentiate effects)

Cocaine
Ecstasy
Heroin

Local anesthetics (benzocaine, lidocaine, procaine)

Methemoglobinemia   Arrhythmia  Seizures
(potentiate effects of common drug)
















Cocaine
Ecstasy
Heroin

Phenacetin

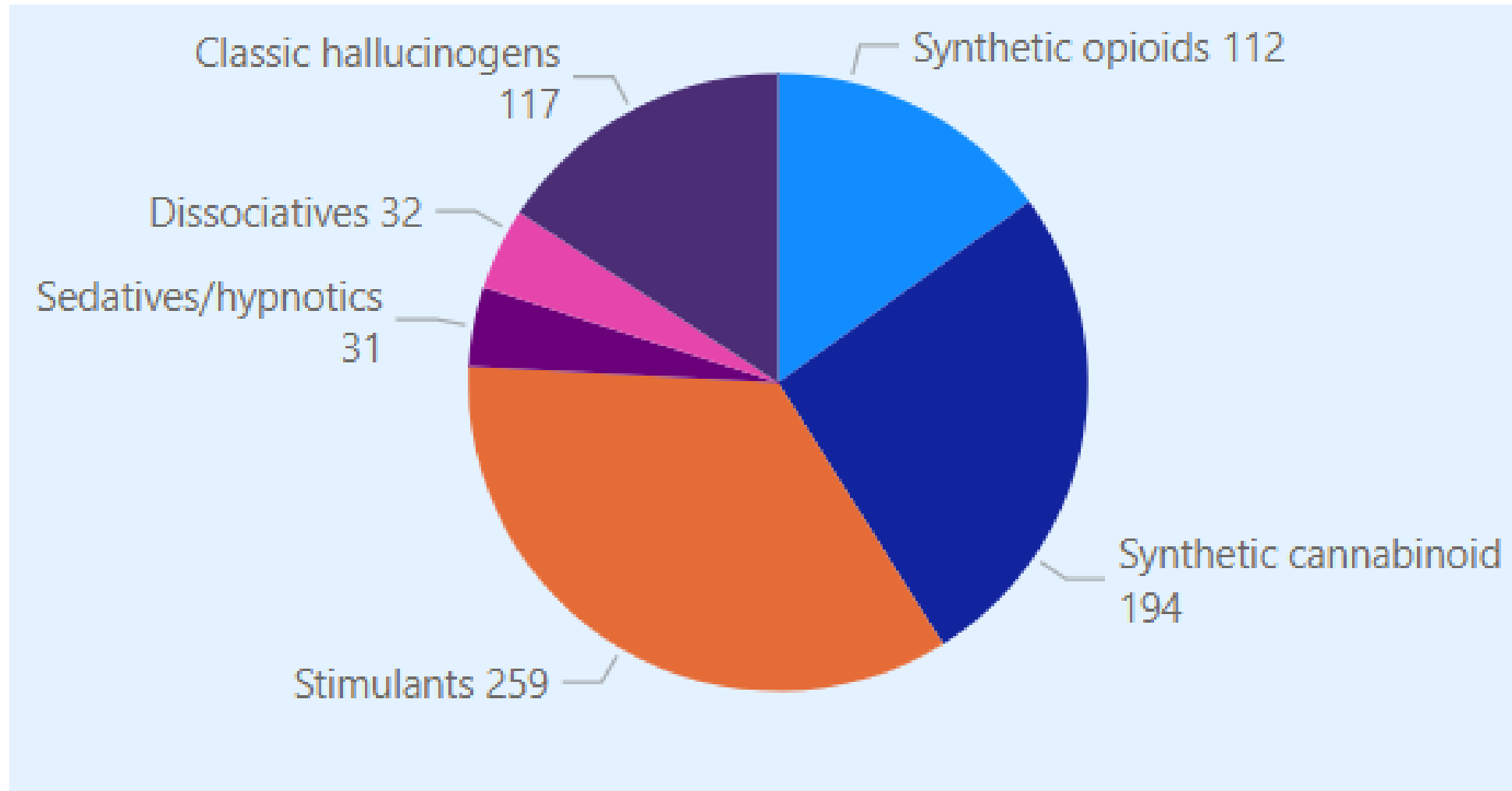
Hematological changes  Nephrotoxicity  Carcinogenic  Sleeplessness 

Cocaine
Ecstasy
Heroin

Adulterants and Health Effects (2)

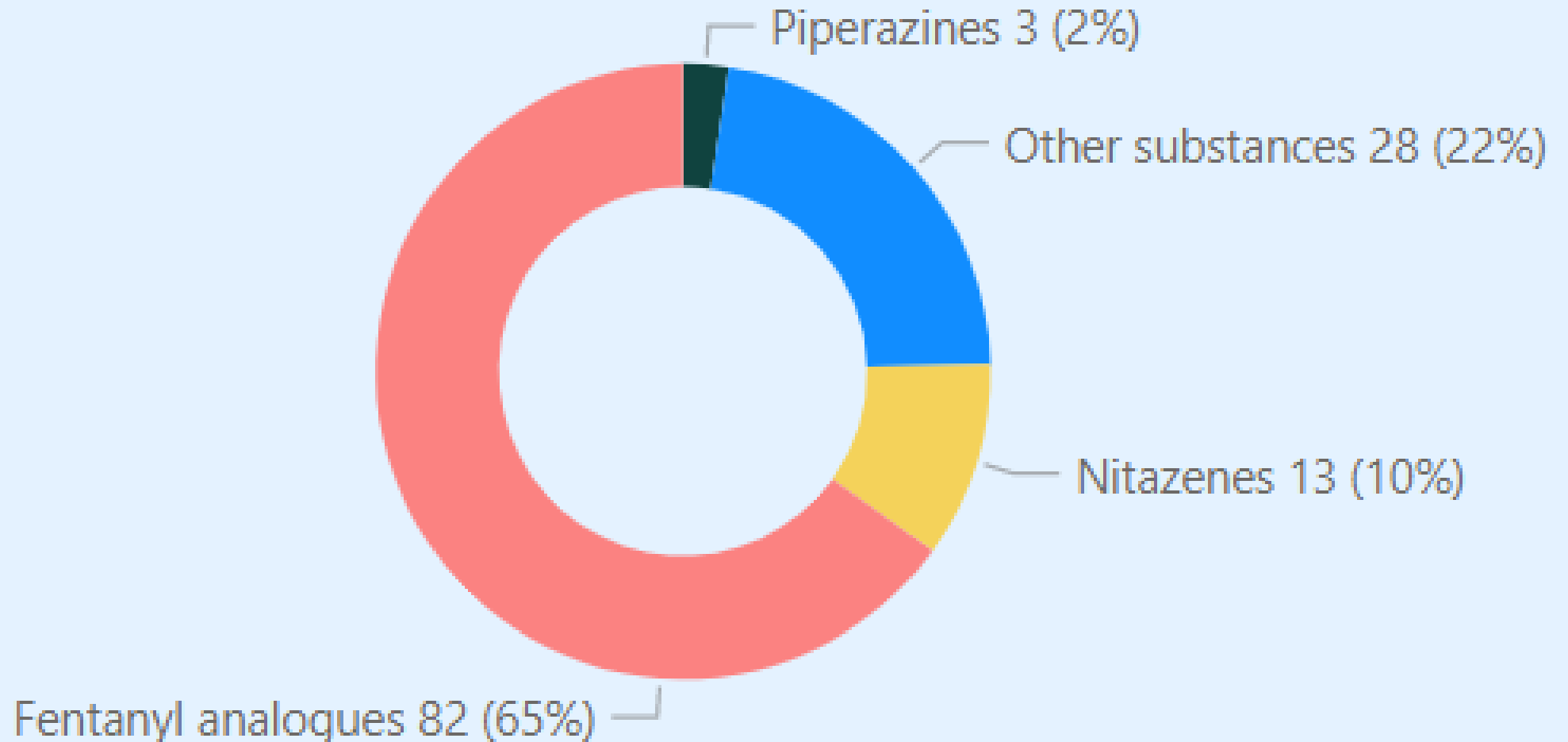
Adulterant and health effects				Found in
Levamisole				Cocaine Heroin
Infections 	Vasculitis 	Kidney disease 	Pulmonary complications 	
Clenbuterol				Heroin
Nausea and vomiting 	Tachycardia 	Arterial hypotension 	Myocardial injury 	
Derivatives of 2 C phenylethylamines (25x-NBOMes)				Ecstasy Heroin LSD
Confusion 	Seizures 	Rhabdomyolysis 	Arterial hypertension 	
Fentanyl and derivatives				Cocaine Heroin LSD
Respiratory depression 	Depression of consciousness 	Cardiorespiratory arrest 		

Distribution of NPS Reported Within Each Drug Category, North America 2013-2023



Synthetic Opioids, North America 2013-2023

Structural groups within this effect group



Synthetic Cannabinoids, North America 2013-2023

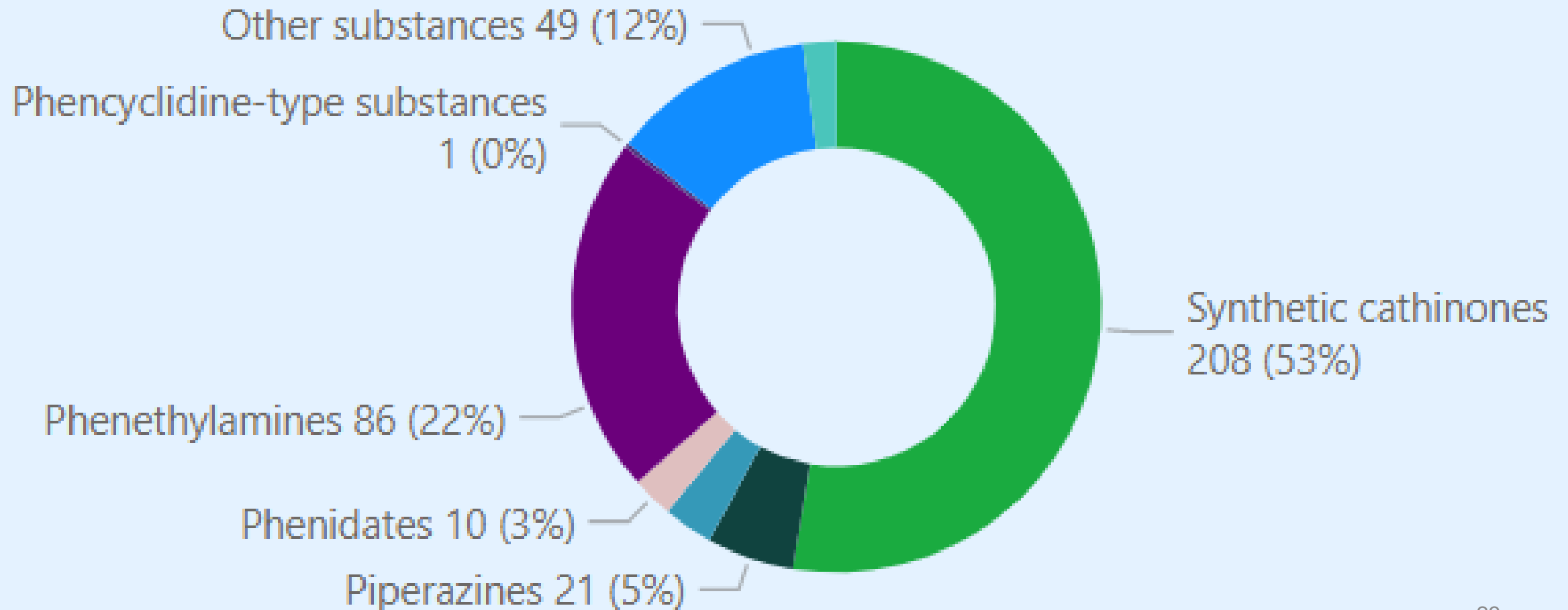
Structural groups within this effect group

Synthetic cannabinoids
335 (100%)



Stimulants, North America 2013-2023

Structural groups within this effect group



(Re)Emerging Synthetic Opioids

- With the void created by this legislation, synthetic opioids developed 6 or 7 decades ago are beginning to re-emerge
- U-compounds – developed in the 1970s; generally have a lower potency compared to fentanyl
- Benzimidazole opioids – developed in the 1950s; potency tends to be comparable to fentanyl analogues such as sufentanil (**approx. 7.5x as potent as fentanyl**)

What about “Rainbow Fentanyl”?



Fake oxycodone M30 tablets containing fentanyl

New Fentanyl Compounds

- Other fentanyl compounds are appearing in heroin, counterfeit pills and in autopsy findings.
- Para-fluorofentanyl was developed through research efforts in the 1960's and classified as a schedule I substance.
- Para-fluorofentanyl is showing up now in seized heroin, counterfeit pills, and autopsy findings.

New Opioid Class

- Benzimidazole was developed in the 1950's as a new opioid analgesic and is now showing up as a heroin adulterant.
- Metonitazene, an opioid in the benzimidazole class, is also showing up more frequently.

Benzimidazole Opioids (Nitazenes)

- Synthetic opioids have begun to emerge on the illicit market globally in 2019 (WHO, 2020)
- Some types (isotonitazine) estimated to be 500 times more potent than morphine (WHO, 2020)
- Appears to be contributing to overdose deaths in Illinois, Indiana, and Ohio (USA Today, 2020)
- Emerging drug so it does not appear on standardized drug tests (USA Today, 2020)
- Continues trend of new synthetic opioids appearing

Nitazene Potency Relative to Fentanyl and Morphine

Legend

1 circle = 1mg morphine

1mg of Morphine

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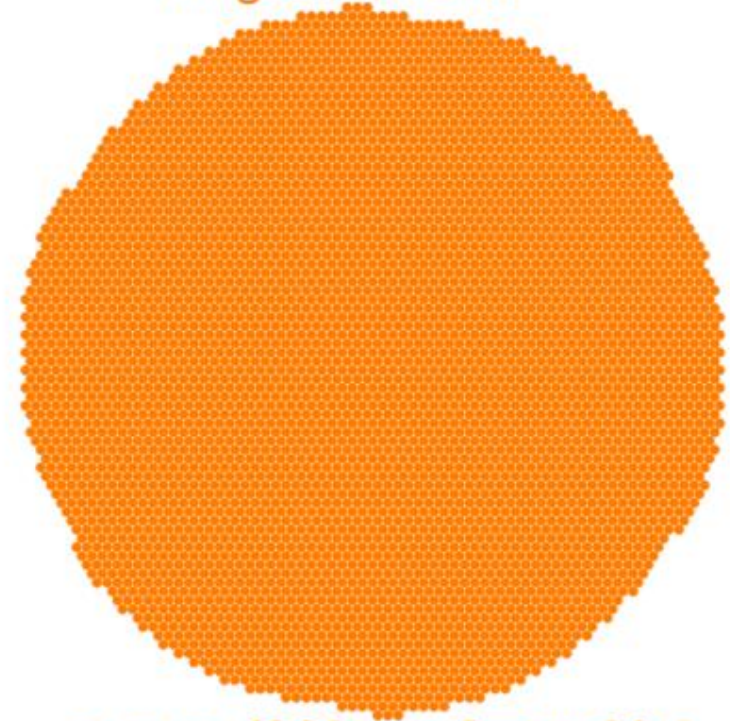
= 1mg of morphine

1mg of Fentanyl



= 100mg of morphine

1mg of Nitazene



= up to 4300mg of morphine

Involvement of New Drugs on Overdose

- In Tennessee the Knox County Regional Forensic Center reported on 770 unintentional overdose deaths.
- 562 (73%) were positive for fentanyl, para-fluorofentanyl, or metonitazene, either alone or in combination:
 - 192 (34%) were positive for fentanyl in the absence of other substances
 - 188 (33%) were positive for fentanyl and methamphetamine
 - 48 (9%) involved para-fluorofentanyl
 - 26 (5%) involved metonitazene

Medical Providers Should be Aware

- Both para-fluorofentanyl and the benzimidazole opioid, metonitazene contributed to unintentional overdose deaths in eastern Tennessee.
- These substances alone are capable of causing respiratory depression leading to death.
- Naloxone is capable of reversing overdose caused by these substances but additional doses may be necessary when fentanyl and these new substances are involved.

Emerging Substance: Xylazine

- Xylazine is a non-opioid sedative, analgesic, and muscle relaxant used in veterinary medicine and not approved for human use.
- It has been found among people who use drugs in Puerto Rico since the early 2000s and referred to as “anestesia de caballo”

Impacts of Xylazine

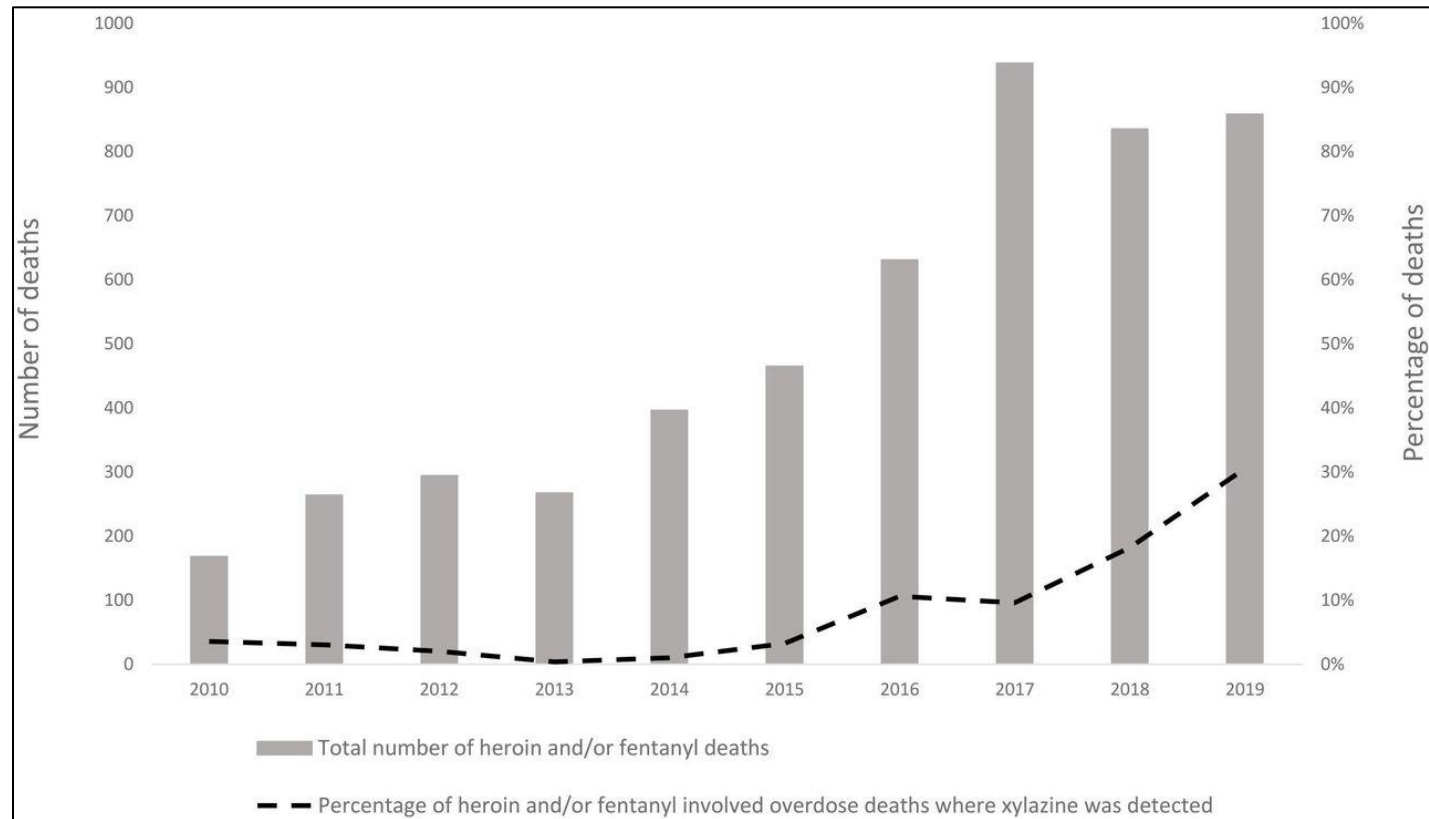
- In humans xylazine can cause hypotension, central nervous system depression, respiratory depression, and bradycardia.
- It also causes open skin ulcers among injectors who may continually inject affected areas for pain relief.

Xylazine in Philadelphia

- Philadelphia street name for xylazine is “tranq”; heroin or fentanyl cut with xylazine is called “tranq dope.”
- The following study examines trends in xylazine detection among post mortem toxicology tests in fatal overdoses in Philadelphia between 2010 and 2019.

Xylazine in Philadelphia (2)

- The Philadelphia Medical Examiner found xylazine in less than 2% of fatal heroin and/or fentanyl overdoses between 2010 and 2015 and an increase to 31% in 2019.



Xylazine in Philadelphia (3)

- Those positive for xylazine were mainly male (76%), between the ages of 35 to 54 (47%), and non-Hispanic white (65%).
- Among 2019 decedents positive for xylazine:
 - 100% were positive for fentanyl,
 - 10% positive for heroin,
 - 12% were positive for methamphetamine,
 - 28% were positive for benzodiazepines,
 - 53% were positive for cocaine.

Xylazine Across the US: Background

- Sharp increases in U.S. overdoses are linked to polysubstance use of synthetic compounds.
- Xylazine is a veterinary tranquilizer long noted in the opioid supply of Puerto Rico and more recently Philadelphia.
- National trends and geographic distribution and health risks are poorly characterized.

Xylazine is Increasingly Detected in Fentanyl Deaths

Xylazine, or "tranq," is a non-opioid sedative

Fentanyl deaths with **xylazine** detected increased **276%** between:

January 2019

2.9%

June 2022

10.9%



Addressing the prevalence of xylazine requires:

Surveillance - Routine testing in suspected overdose deaths

Prevention - Further investigation of its effects on humans

Treatment - Medical care such as respiratory and cardiovascular support

Source: Kariisa M, O'Donnell J, Kumar S, Mattson CL, Goldberger BA. Illicitly Manufactured Fentanyl–Involved Overdose Deaths with Detected Xylazine – United States, January 2019–June 2022. MMWR Morb Mortal Wkly Rep 2023;72:721–727.

Xylazine Attitudes among People Who Use Drugs and have Xylazine Awareness – Ohio, 2023-2024

Characteristic	Xylazine awareness ^a , Yes
	No. (%)
Total	293 (100.0)
How do you feel about using xylazine?	
I would rather use xylazine than other drugs	13 (4.4)
I use xylazine when it is available, but it isn't my 1st choice	16 (5.5)
I don't try to use xylazine, but I'm not worried about it being in my drugs	42 (14.3)
I do not want to use xylazine and try to avoid it	214 (73.0)
Other ^b	8 (2.7)
How important is it to know if xylazine is in your drugs?	
Not important at all	19 (6.5)
Slightly important	20 (6.8)
Moderately important	32 (10.9)
Very important	92 (31.4)
Extremely important	130 (44.4)

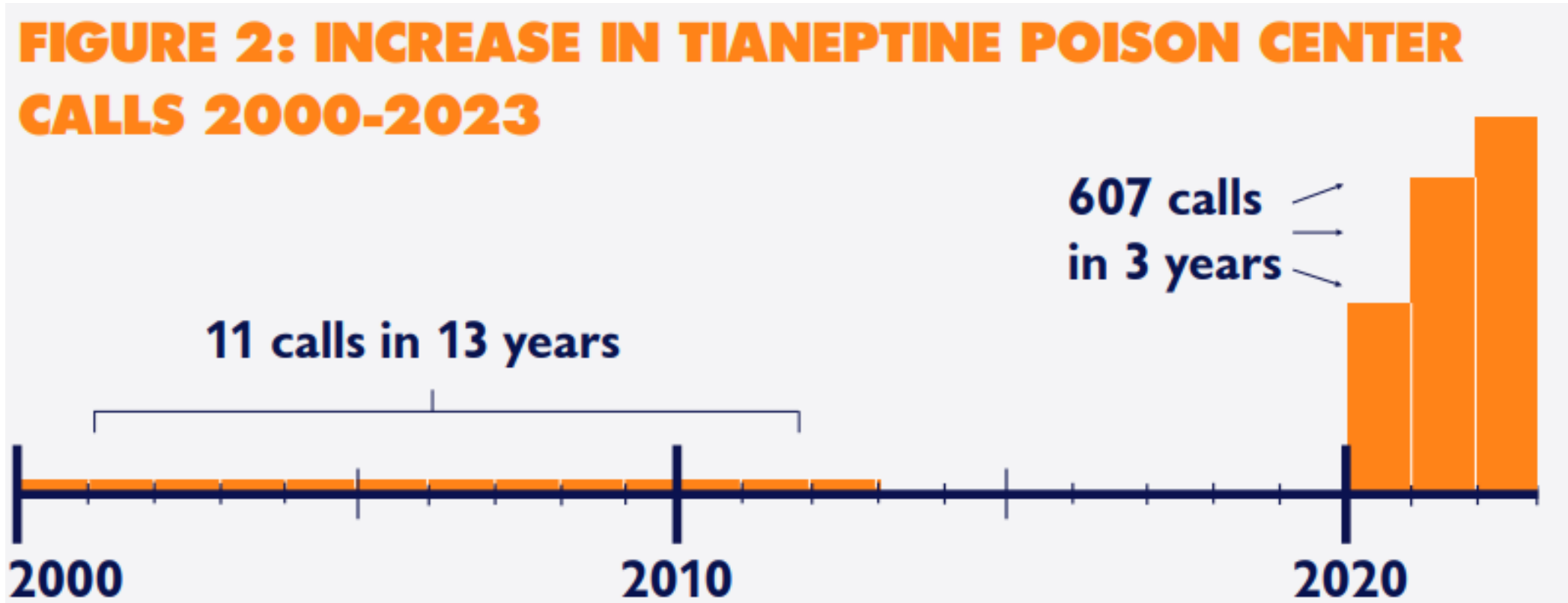
^aRespondents were asked, "Before today, had you ever heard of xylazine being present in street drugs? (Xylazine is also known as tranq, tranq dope, Philly dope, sleep cut, or zombie drug.)" Missing responses were excluded from analyses

^bIncluded responses "don't know," "NA," "Not sure," etc

What about Medetomidine?

- Medetomidine is an alpha-2 agonist, belonging to the same family of drugs as xylazine and clonidine
- Medetomidine is the latest CNS depressant to appear as an adulterant alongside fentanyl.
- Recent mass overdose outbreaks in Philadelphia, Chicago, and elsewhere have all been associated with fentanyl or heroin drug products containing medetomidine, as well xylazine and/or other substances
- Severe adverse effects have been noted, including heightened sedation and profound bradycardia

Increase in Tianeptine in Poison Control Calls, 2000-2023



Rise in Bromazepam Seizures, 2016-2023

- First appeared in US drug market in 2019
- Most frequently mixed with fentanyl
- Sedative effects pose significant health risks, especially when consumed with opioids



Synthetic Cannabinoids (1)

- Wide variety of herbal mixtures
- Marketed as “safe” alternatives to cannabis
- Brand names include: “Spice,” “K2,” fake weed, “Yucatan Fire,” “Skunk,” “Moon Rocks,” herbal incense, “Crazy Clown,” “Herbal Madness”
- Labeled “not for human consumption”
- Contain dried, shredded plant material (inert) and chemical additives that are responsible for their psychoactive effects.



Synthetic Cannabinoids (2)

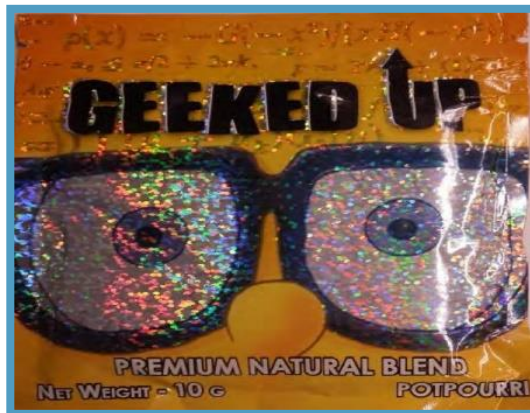
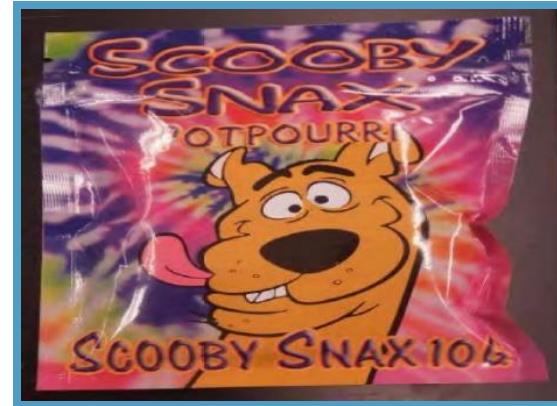
- Synthetic cannabinoids are often associated with adverse health risks due to potency
- Neurological effects (psychosis, agitation, paranoia, confusion)
- Psychiatric episodes such as hallucinations, delusions, delirium and self-harm
- Physical ailments (tachycardia, hypertension, arrhythmia, chest pain, GI distress, kidney injury, nausea, vomiting, fever)

Synthetic Cannabinoids (3)

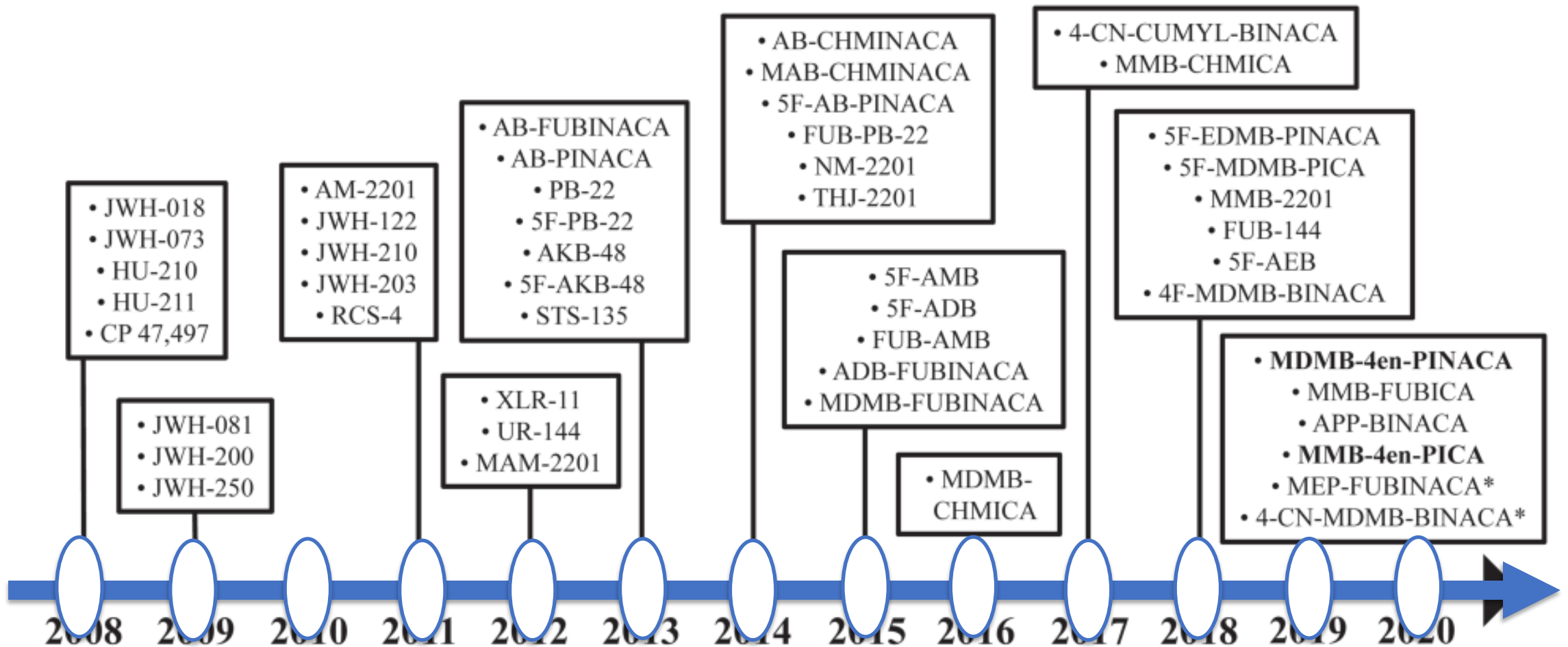
- Mainly used by smoking (alone or with cannabis); may also be prepared as an herbal infusion for drinking.
- Many of the active chemicals most frequently found in synthetic cannabis products have been classified by the DEA as Schedule I controlled substances, making them illegal to buy, sell, or possess.
- Multiple “generations” of drugs.



Synthetic Cannabinoid Packaging



Cannabinoids by Year



*NFLIS Snapshot Report

Factors Associated with Synthetic Cannabinoid Popularity

- They induce psychoactive effects
- They are readily available in retail stores and online
- The packaging is highly attractive
- They are perceived as safe drugs
- They are not easily detectable in urine and blood samples

Six States Report Cases of Kidney Damage Linked to Synthetic Cannabinoids

- Sixteen cases of kidney damage reported by CDC
 - All admitted to hospital
 - Five required hemodialysis
- Fifteen of the patients were male; ranged in age from 15 to 33, no history of kidney disease
- In early Feb 2013, UA-Birmingham reported 4 cases of previously healthy young men, whose acute kidney injury was associated with synthetic cannabis
 - Symptoms of nausea, vomiting, and abdominal pain
 - All four men recovered kidney function, and none required dialysis

Synthetic Cannabinoid Use Leads to Dangerous Symptoms in Pregnant Women

- Leads to **symptoms similar to** those caused by dangerous conditions known as **preeclampsia and eclampsia**
- Preeclampsia is marked by **high blood pressure** and a **high level of protein in the urine**
- Preeclampsia can lead to eclampsia, which can cause a pregnant woman to **develop seizures or coma**, and in **rare cases is fatal**

Case Example: Synthetic Cannabinoid Use among Pregnant Woman

- A woman (35 weeks pregnant) suffered a seizure and appeared agitated
- High blood pressure and protein in urine, treated for eclampsia
- An emergency C-section was performed (baby in distress)
- The woman screened negative for drugs, but an anonymous caller reported the woman regularly smoked “Spice Gold,” a synthetic cannabinoid.
- Spice Gold cannot be detected with a standard urine test.
- The baby tested negative for drugs.
- The woman required psychiatric care for psychotic behavior the day after delivery.
- *“This was not a pregnancy problem but a drug problem. Eclampsia is cured with delivery of the baby, but she did not get better after delivery.” (Dr. Cindy Lee)*

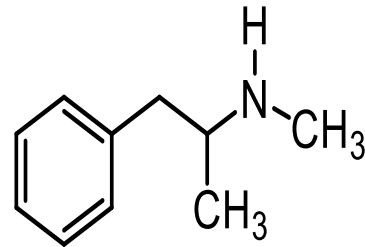
Synthetic Cathinones

- Could be MDPV, 4-MMC mephedrone, or methylone
- Sold on-line with little info ingredients, dosage, etc.
- Advertised as legal highs, legal meth, cocaine, or ecstasy
- Taken orally or by inhaling
- Serious side effects include tachycardia, hypertension, confusion or psychosis, nausea, convulsions
- Labeled “not for human consumption” to get around laws prohibiting sales or possession

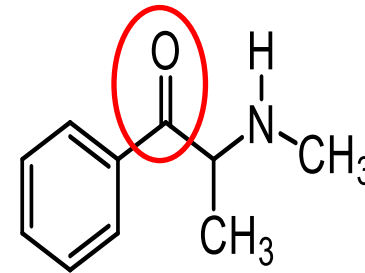
Synthetic Cathinone Packaging



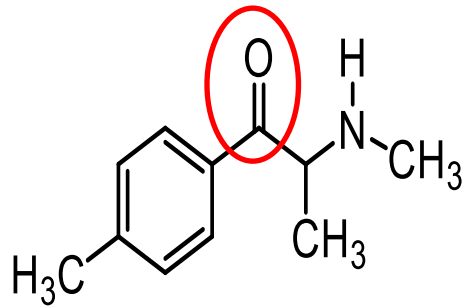
Synthetic Cathinones are b-keto ('bk') Analogs of Amphetamine



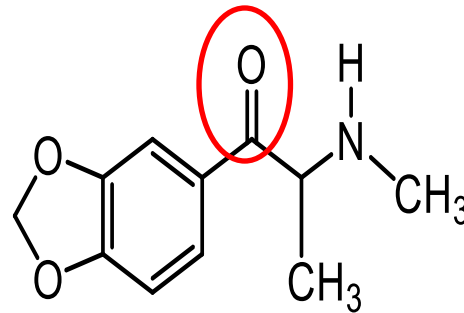
Methamphetamine



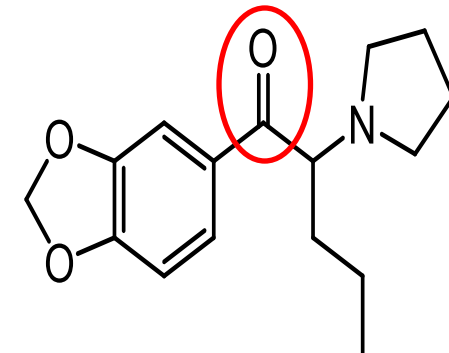
Methcathinone



4-Methylmethcathinone
(Mephedrone)



3,4-Methylenedioxymethcathinone
(Methylone)



3,4-Methylenedioxypyrovalerone
(MDPV)

Clinical Symptoms of Synthetic Cathinone Use in Patients Admitted to the Emergency Department (N=236)

Symptom	Prevalence
Agitation	82%
Combative/Violent behavior	57%
Tachycardia	56%
Hallucinations	40%
Paranoia	36%
Confusion	34%
Myoclonus/Movement disorders	19%
Hypertension	17%
Chest pain	17%
CPK elevations	9%

Effects of Mephedrone

Intended Effects:

- Euphoria
- Stimulation
- Enhanced music appreciation
- Decreased hostility
- Improved mental function
- Mild sexual stimulation

Unintended (Adverse) Effects:

- Bruxism (teeth grinding)
- Dilated pupils
- Poor concentration
- Problems focusing visually
- Poor short-term memory
- Hallucinations
- Delusions

Effects of Methylone

- Central Nervous System stimulation
- Euphoria or dysphoria
- Anxiolysis/Anxiogenesis
- Increase in sociability
- Insomnia
- Restlessness
- De-realization/
De-personalization
- Hallucinations
- Psychosis
- Tachycardia (rapid pulse)
- Hypertension (high BP)
- Hyperthermia
- Sweating
- Dilated pupils
- Nystagmus
- Trismus (inability to open the mouth)
- Bruxism (teeth grinding)
- Anorexia
- Nausea and vomiting

Synthetic Cannabinoids – Clinical Presentation

- Persistent depression
- Memory problems (can last for several weeks)
- Blunted affect
- Difficulty focusing
- Difficulty participating in clinical until stabilized
- Users also report elevated mood, relaxation, and altered perception
- Psychotic effects, such as extreme anxiety, paranoia, and hallucinations

Sample Clinical Treatment Protocol for Synthetic Cannabinoid Users

- Direct individual to emergency room via ambulance
- Consult a regional Poison Control Center
- Acute management consists of:
- Supportive care with the use of benzodiazepines, if needed, to control agitation and anxiety
- Observe until resolution of abnormal vital signs, vomiting, and psychiatric symptoms

Recognizing Synthetic Cathinone Intoxication

- Present with severe sympathetic stimulation:
 - Tachycardia
 - Hypertension
 - Hyperthermia
 - Seizures
- Present with profoundly altered mental status:
 - Severe panic attacks
 - Agitation
 - Paranoia
 - Hallucinations
 - Suicidal behavior



Sample Clinical Treatment Protocol for Synthetic Cathinone Users

- Supportive care
- Aggressive sedation with benzodiazepines (for agitation, seizures, tachycardia, and hypertension)
- Significant hyperthermia may require passive or active cooling
- Lab studies including electrolytes, renal and liver function tests, cardiac markers, and creatine kinase should be considered

Public Health Measures to Manage Fentanyl

- Continued need for harm reduction methods at a public health level
- This might include overdose education, naloxone distribution, and Good Samaritan Laws
- Off-label use of Fentanyl Test Strips (FTS) has been a more recent addition
- FTS should have good sensitivity and specificity
 - A 2019 study compared Raman Spectroscopy, Fourier-transform infrared spectroscopy with FTS from a Canadian biotech company
 - FTS had highest sensitivity and specificity

Public Health Measures to Manage Fentanyl: FTS

- FTS were originally developed to test urine in clinical settings
- Low cost and ease of use have transitioned product to wider use
- One study found that younger individuals (18-35) had high levels (more than 90%) of willingness to use FTS
- Recent studies indicate that use of FTS prompted reduced use and other informed choices among individuals using substances

Public Health Measures to Manage Fentanyl: Understanding Risk Factors

- Use of heroin and other drugs is influenced by social and physical conditions around preparation, consumption, and experience of substances
- These aspects of the “risk environment” generate much of the risk associated with overdose
- Addressing these elements create risk mitigation methods
- Gathering perspectives from individuals using FTS can help to tailor processes

Public Health Measures to Manage Fentanyl: Macro Factors and Interventions

Macro Factors

- Trafficking and distribution routes
- Population mobility and mixing
- Gender inequalities and risk
- Stigmatization and marginalization
- Community advocacy
- Lack of health service resources
- Uncertainty of economic transitions
- Health policy
- Laws around possession and health rights

Possible Interventions

- Changes to trafficking interdiction policy
- Cross-border intervention and interventions at train/bus/truck stops
- Fostering collective action with policy change
- Mass media and social marketing for harm reduction
- Strengthening civil society infrastructure and self-help
- Laws governing employment rights
- Investment in harm reduction relative to enforcement
- Legal reform enabling harm reduction and protection of rights
- National policy changes regarding public health strategy

Public Health Measures to Manage Fentanyl: Micro Factors and Interventions

Micro Factors

- Drug using and injecting locations
- Prisons and detention centers
- Social and peer group “norms”
- Policing practices and “crackdowns”
- Community health and welfare access and delivery
- Cost of living and health materials
- Lack of income generation and employment
- Availability of sterile needles and syringes
- Access to housing

Possible Interventions

- Safer drug using sites (sharps disposal, supervised injecting facilities)
- Prison-based harm reduction interventions
- Social network and peer-based intervention
- Police partnership and training
- Low threshold accessible services
- Subsidized and free treatment and prevention materials
- Micro-economic enterprise and employment schemes
- Pharmacy-based syringe provisions
- Neighborhood housing development

What do you do if someone has taken a Synthetic Drug?

- Call your local poison center at 1-800-222-1222
- 57 poison centers around the country have experts waiting to answer your call.
- The experts at the Center can help you decide whether someone can be treated at home, or whether he or she must go to a hospital.
- Dial 9-1-1 immediately if they:
- Stop breathing
- Collapse
- Have a seizure

...or if they have taken one of these and are having physical symptoms or behaving in a way that is concerning to you

Strategies to Address Use of Synthetics

- Strategies should be built on science, evidence, and knowledge to be effective
- Practical cross-cutting tools that are available and accessible enhance action
- Utilize existing frameworks that incorporate international, regional, national, and local action steps

United Nations Toolkit on Synthetic Drugs



<https://syntheticdrugs.unodc.org/syntheticdrugs/en/toolkit-index.html>

Early Warning Systems

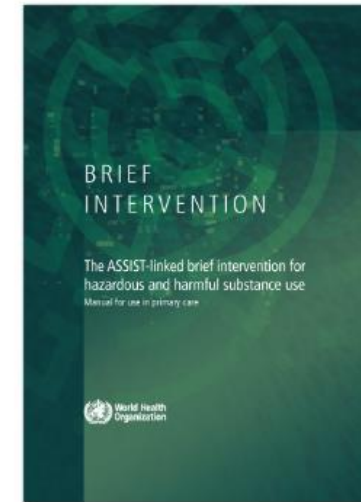
- Early Warning System for the Americas (SATA)
- Monitors and reports on emerging drug threats made available throughout North and South America
- http://www.cicad.oas.org/Main/Template.asp?File=/oid/sata/default_eng.asp

Lists of Precursors

- International Narcotics Board Red List
- List of precursors and chemicals that are typically found in illicit manufacture of psychotropic substances
- Contains 11 pages of different chemicals and medications and the associated precursor
- https://www.incb.org/incb/en/precursors/Red_Forms/red-list.html

Prevention Strategies: WHO and UNODC

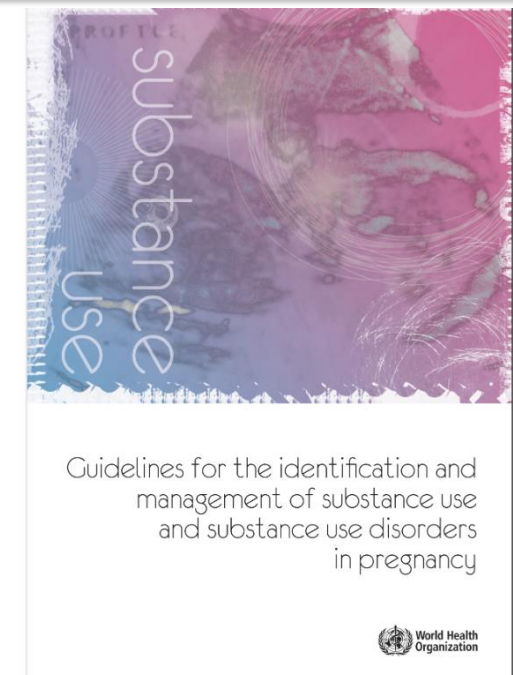
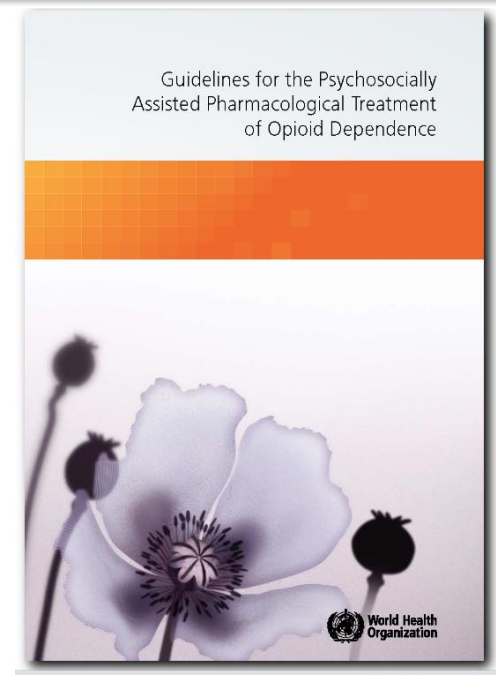
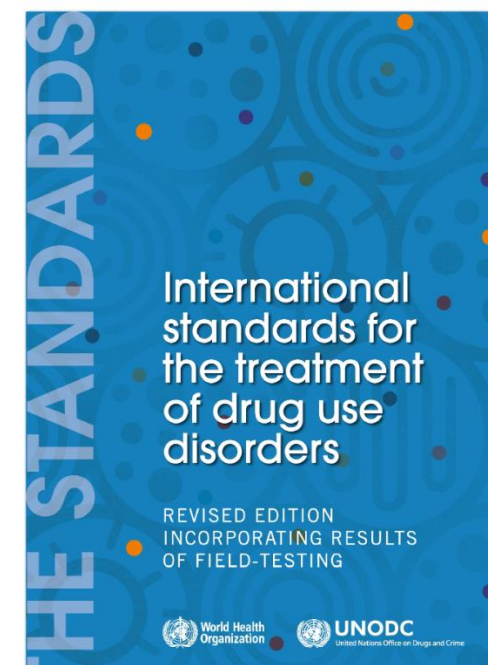
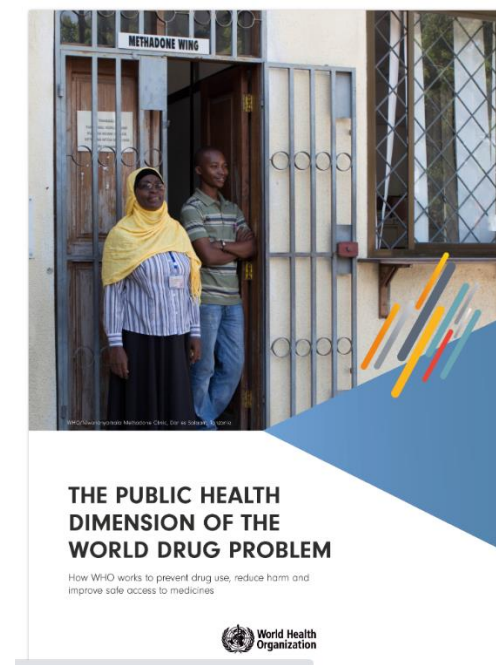
- Use of prevention strategies to reduce the continued health burden of substance use
 - <https://syntheticdrugs.unodc.org/syntheticdrugs/en/prevention/evidence/system.html>
- Integrated networks of intervention and policy:
 - Supportive policy and legal framework
 - Scientific evidence and research
 - Coordination between multiple sectors
 - Training of policy makers and practitioners
 - Commitment to providing adequate resources to sustain the system in the long term



Guidelines For Treatment: WHO and UNODC

- <https://syntheticdrugs.unodc.org/syntheticdrugs/en/treatment/managementDUD/identification.html>
- Recommends incorporating aspects of:
 - Outreach services
 - Screening and brief intervention
 - Inpatient and outpatient treatment
 - Evidence-based pharmacological treatment and psychosocial interventions
 - Long-term residential treatment, rehabilitation and recovery-support services

Resources



Resources for Continued Learning

- American Association of Poison Control Centers, www.aapcc.org
- Drug Enforcement Administration, www.dea.usdoj.gov
- European Monitoring Centre for Drugs and Drug Addiction, www.emcdda.europa.eu
- National Institute on Drug Abuse, www.nida.nih.gov
- Office of National Drug Control Policy, www.ondcp.org
- Pacific Southwest ATTC, www.psattc.org (refer to *Synthetic Drugs Training Package*)

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- Opioid Response Network



Pacific Southwest

RURAL OPIOID TECHNICAL

ASSISTANCE REGIONAL CENTER

Thank you! Feel free to reach out –

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To join the Pacific Southwest ROTA-R mailing list
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