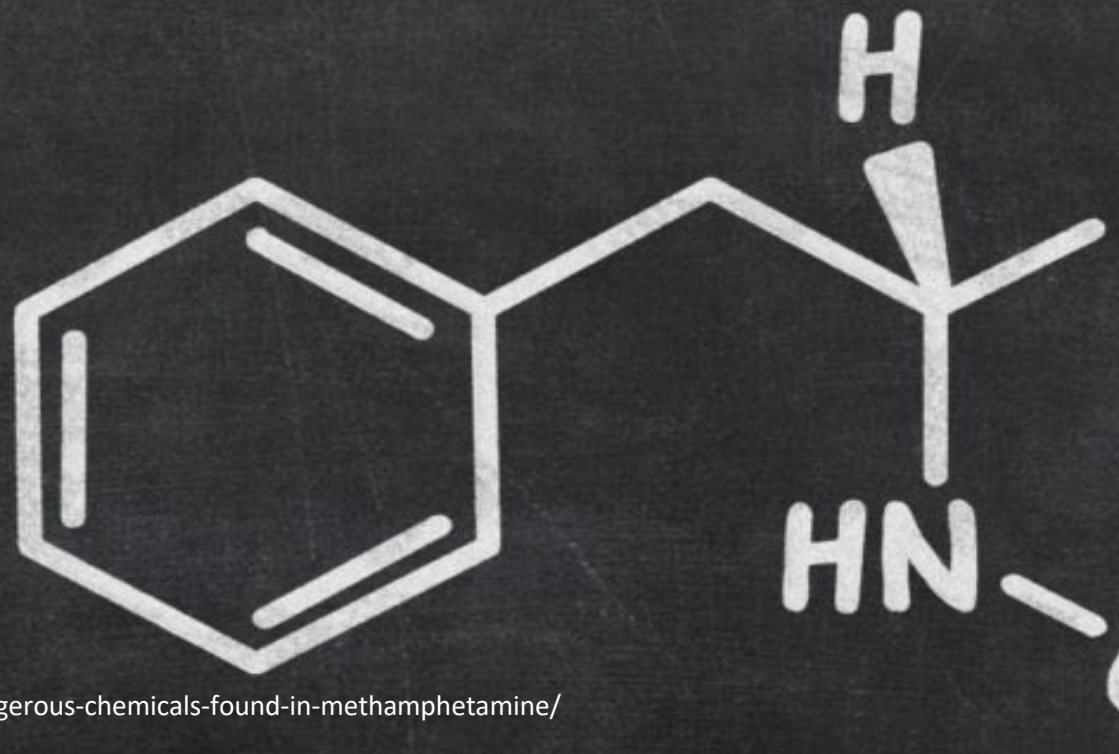
Methamphetamine

$C_{10}H_{15}N$



Bob Lutz, MD MPH
WAPC
08.07.2024

https://www.deconsystems.com.au/dangerous-chemicals-found-in-methamphetamine/

learning objectives

what is methamphetamine

trends – illicit usage to include polysubstance, overdoses, availability/supply

effects

treatment considerations

public health response

history

methamphetamine - Nagai Nagayoshi, a Japanese scientist, was the first person to synthesize methamphetamine in 1883. In 1919, another Japanese scientist, Akira Ogata, developed the crystalized form of meth that is most common today

amphetamines – the first amphetamine, phenylisopropylamine, was synthesized in 1887 by Lazăr Edeleanu, a Romanian scientist working in Germany

1932 - US patent declared Gordon Alles the inventor of amphetamine sulfate and amphetamine hydrochloride

WW II

1939 - the Blitzkrieg's success attributed partly to the use of Pervitin—methamphetamine—among German soldiers

mid-1940s – British & American militaries settle on Benzedrine to combat fatigue and boost morale. especially with popular with pilots and air crews, who often had to fly long, grueling bombing raids late into the night. By 1943 a package of Benzedrine pills had its place in the emergency kit of every American bomber. Two years later a survey of European-theater fighter pilots who frequently flew long missions showed that around 15% frequently used Benzedrine.

Japanese, U.S., British and German military are reported to have used the stimulant to enhance endurance and ward off fatigue on long campaigns

Kamikaze pilots received high doses of Pervitin before suicide flight missions. Japanese factory workers also used methamphetamine to work longer hours

The German army ordered front-line soldiers and fighter pilots to take military-issued stimulants that contained a combination of methamphetamine and cocaine

https://www.sciencehistory.org/stories/magazine/fast-times-the-life-death-and-rebirth-of-amphetamine/; https://www.history.com/topics/crime/history-of-meth

Benzedrine aka “bennies”

Benzedrine’s commercial success

- study aid for college students as early as the 1930s
- diet and mood pill for housewives in the 1950s and 1960s
- muse and energy booster to artists during the Beatnik period of the 1960s (Jack Kerouac and Allen Ginsberg)
- chemical copilot for long-haul truckers
- “speed” that roiled the Flower Children
- CA biker gangs

similar but different

legal status – Schedule II stimulant

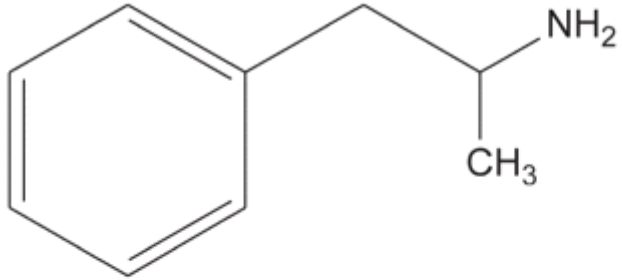
high potential for abuse with a currently

recognized (limited) medical use – obesity

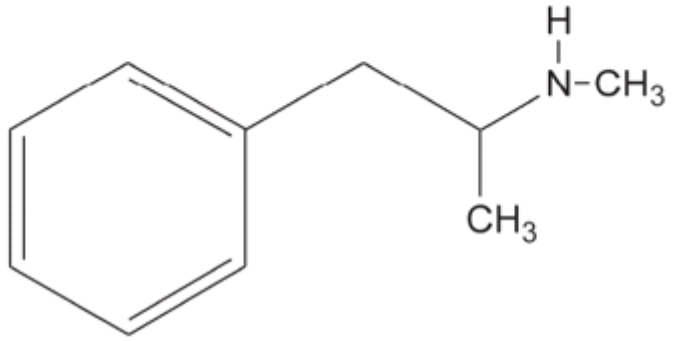
& ADHD, narcolepsy (amp)

llicit use - illegal

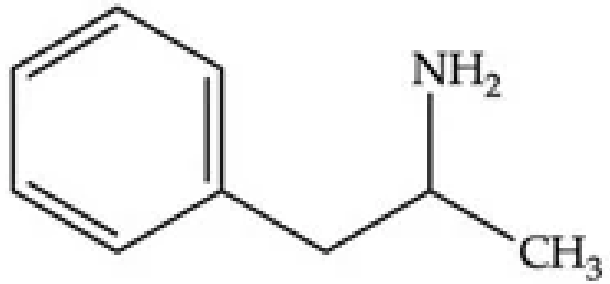
Amphetamine



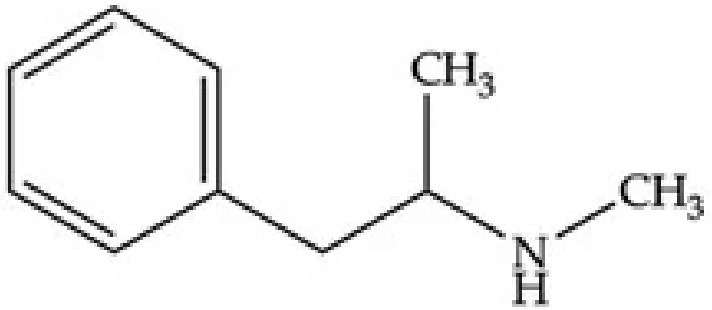
Methamphetamine



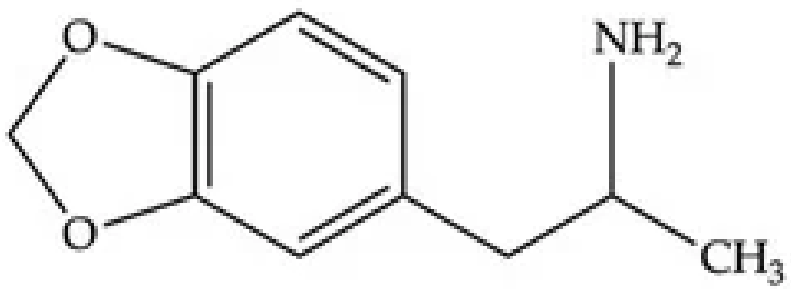
also similar but different



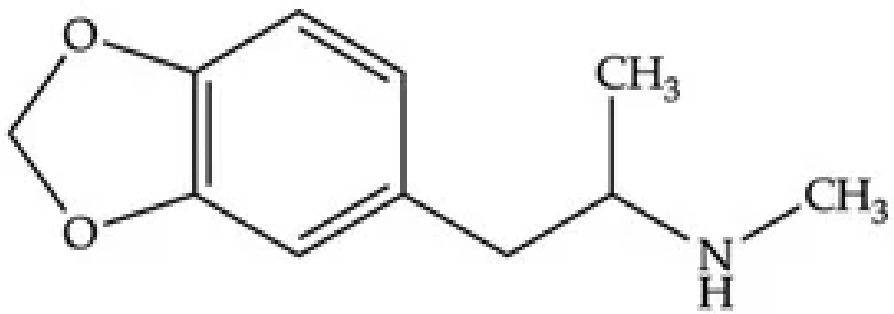
amphetamine



methamphetamine



3,4-methylenedioxyamphetamine
(MDA)



3,4-methylenedioxymethamphetamine
(MDMA)

prescription amphetamines

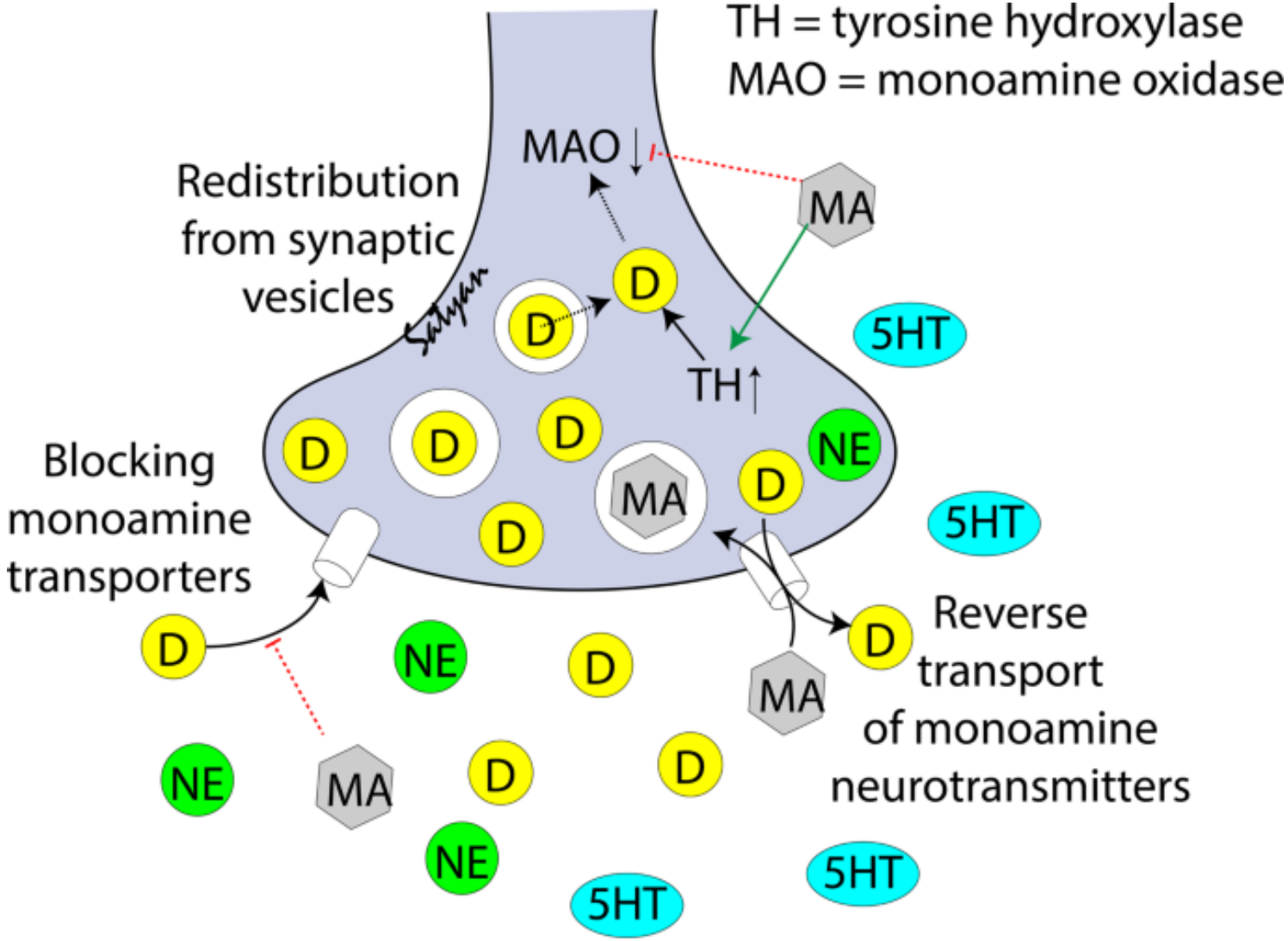
Adderall (racemic amphetamine and dextroamphetamine)

Ritalin (methylphenidate)

Dexedrine (dextroamphetamine)

Focalin (dexmethylphenidate)

Vyvanse (lisdexamfetamine)



High concentration of dopamine (D), norepinephrine (NE) and serotonin (5HT)

pharmacodynamics

primarily hepatic metabolism

metabolism not altered by chronic exposure - dose escalation arises from pharmacodynamic rather than pharmacokinetic tolerance

~70% of a methamphetamine dose excreted in the urine within 24 hours - 30–50% as methamphetamine, up to 15% as 4-hydroxymethamphetamine and 10% as amphetamine

with a long terminal urinary half-life of 25 hours, methamphetamine accumulates in the urine with repeated dosing (7days)

effects

acute subjective effects diminish over 4 hours, while cardiovascular effects tend to remain elevated

although dosing patterns vary substantially between regular methamphetamine users, a typical pattern of use appears to consist of 4 doses daily, in binges lasting 4 days

self-reported data indicate illicit doses of 50–500 mg totaling up to 4 g/day

clinical pharmacokinetics

Route	*Dose*	*Bioavailability*	*C_{max} (µg/l)*	*T_{max} (minutes)*	*$T_{1/2}$ (hour)*	*Time to peak effect*
Intravenous	30 mg	100%	108±22 (64–164)	6± 11	9.1± 0.8 (8–16)	<15 minutes
Smoking	30 mg	67%; 90± 10%	47± 6	150± 30	12± 1 (8–17)	18± 2minutes
Oral	30 mg	67± 3%	94.1 (62–291)	216 (180–300)	9.1 (3–17)	180 minutes
Intra- nasal	50 mg	79%	113± 8	169± 8	11± 1	≤15 minutes

https://onlinelibrary.wiley.com/doi/full/10.1111/j.1360-0443.2009.02564

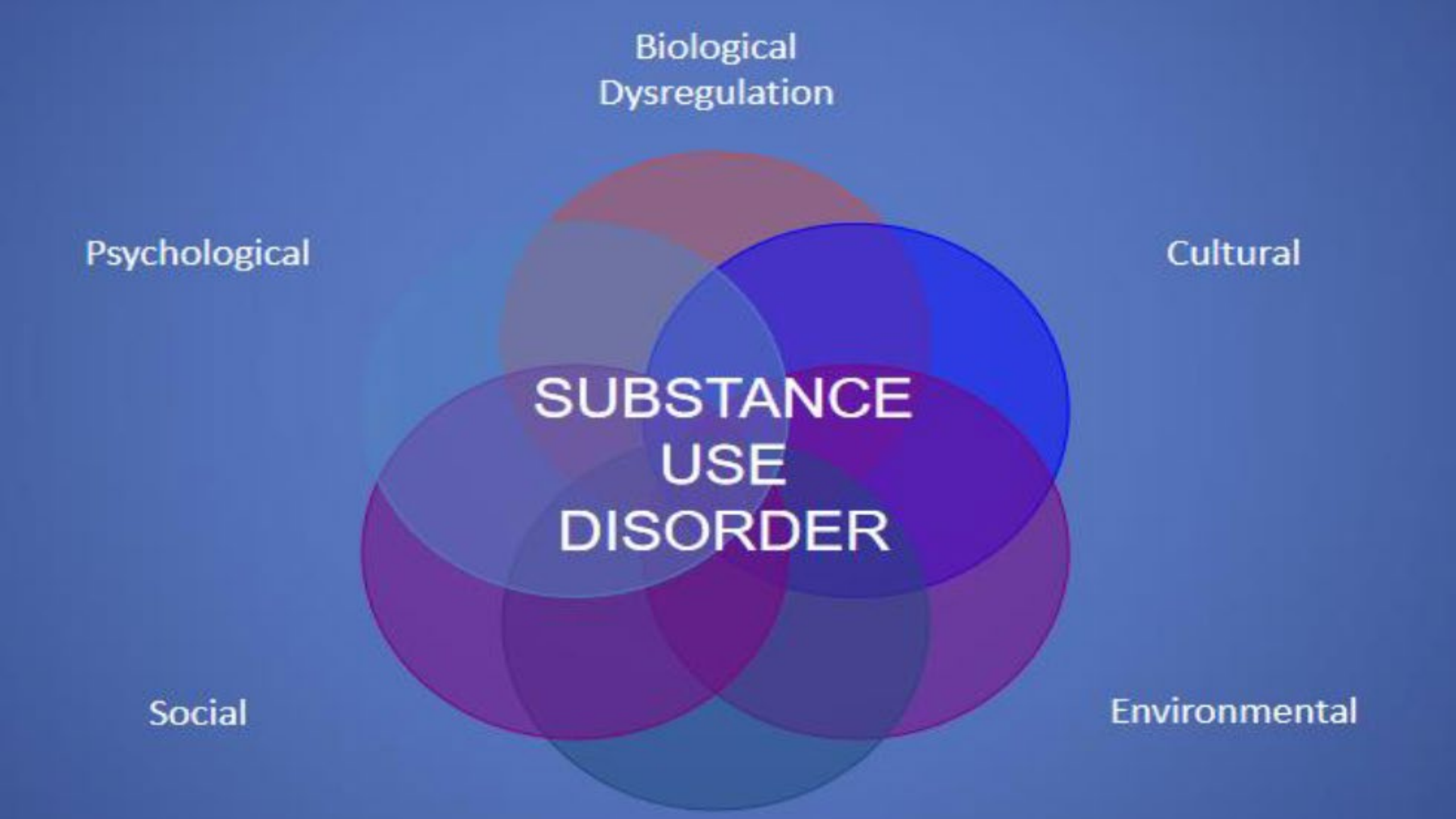
Why People Use Drugs

TO FEEL GOOD

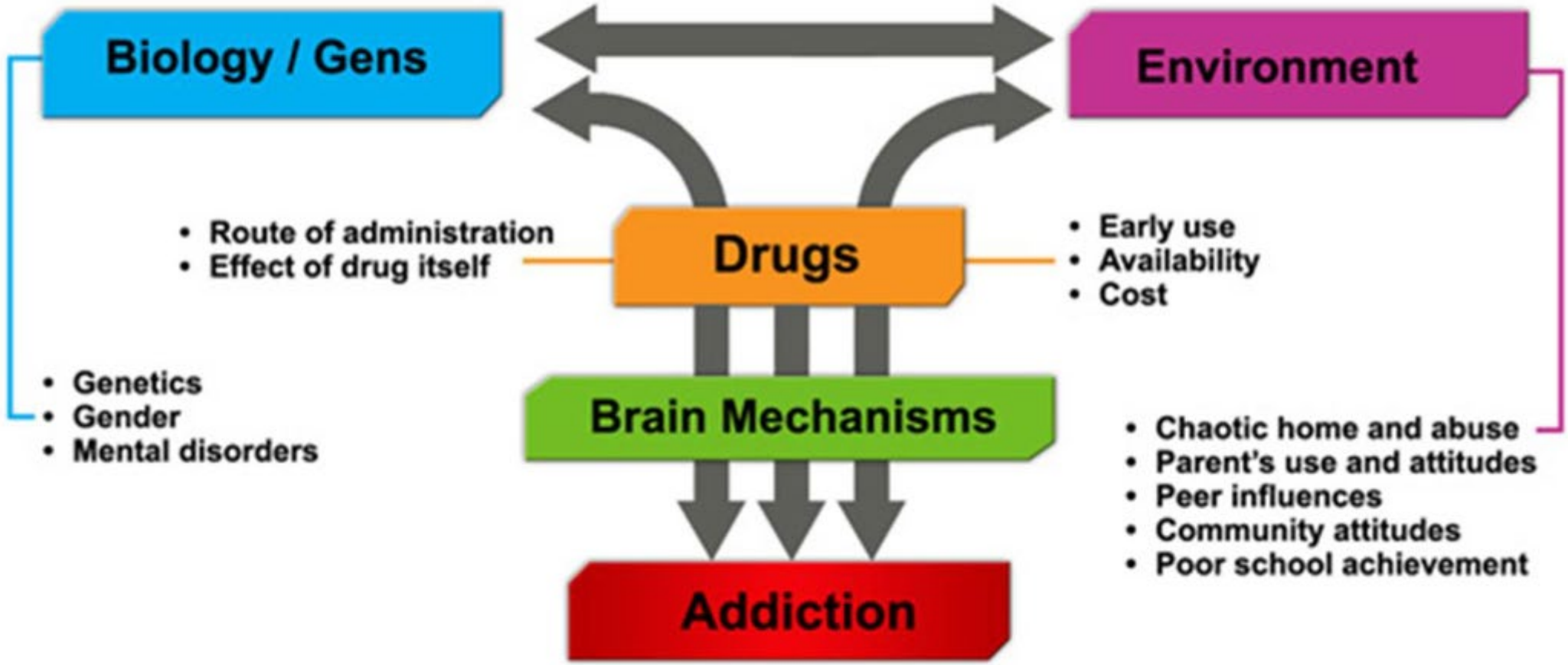
…and have
novel feelings,
sensations,
experiences AND
to share them

TO FEEL BETTER

…and lessen
anxiety, worries,
fears,
depression,
hopelessness
despair


Biological
Dysregulation
Psychological
Cultural
SUBSTANCE
USE
DISORDER
Social
Environmental

Factors Leading to Addiction



street terms

batu, biker’s coffee, black beauties, chalk, chicken feed, crank, crystal, go-fast, hiropon, ice, meth, methies quick, poor man’s cocaine, shabu, shards, speed, stove top, tina, trash, tweak, uppers, Ventana, vidrio, yaba, yellow bam, clear

goofball – mixture of meth with opioid (fentanyl, heroin)

meth labs & the crystal meth epidemic

1980 - amphetamine's key chemical, phenyl-2-propanone, put under federal control

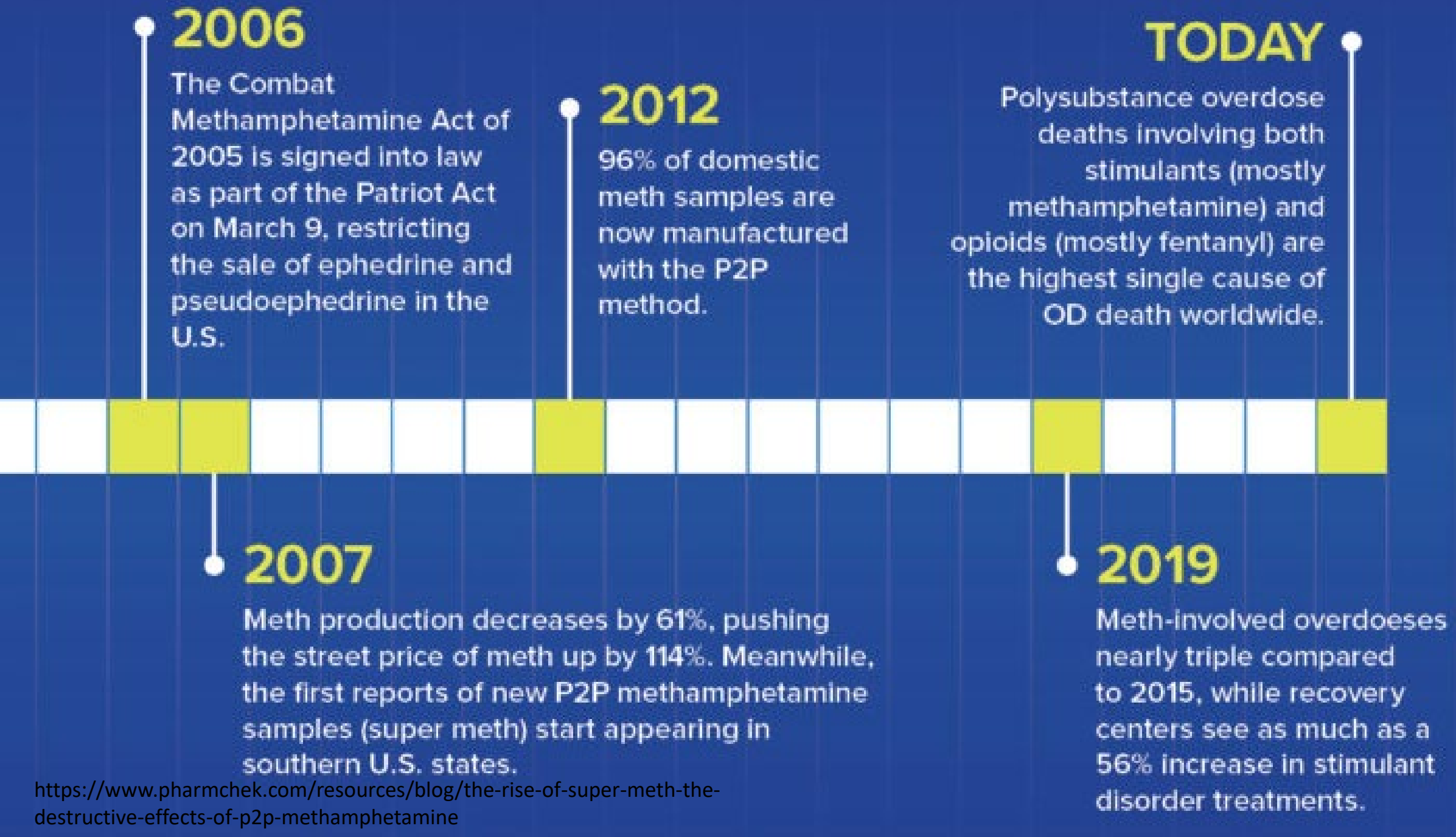
the ‘cooks’ making the drug for West Coast motorcycle gangs discover ephedrine (or pseudoephedrine) in OTC cold medications →methamphetamine (2x more potent) & easily made from household products

80s – 00s - DEA attempts to regulate sales of OTC cold medications, pharmaceutical industry fights back

" … in the protection of the public interest, there were two competing goals: keeping the ingredient in the hands of the American consumer but keeping it away from the criminal. We all thought we could find a way to do this, but unfortunately we felt DEA was confused about who was the bad guy." – Allan Rexinger, former lobbyist for the pharmaceutical industry

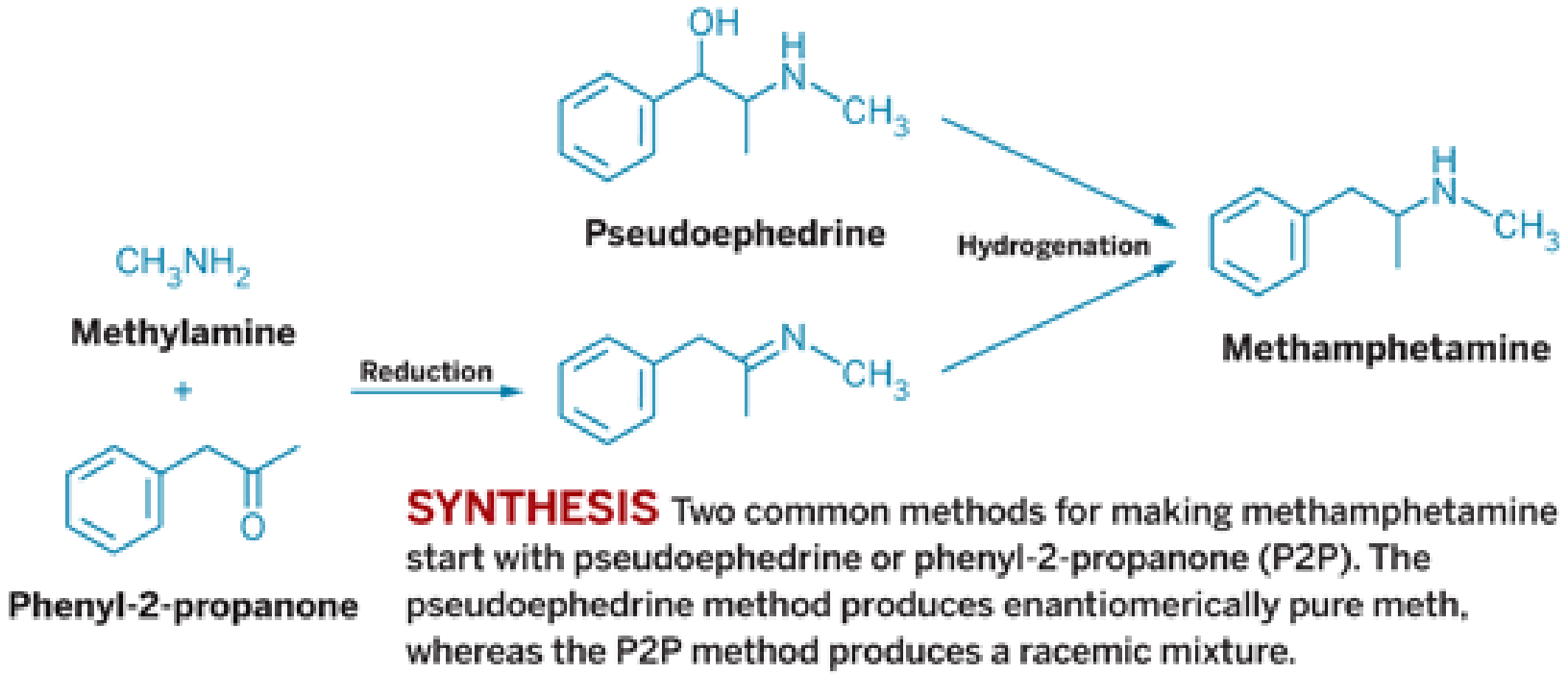
2005 - Combat Methamphetamine Epidemic Act of 2005 as part of the PATRIOT Revision Act mandates pseudoephedrine be put under lock and key in stores nationwide

https://www.pbs.org/wgbh/pages/frontline/meth/etc/cron.html



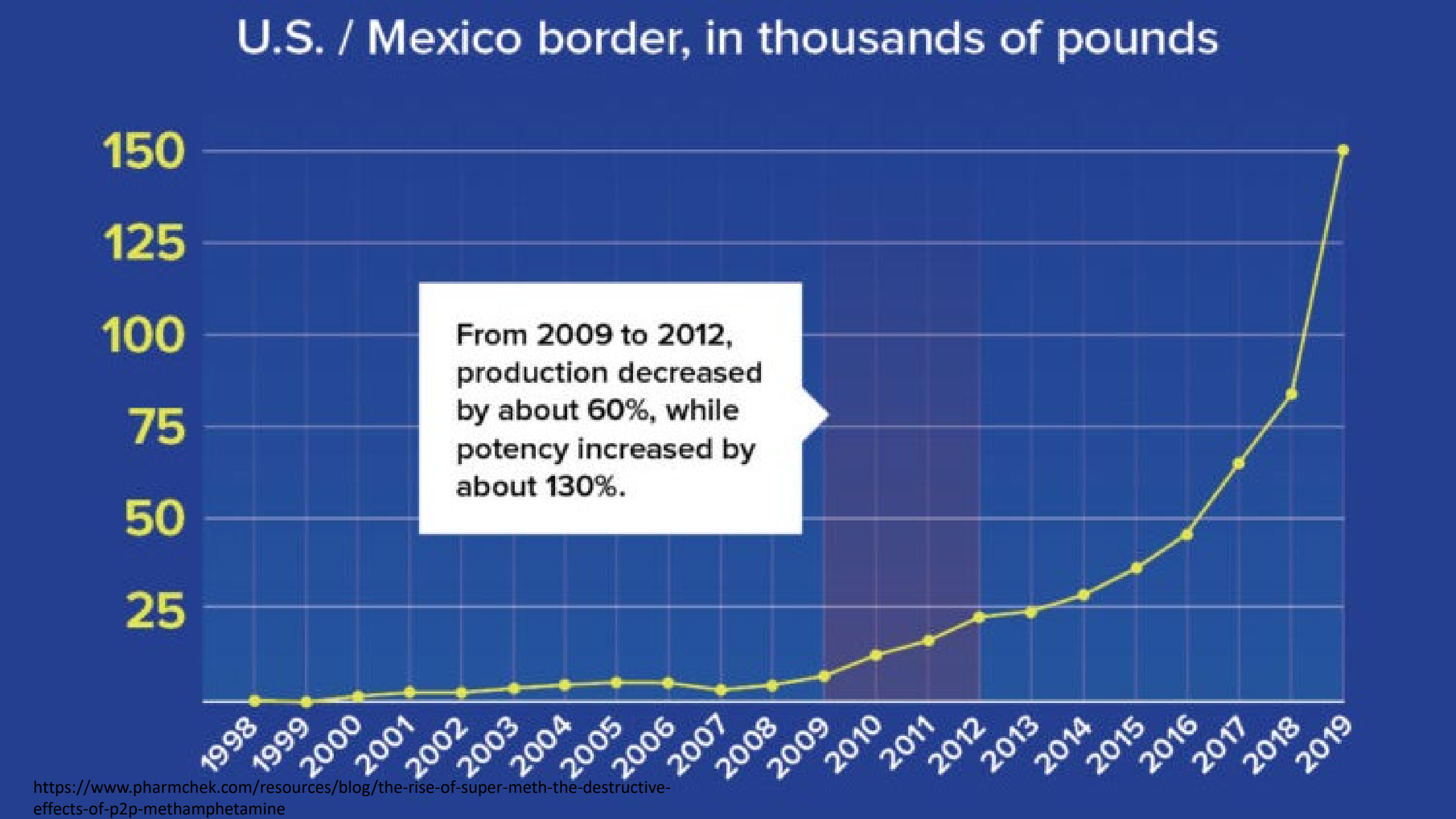
https://www.pharmchek.com/resources/blog/the-rise-of-super-meth-the-destructive-effects-of-p2p-methamphetamine

“cooking”

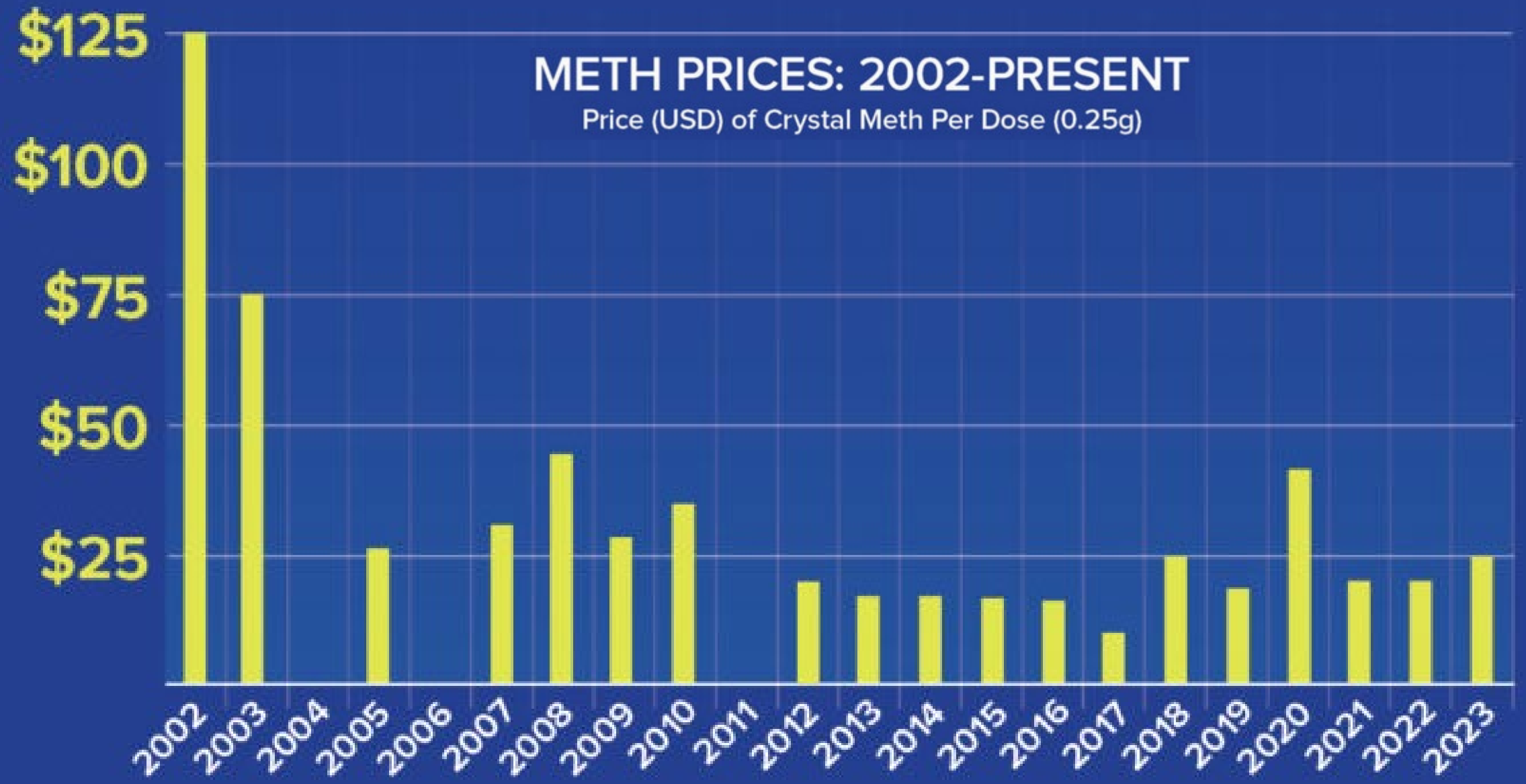


cooked in clandestine laboratories by a variety of methods commonly using precursors such as ephedrine, pseudoephedrine, 1-phenyl-2-propanone (P-2-P), and P-2-P precursors

https://cen.acs.org/articles/86/i36/Student-Suspected-Making-Meth.html



https://www.pharmchek.com/resources/blog/the-rise-of-super-meth-the-destructive-effects-of-p2p-methamphetamine



https://www.pharmchek.com/resources/blog/the-rise-of-super-meth-the-destructive-effects-of-p2p-methamphetamine

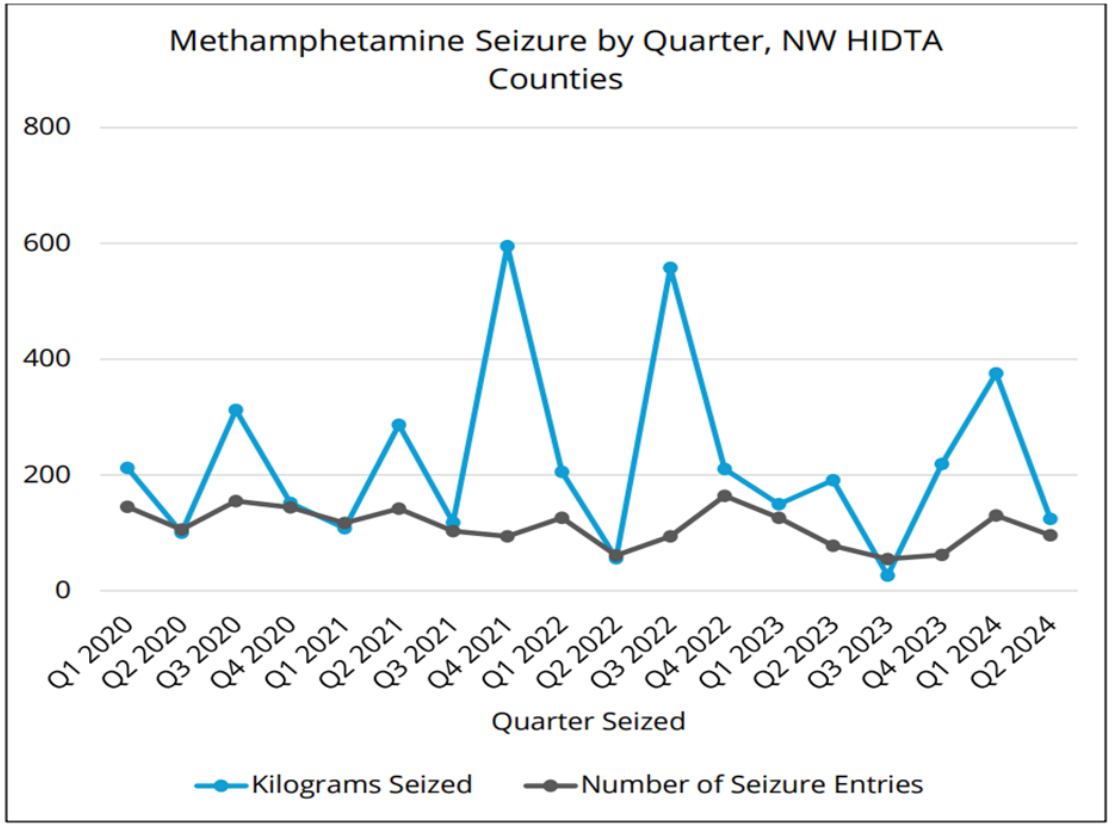
Northwest High Intensity Drug Trafficking Area (NW HIDTA)

meth exhibits consistently high purity, averaging roughly 97% in the Pacific Northwest (slightly higher than the national average)

most common form of methamphetamine from seizures is in the crystal or shard form; meth powder less commonly encountered

meth represents a larger percentage of Northwest HIDTA seizures compared with most other HIDTAs nationwide

stimulant drug seizures



* The figure above excludes large amounts seized entering Canada from the Washington. Data from 2024 quarter 2 are preliminary.

statewide data from Northwest HIDTA task force counties (Benton, Clark, Grant, King, Pierce, Snohomish, Skagit, Spokane, Thurston, Whatcom, and Yakima) and may not be representative of the entire state

while kilograms of meth seized have varied, the number of seizures has remained relatively stable over the past few years (compared to other substances such as fentanyl)

meth is seized at comparable rates in both eastern & western regions of Washington

Northwest High Intensity Drug Trafficking Area (NW HIDTA)

Where are stimulants coming from?
meth generally enter the U.S. through Mexico

Are drugs (like cannabis) actually being laced with meth?
We have not seen cannabis being laced with methamphetamine. While poly-substance use with methamphetamine is common, it is less common to see non-stimulant substances laced with methamphetamine.

Results from the 2023 Syringe Services Program Health Survey

Caleb Banta-Green, PhD, MPH, MSW & Alison Newman, MPH

Center for Community-Engaged Drug Epidemiology, Education, and Research

UW Addictions, Drug & Alcohol Institute

ADAI
ADDICTIONS, DRUG & ALCOHOL INSTITUTE

UNIVERSITY of WASHINGTON

where to find data online

> Center for Community-Engaged Drug Education, Epidemiology and Research > Surveys and Interviews with People Who Use Drugs

Surveys and Interviews with People Who Use Drugs

The team at ADAI's Center for Community-Engaged Drug Education, Epidemiology, and Research (CEDEER) regularly collects community-level data directly from people who use drugs to learn more about their needs to help shape relevant and impactful services and policies. The WA State Syringe Service Program Health Survey is conducted every two years, followed by qualitative interviews on opposite years with people who use drugs.

+ Washington State Syringe Service Program Health Surveys
+ Qualitative Interviews
+ Overview & Perspectives of Syringe Services Programs in WA

This work is funded by the WA Health Care Authority, Division of Behavioral Health and Recovery.

https://adai.uw.edu/cedeer/community-surveys/

Table 4. Substances used in past week compared to "main drug" *n=1,667*				
	Used in past week		**Identified as "main" drug**	
	n	%	n	%
Methamphetamine	1,484	**89%**	650	**39%**
Fentanyl	1,018	**61%**	648	**39%**
Powder or crack cocaine	398	**24%**	70	**4%**
Heroin	267	**16%**	108	**7%**
Benzodiazepines	178	**11%**	4	**<1%**
Meth and fentanyl used together[4]	n/a	n/a	94	**6%**

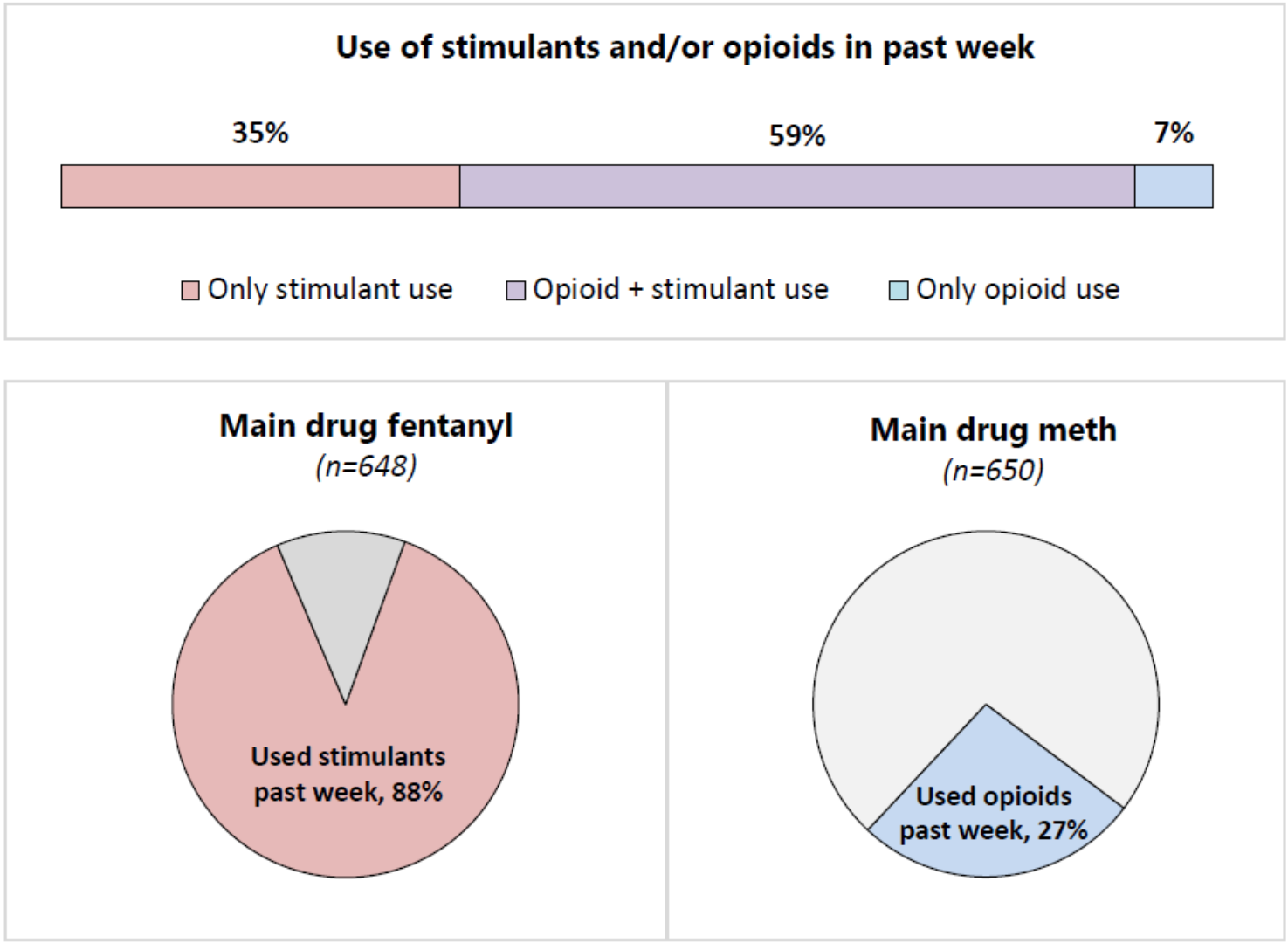


Figure 1. Patterns of stimulant and opioid use in past week.

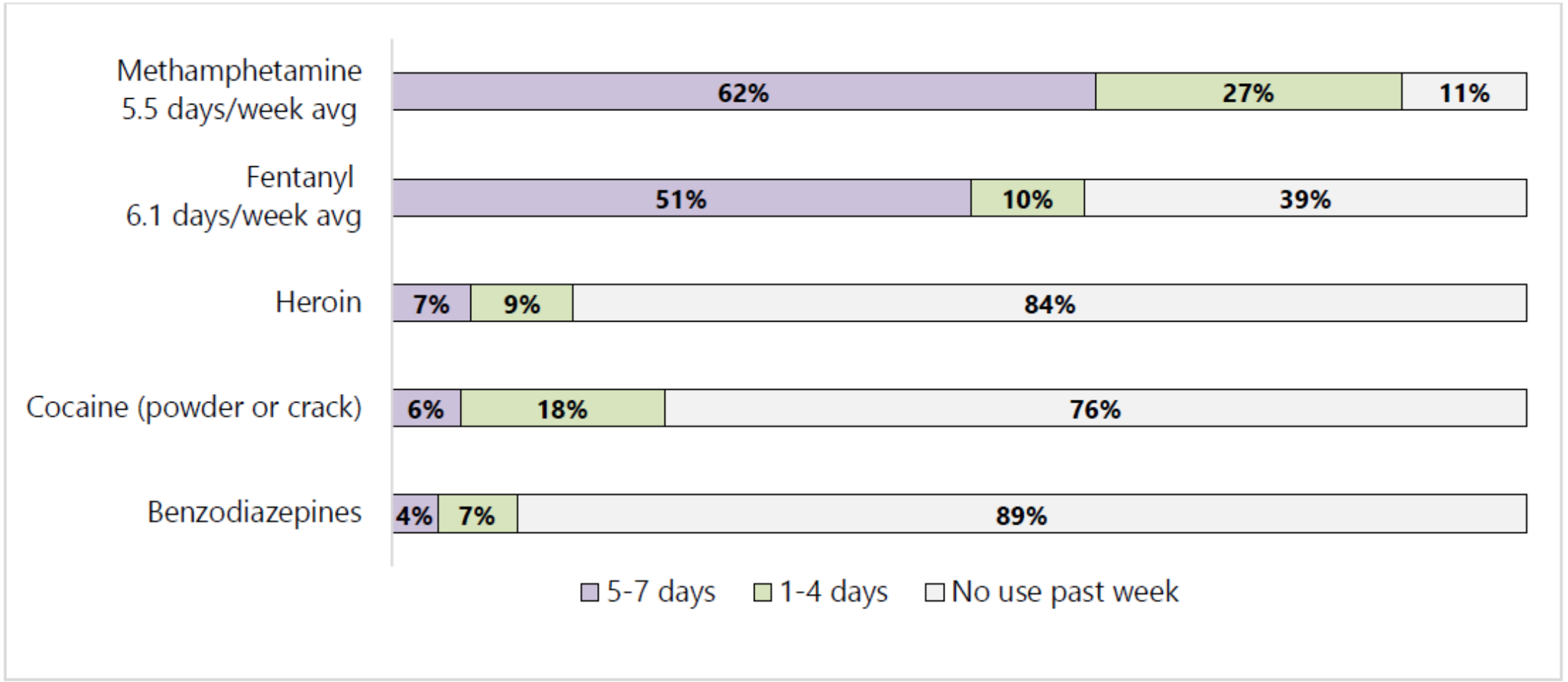


Figure 2. Frequency of drug use in past 7 days. *n=1,667*

smoking & injection

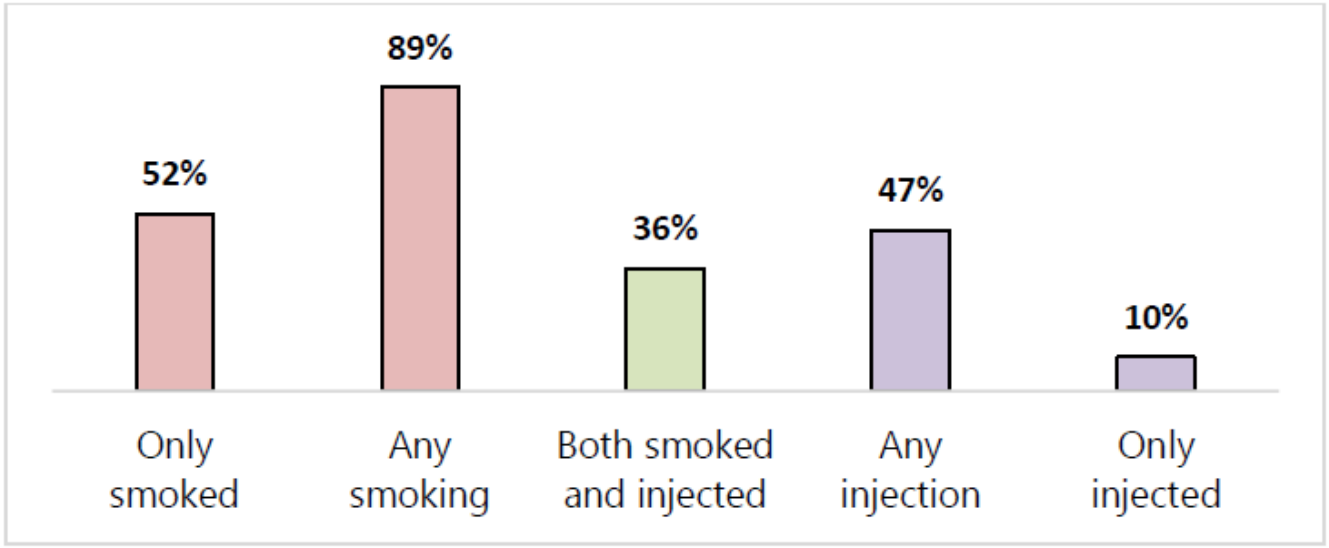
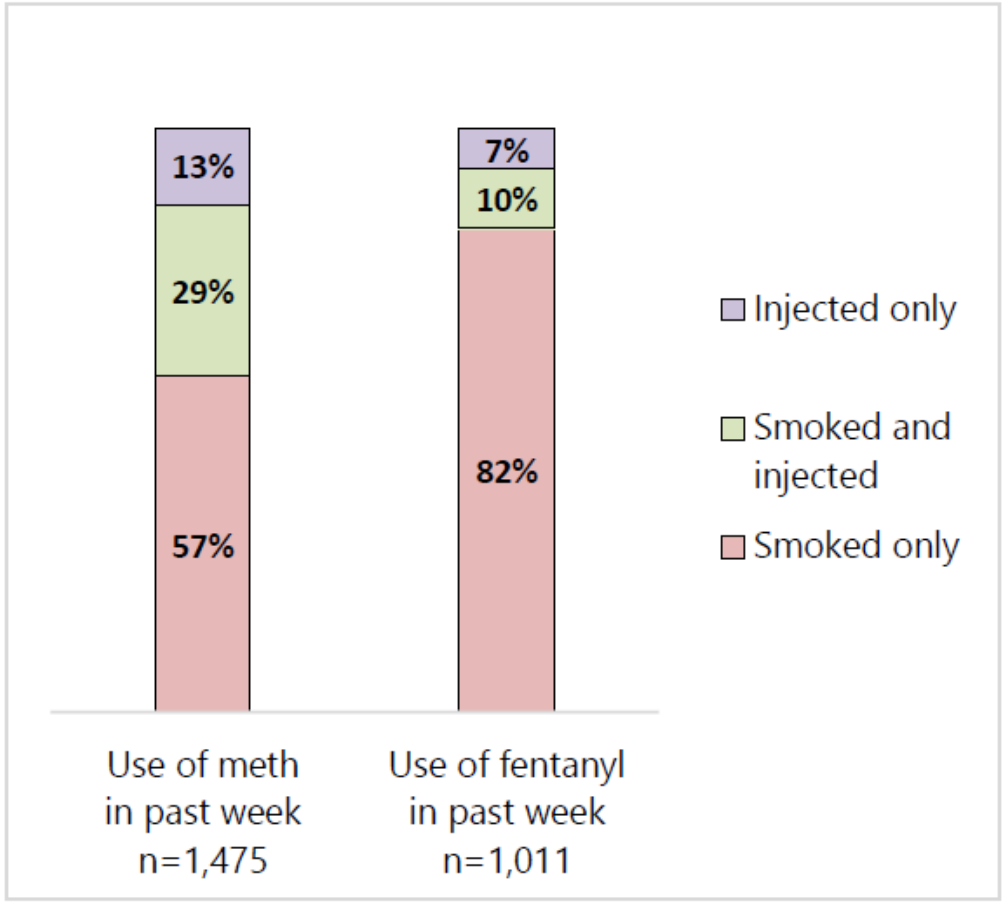


Figure 4. Routes of drug administration in past week. n=1,667



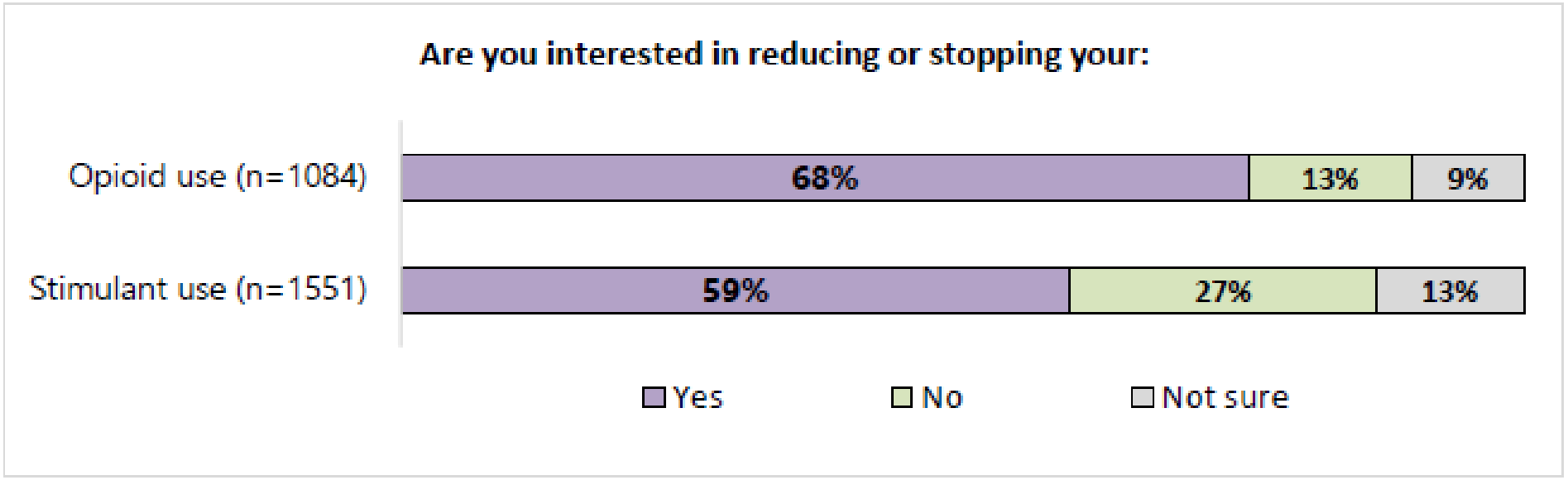
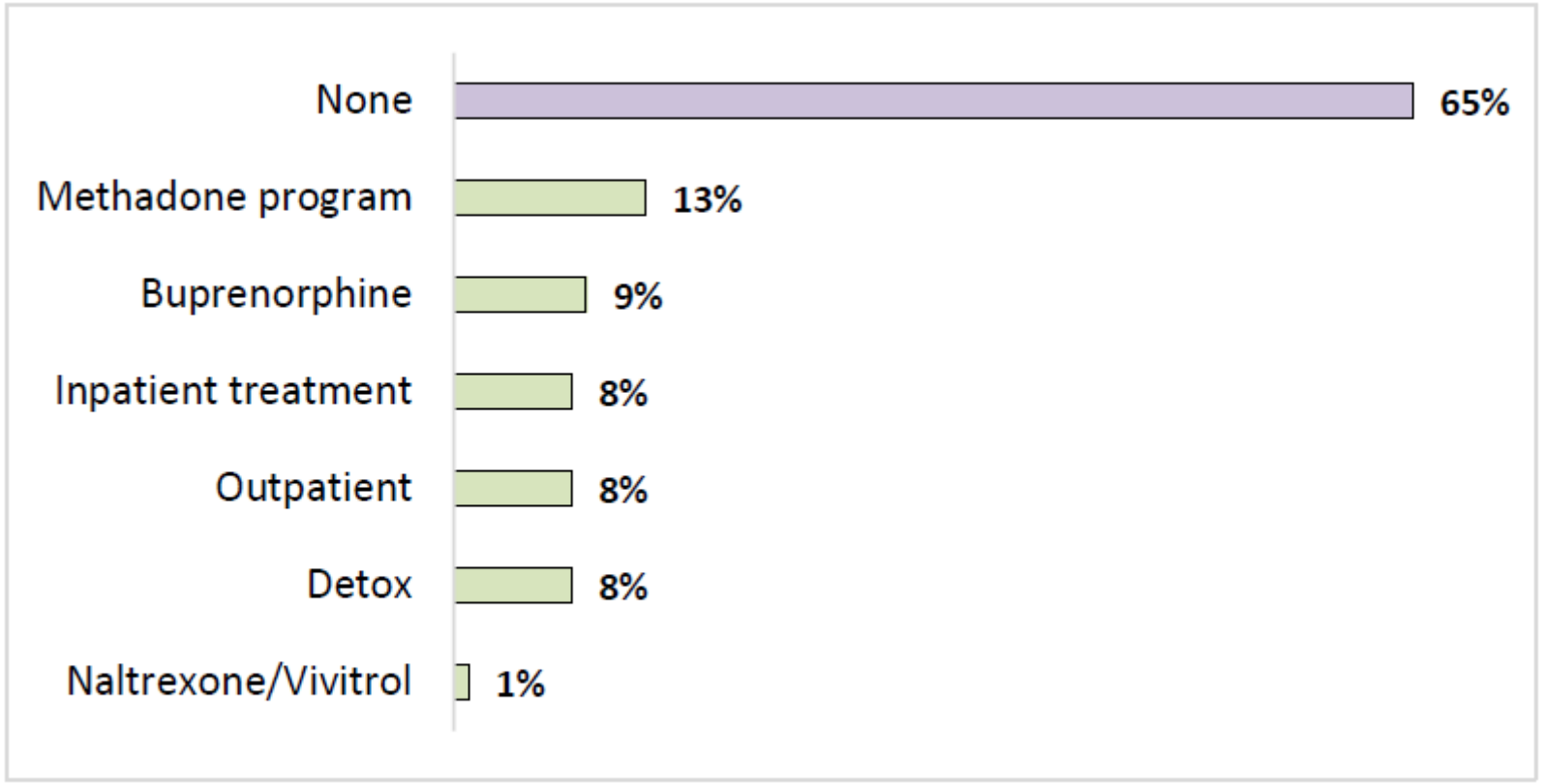


Figure 10. Interest in reducing or stopping drug use, among those who had used opioids or stimulants in the past week.

drug treatment in the past year



32% said there was *"a time in the past year when you tried to get help to stop or reduce your drug use but didn't/couldn't get it"*

Table 5. Barriers faced when trying to get help to reduce drug use n=357 responses given	
Availability/access problem (e.g., long waitlists, no treatment beds, no place to get MOUD, no I.D., no help to navigate entry)	**23%**
Lack of transportation	**12%**
Personal motivation (e.g., couldn't follow through, got scared)	**11%**
"Being homeless" (e.g., no phone, no place to store belongings, camp "sweeps" prevented follow through)	**7%**
Restrictive program issues or rules (e.g., strict appointment/attendance rules)	**6%**
No insurance/cost too high	**6%**

priorities

respondents were asked to identify the “top need in your life right now” and their open responses were coded. The **largest percentage (44%) said housing was their top need**, followed by other needs:

housing - 44%

income or job - 15%

to stop or reduce drug use - 9%

positive relationships, social support, friendship, “love,” - 6%

basic survival needs (e.g., food, water, personal safety, tent/tarp, clothing) - 6%

Other needs mentioned included mental health supports, drug treatment, stability, transportation, sense of purpose, and help with legal issues or getting an identification card.

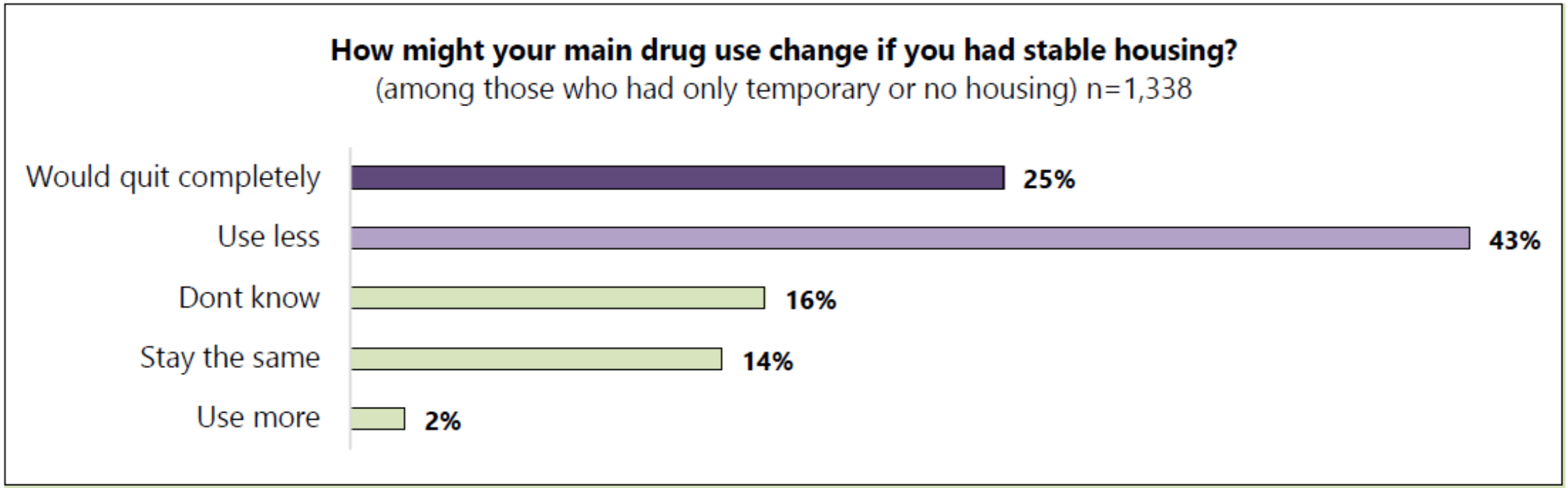


Figure 3. How participants felt stable housing might impact their drug use.

2021 SSP survey of people who use meth

"I WOULD LIKE TO HAVE KIND OF A NORMAL LIFE, WHATEVER NORMAL IS."

Reasons to Cut Back or Quit Meth

Most people shared reasons for wanting to cut back or quit. The most common reasons were:

- Family and relationships
- Desire for a "normal life"
- Physical health
- Mental health

What Helps or Would Help

People shared what has been or would be helpful. The most common responses were:

- Relationships and social connections with peers, friends, family, & even pets
- Substance use services: Support groups, case managers, SSPs, substance use treatment
- Personal factors: Internal drive, spirituality, staying positive, setting goals, accountability
- Purposeful activities and employment
- Housing
- Medications for mental health issues or opioid use disorder

https://adai.uw.edu/perspectives-meth-use/

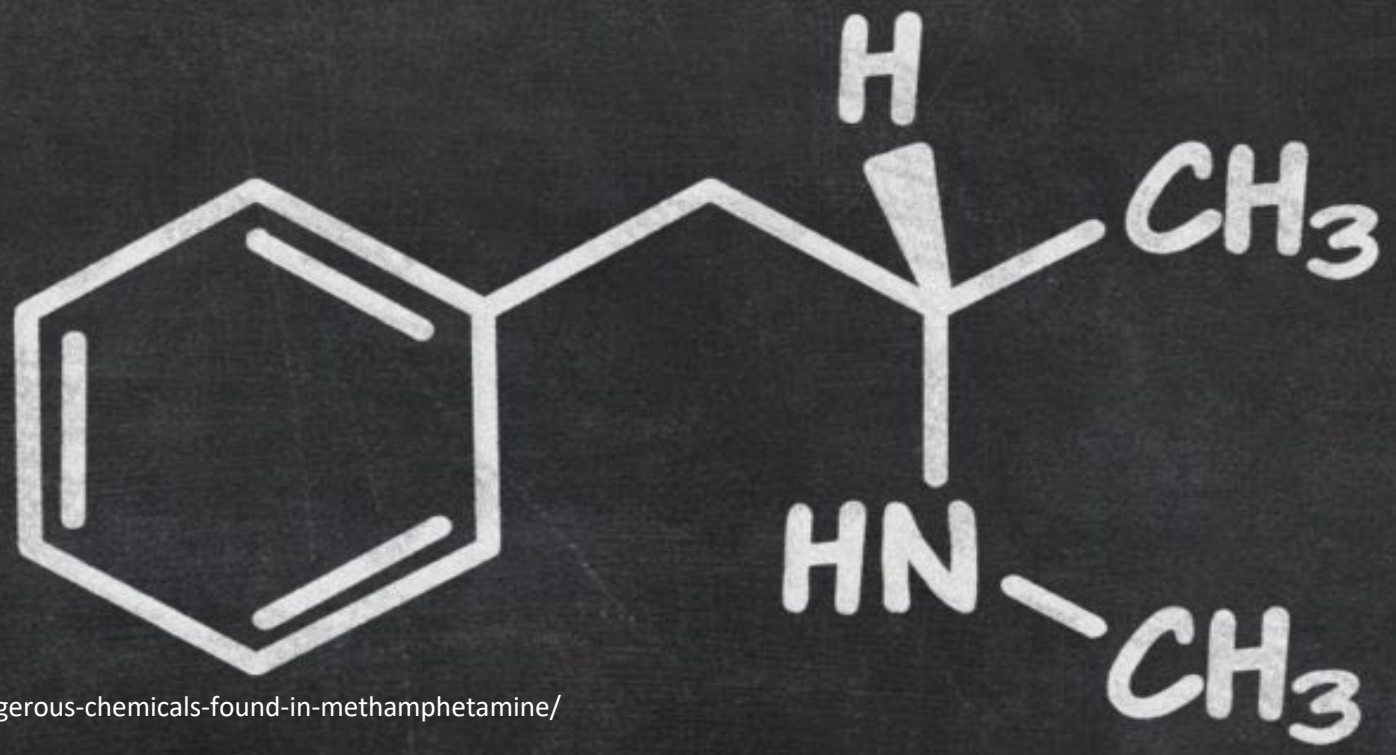
the high prevalence of stimulant use among people who use opioids reinforces the need to address opioid use, opioid overdose risk, and treatment of opioid use disorder within a polysubstance use context

given the high prevalence of drug smoking and the greater health risks from drug injection, all **SSPs should be supported by policy and funding to distribute safer smoking supplies**

housing is a crucial and substantial need, and most participants said that stable housing would have a positive impact on reducing or stopping their drug use.

Methamphetamine

$C_{10}H_{15}N$



https://www.deconsystems.com.au/dangerous-chemicals-found-in-methamphetamine/

short-term effects

euphoria

insomnia, increased attention & wakefulness, decreased fatigue

violent, bizarre, & erratic behavior, agitation, psychosis – paranoia, visual & auditory hallucinations(parasitosis), delusions

increased distractibility & irritability, decreased inhibition

panic attacks

decreased appetite, nausea

abscesses & cellulitis (spider bites)

neurotic excoriations & prurigo nodularis (“speed bumps”)

increased risk for 1° & 2° syphilis, HIV

long-term effects

physical & psychological dependence

changes in neuroanatomy & function similar to Alzheimer disease, epilepsy, and stroke

changes in cognition & motor skills

anxiety, confusion, insomnia, mood disturbances, and violent behavior

psychosis – paranoia, visual & auditory hallucinations, delusions

increased distractibility & irritability

memory loss

mood disturbances

disorientation, apathy, confusion, and exhaustion

long-term effects

weight loss & malnutrition
poor personal hygiene
“meth mouth” (maxillary artery vasoconstriction, xerostomia, poor hygiene)
chronic skin picking (delusions of parasitosis)
vascular damage to heart and brain
endocarditis
noncardiogenic pulmonary edema & pulmonary hypertension
acute and chronic cardiomyopathy
chronic hypertension
renal failure

use during pregnancy

increase rates of prematurity

placental vasoconstriction & abruption

spontaneous abortion

fetal changes

- small for gestational age
- lethargy
- cardiac & neurological abnormalities
- congenital syphilis

effects – infants & children

decreased arousal, increased stress, and poor quality of movement

by ages 1 and 2, toddlers show delayed motor development

preschool and school-age children with subtle but significant attention impairments

more likely to have cognitive and behavioral issues in school related to difficulties with self-control and executive function

“tweaking”

sleep disturbance (3-15 days)

increased need for meth to achieve original high → frustration, irritability & unpredictable behavior → violence – DV, spontaneous offenses, danger to others or themselves.

may behave normally and have clear eyes, concise speech, and brisk movements; but eye movement much faster than normal, minor quiver voice & jerky movements

concurrent use of depressant (e.g., alcohol or opioids) → increases paranoia, irritability, & frustration

EXTREME CAUTION

“overamping”

psychological	physical
confusion	nodding off
restlessness	jerking movements, tremors
hypervigilance	unable to stay still
panic attack	chest pain/tightness
paranoia	irregular breathing
suicidal ideation	hyperthermia, sweating, +/- chills
increased aggressiveness	teeth grinding
agitation	tachycardia

“overamping” risk factors

higher doses

lower tolerances

sleep deprivation

using multiple days in a row, especially without sleeping

setting or environment e.g., at a stranger’s house

changes in how used, mixing

underlying physical health

presentation of meth intoxication

mydriasis (dilated pupils)

altered mental status, hemorrhagic stroke

acute psychosis (tactile hallucinations, delusions, severe paranoia), agitation/irritability, violent behaviors, coma, seizure

tachycardia and hypertension (catecholamine excess)

bradycardia & hypotension (catecholamine depletion)

https://www.ncbi.nlm.nih.gov/books/NBK430895/

presentation of meth intoxication

dysrhythmia (atrial & ventricular), chest pain, myocardial infarction, aortic dissection, CHF

shortness of breath (pulmonary edema)

gastrointestinal distress (acute mesenteric vasoconstriction)

renal failure (rhabdomyolysis, tubular necrosis)

hyperthermia

OD - life-threatening intoxication characterized by hypertension, tachycardia, severely agitated delirium, hyperthermia, metabolic acidosis, and seizures

https://www.ncbi.nlm.nih.gov/books/NBK430895/

treatment of meth intoxication

benzodiazepines – escalated dosing

antipsychotics – agitation

diphenhydramine – sedation, prevent dystonia

“B-52” – Haldol (5mg) + diphenhydramine (50mg) + lorazepam (2mg)

labetalol – tachycardia + hypertension refractory to sedation

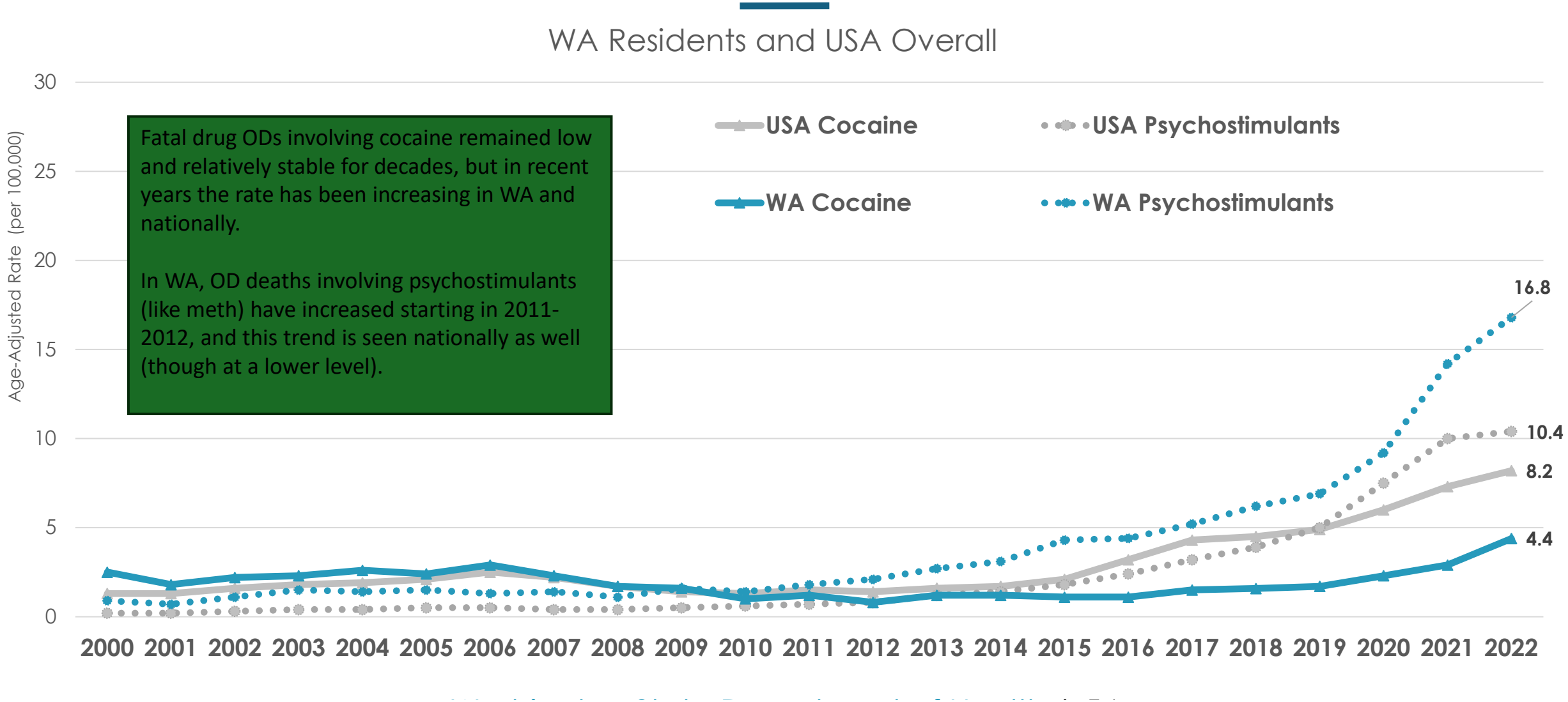
metoprolol – tachycardia without hypertension

STIMULANT OD DEATHS IN WASHINGTON STATE

RECENT UPDATES WITH PRELIMINARY 2023 & 2024 DATA (DATA AS OF 22JULY2024)

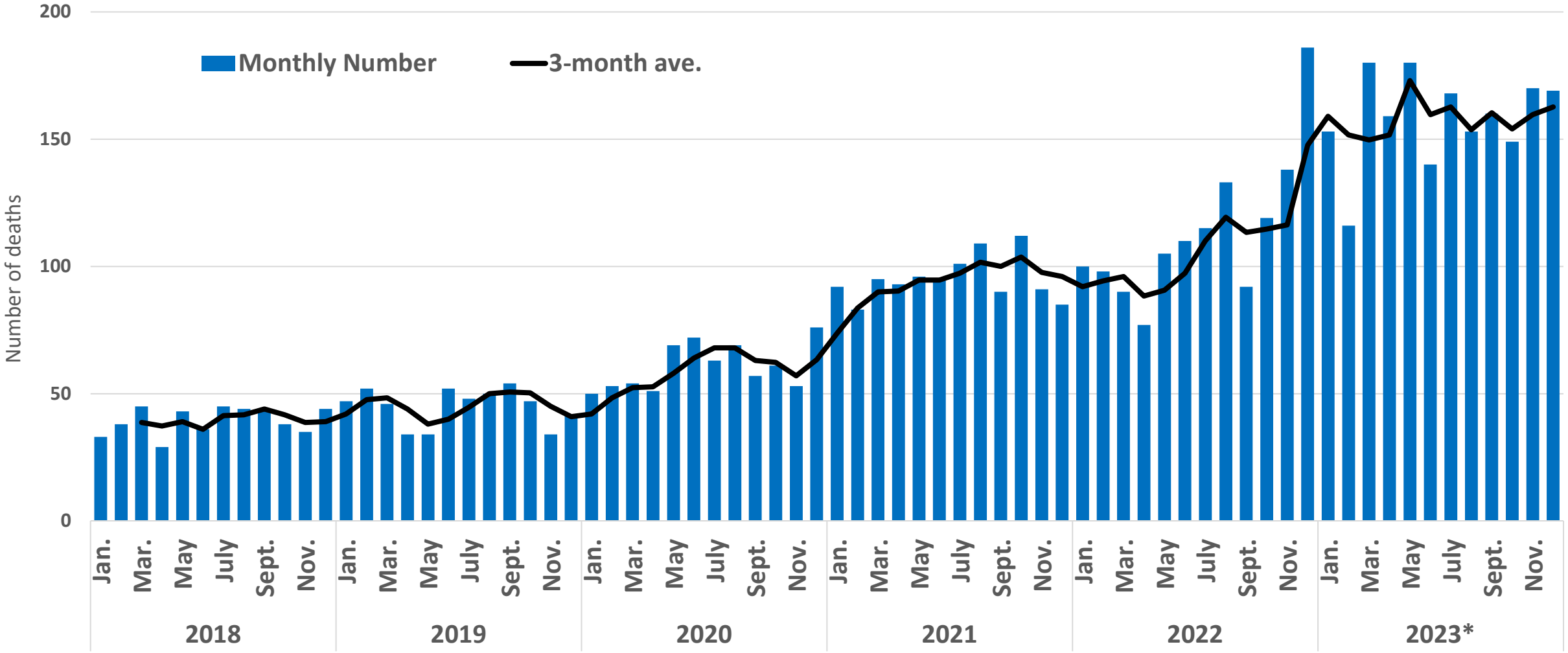
Injury and Violence Prevention/Surveillance and Evaluation, WA DOH
July 2024

OD death rate by drug type, USA & WA (2000-2022)



WA Data Source: Washington State Department of Health, Center for Health Statistics, Death Certificate Data. Data last updated on July 22, 2024.
USA Data Source: CDC WONDER

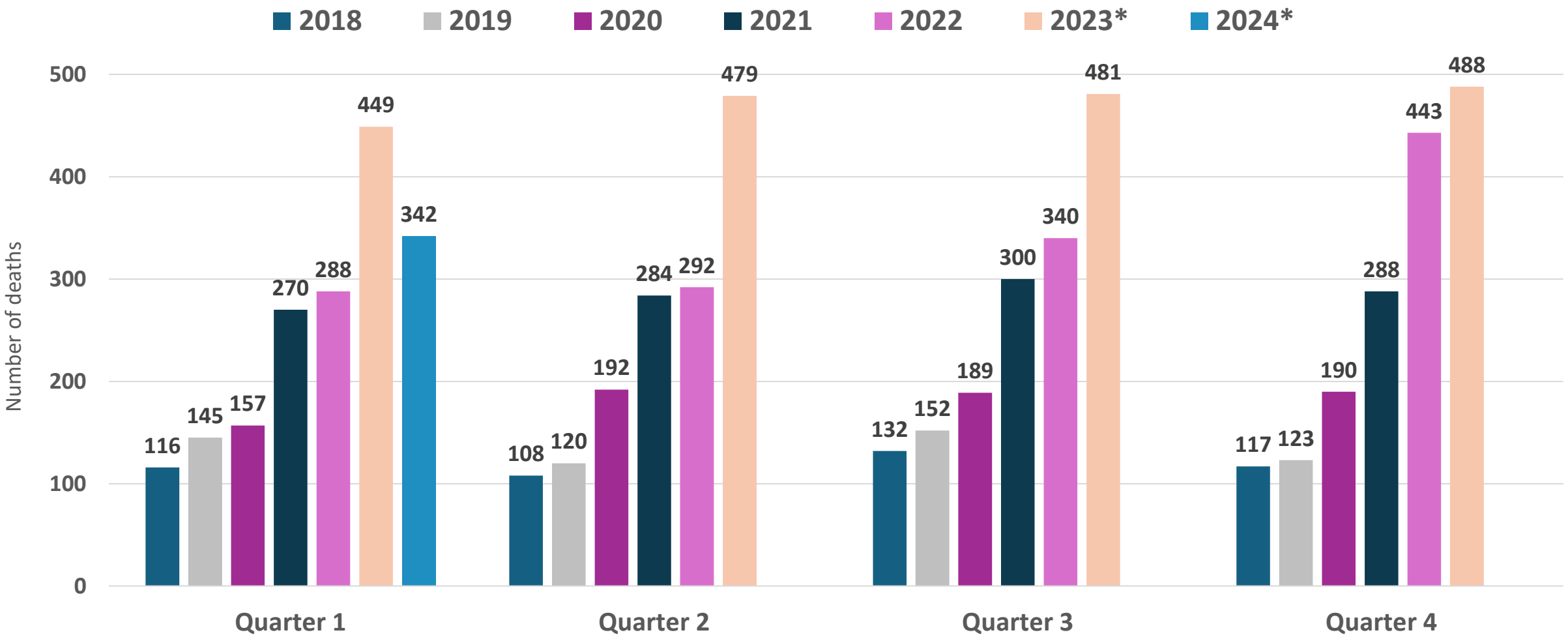
number of OD deaths - psychostimulant by month and 3-month average (2018-2023*)



*2023 data is preliminary and expected to change.

WA Data Source: Washington State Department of Health, Center for Health Statistics, Death Certificate Data. Data last updated on July 22, 2024.

number of OD deaths involving a psychostimulant by quarter (2018-2024*)



*2023 and 2024 data are preliminary and expected to change.

Data Source: Washington State Department of Health, Center for Health Statistics, Death Certificate Data.. Data last updated: July 22, 2024.

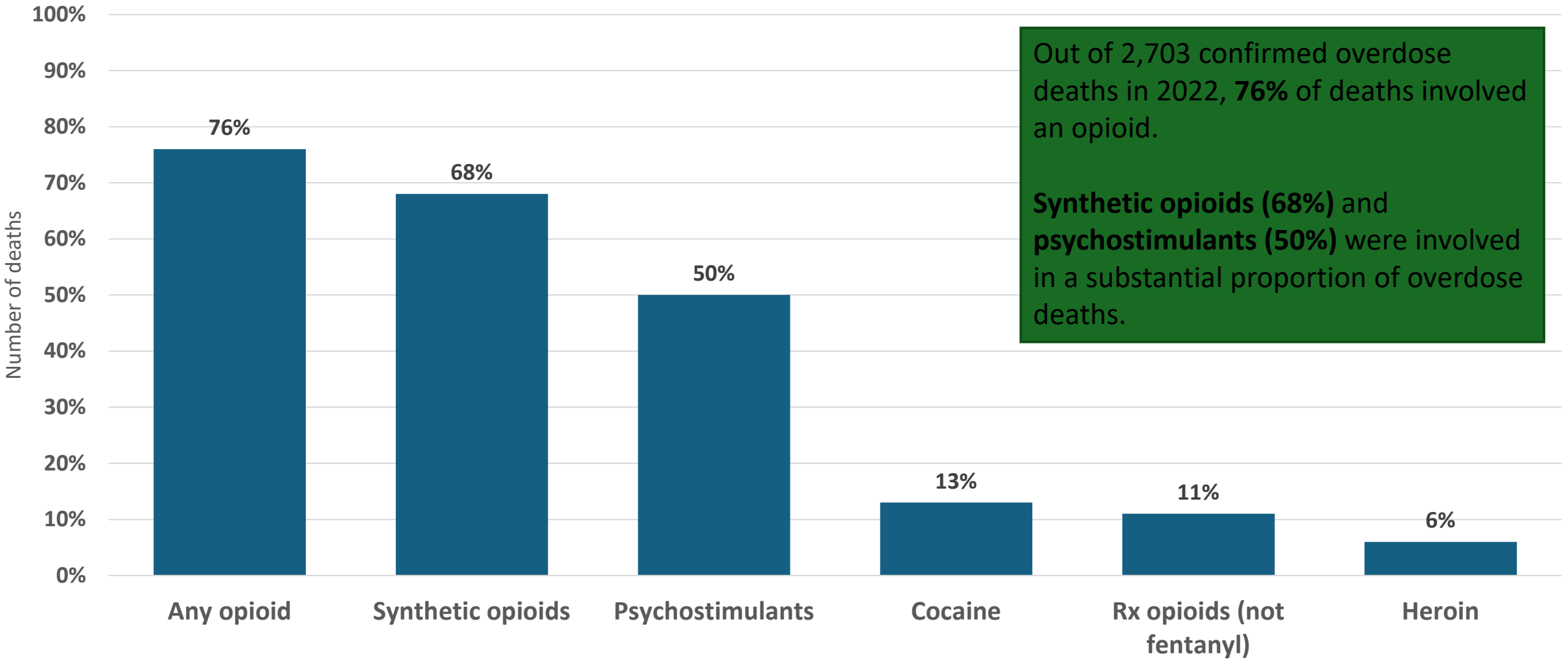
confirmed OD deaths by drug (2018-2024*)

Drug Type	2018	2019	2020	2021	2022	*2023**	*2024**
Any Drug	1181	1259	1731	2264	2703	*3432*	*866*
Any Opioid	744	827	1194	1619	2048	*2798*	*706*
Heroin	329	347	384	344	154	*67*	*<10*
Synthetic Opioids	224	337	672	1214	1850	*2622*	*668*
Rx Opioid (not Fentanyl)*	305	267	328	402	303	*372*	*71*
Psychostimulants	473	540	728	1142	1363	*1897*	*475*
Cocaine	129	132	187	232	361	*594*	*142*

* 2023 data are preliminary and will change
* Rx Opioid: T40.2 and T40.3

Source: WA DOH death certificates
Data as of: 22July2024

proportion of drug types involved in OD deaths (2022)



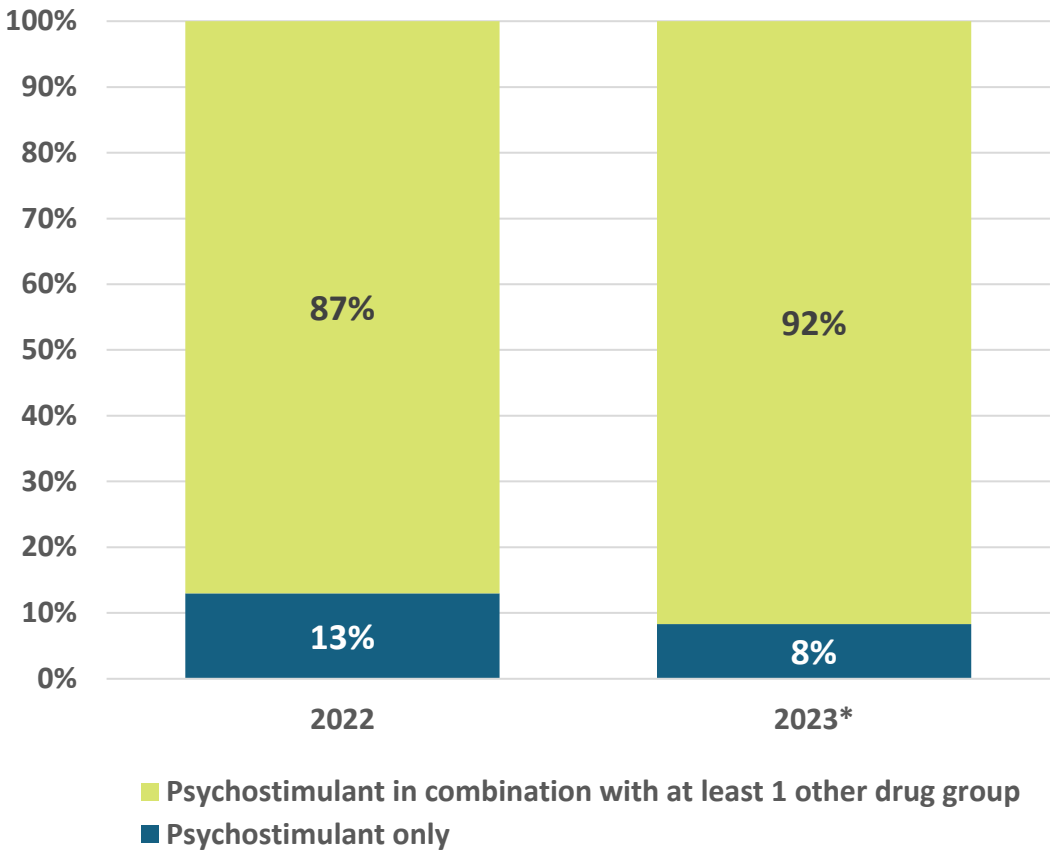
Out of 2,703 confirmed overdose deaths in 2022, **76%** of deaths involved an opioid.

Synthetic opioids (68%) and **psychostimulants (50%)** were involved in a substantial proportion of overdose deaths.

Source: WA DOH death certificates

polysubstance OD deaths among psychostimulant-involved drug overdose deaths (2022-2023*)

Percent of drug overdose deaths involving a psychostimulant alone and in combination with at least 1 other drug type



*2023 data are preliminary and expected to change.

Most common co-occurring substances listed on death certificate:

- Synthetic opioids: 2022: 64%; 2023*: 76%
- Cocaine: 2022: 10%; 2023*: 13%

Top 5 leading drug combinations

(2023, n=1739 drug overdose deaths involving a psychostimulant and at least 1 other drug type):

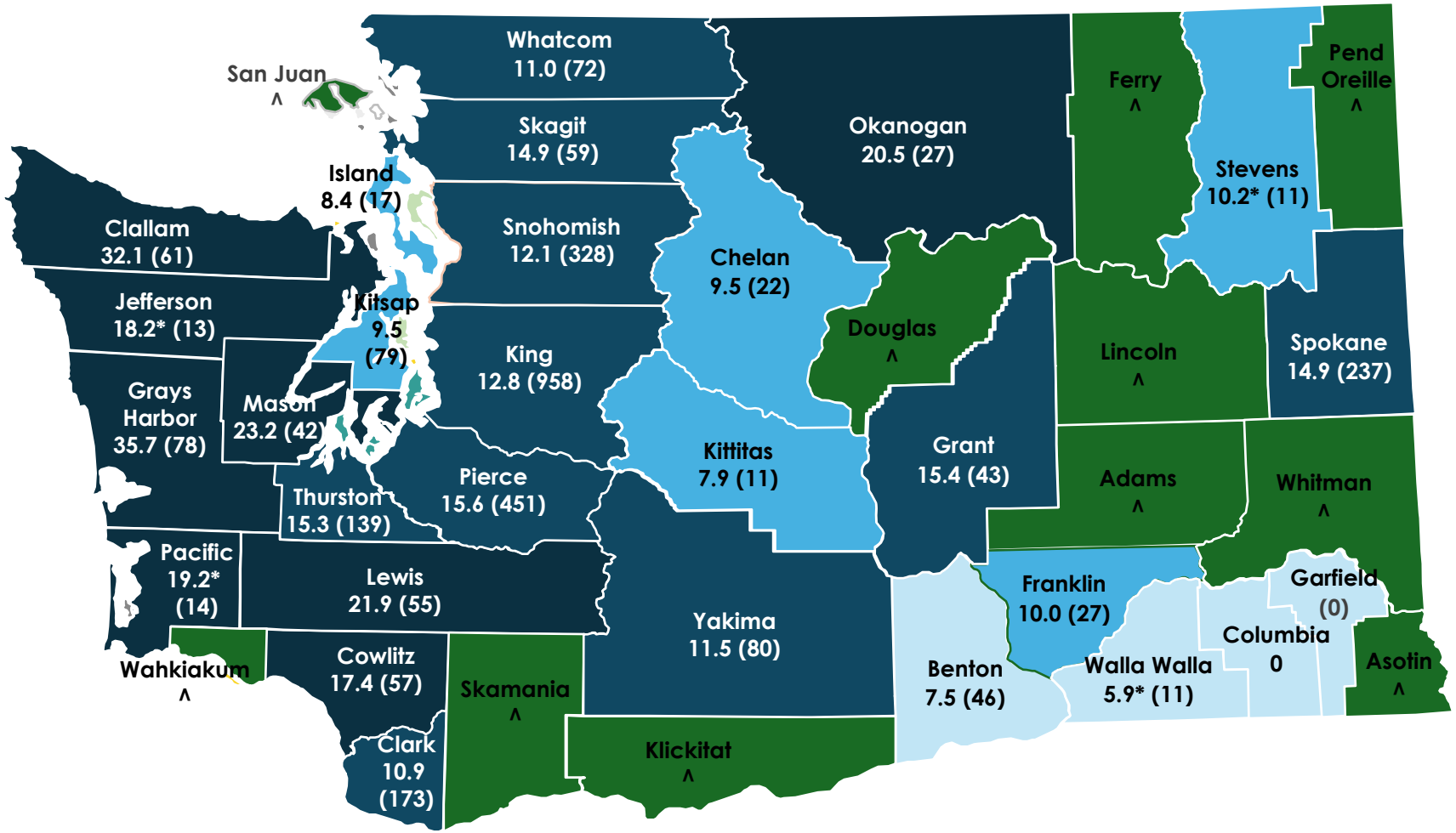
- Psychostimulants and: Synthetic opioids: 54%
- Psychostimulants and: Synthetic opioids and Cocaine: 9%
- Psychostimulants and: Synthetic opioids and Alcohol: 3%
- Psychostimulants and: Synthetic opioids and Prescription opioid**: 3%
- Psychostimulants and: Synthetic opioids and Sedative: 3%

**Prescription opioid includes natural and semi-synthetic opioids and methadone (T40.2 and T40.3).

Data Source: WA DOH death certificates

Psychostimulant OD death rates (and counts) by county (2020-2022)

(State Age-Adjusted Rate = 13.4 per 100,000)



Drug overdose death rate quartiles
(Rate per 100,000)

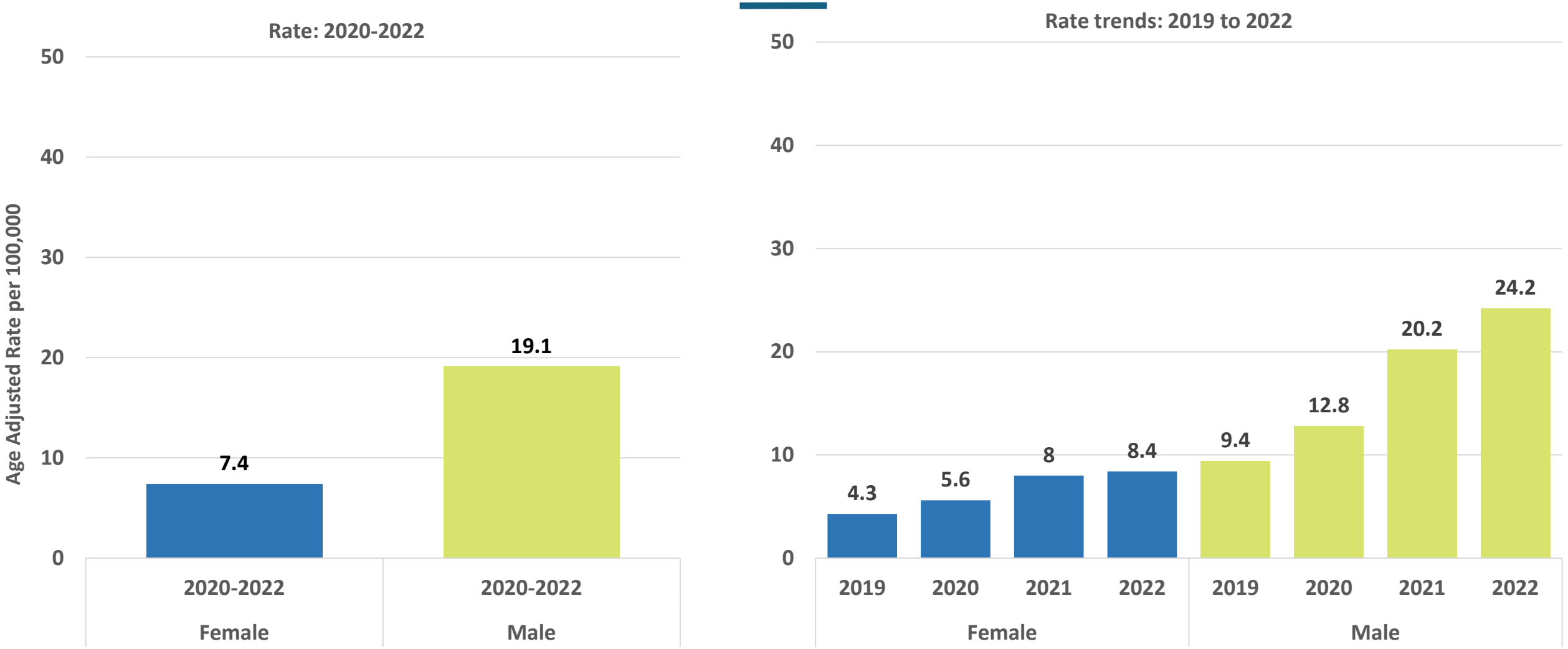
- Less than 7.9
- 7.9 to <10.9
- 10.9 to <16.5
- 16.5 and higher
- Rate/Count is suppressed

^: Rate/Count is suppressed in county with 9 or fewer deaths.
*: Rate is not reliable in county with 16 or fewer deaths

Data Source: Washington State Department of Health, Center for Health Statistics, Death Certificate Data.

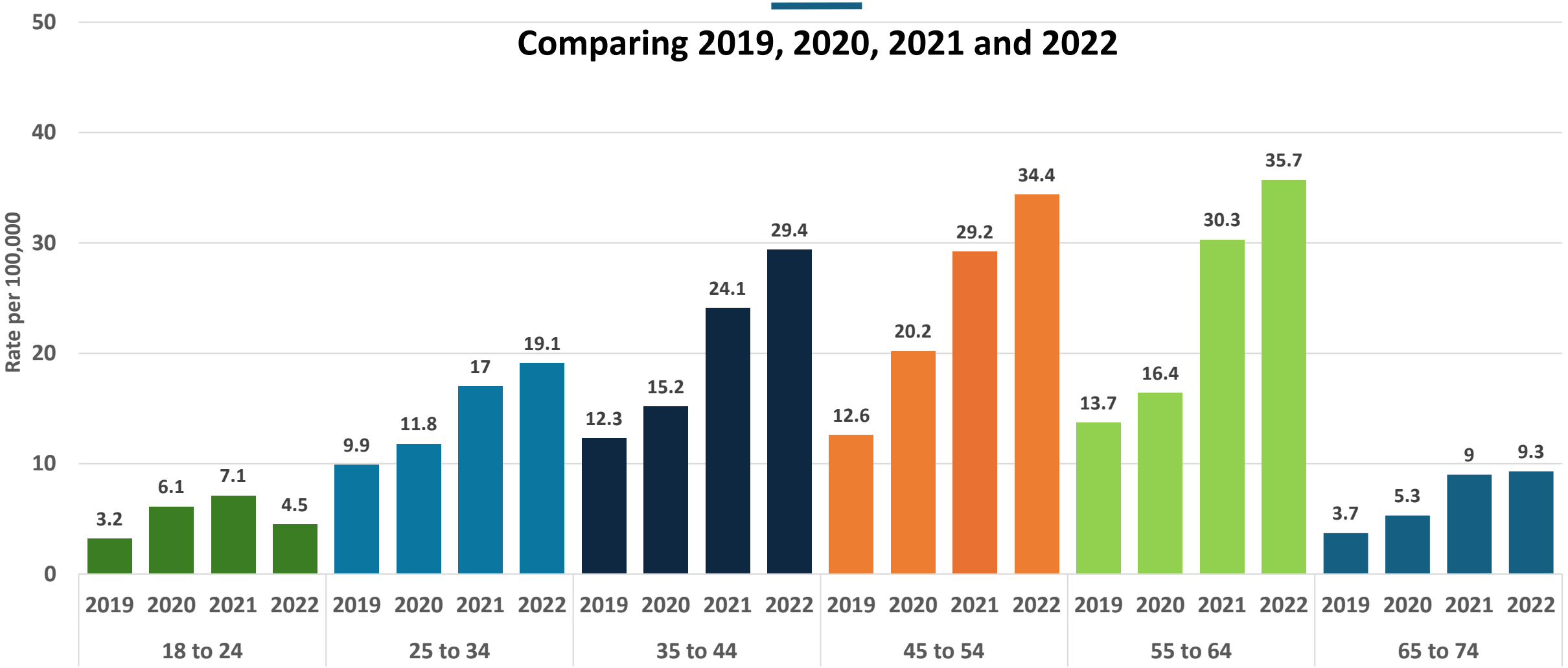
2022 data are finalized.

Psychostimulant OD death rates by sex



Source: WA DOH death certificates

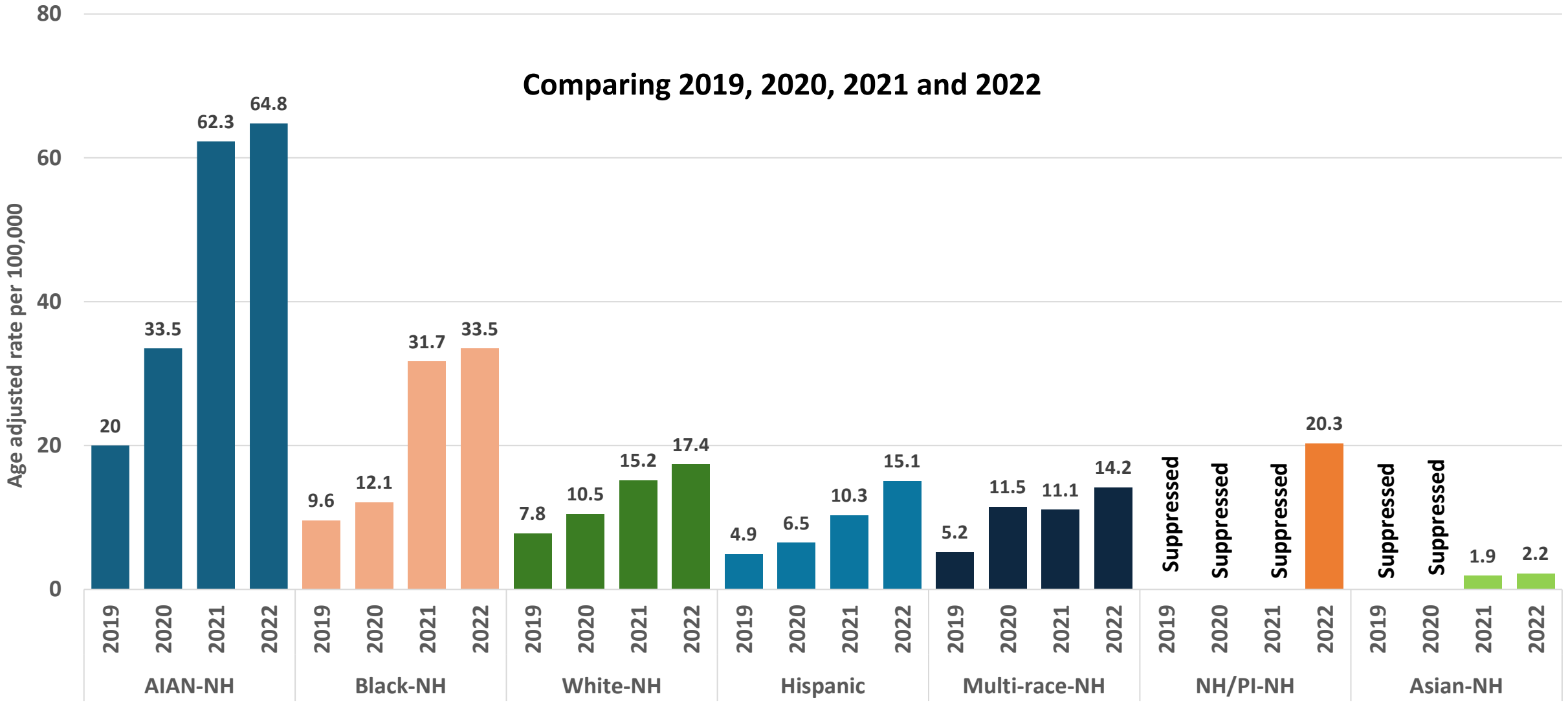
Psychostimulant OD death rates by age



Ages 9 and under, 10 to 17, and 75+ are suppressed due to small counts.

Source: WA DOH death certificates

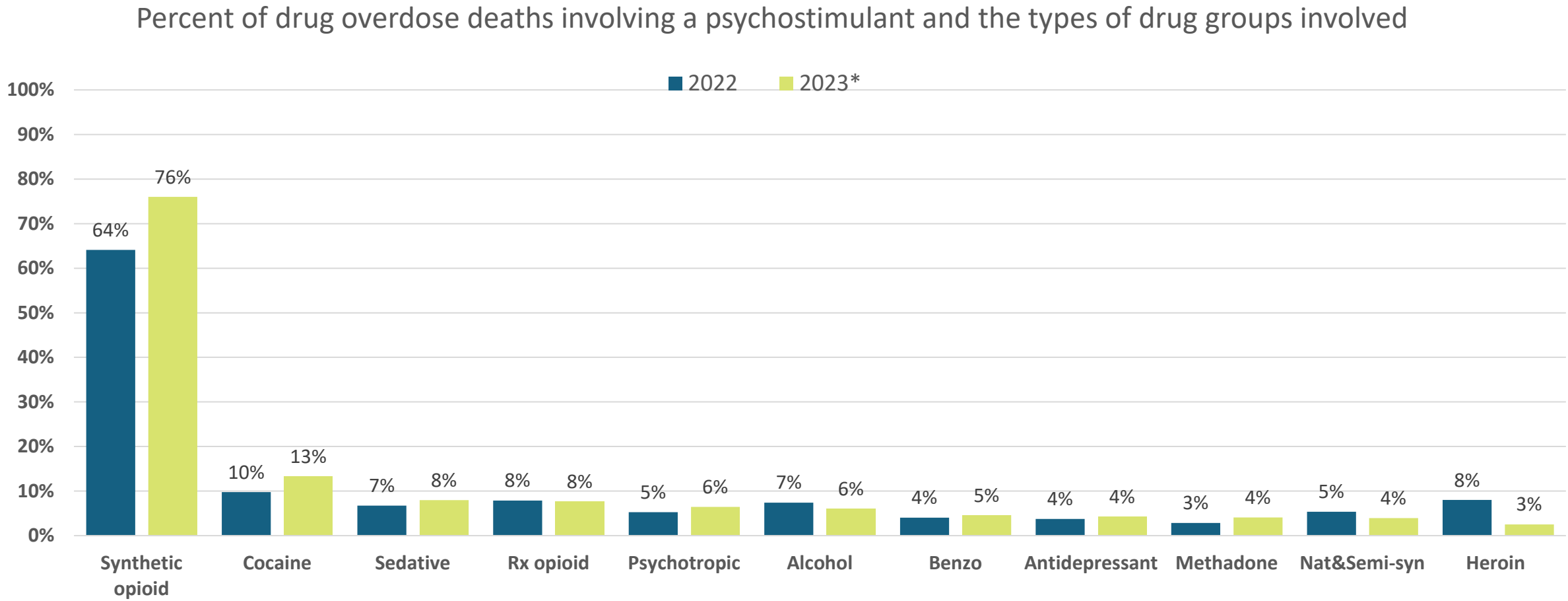
psychostimulant OD death rates by race/ethnicity



NH/PI: Native Hawaiian and Pacific Islander

Source: WA DOH death certificates

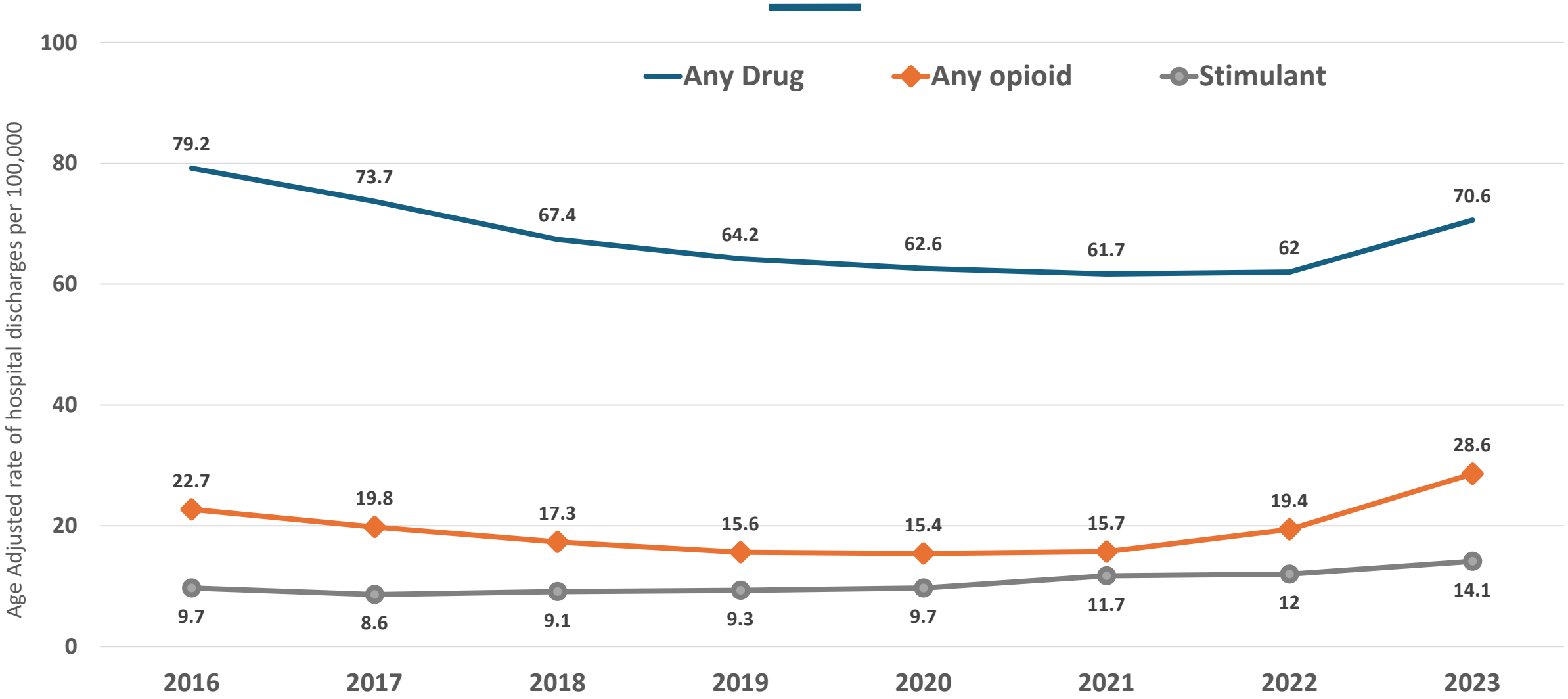
polysubstance OD deaths among psychostimulant-involved drug overdose deaths (2022-2023*)



*2023 data are preliminary and may change.

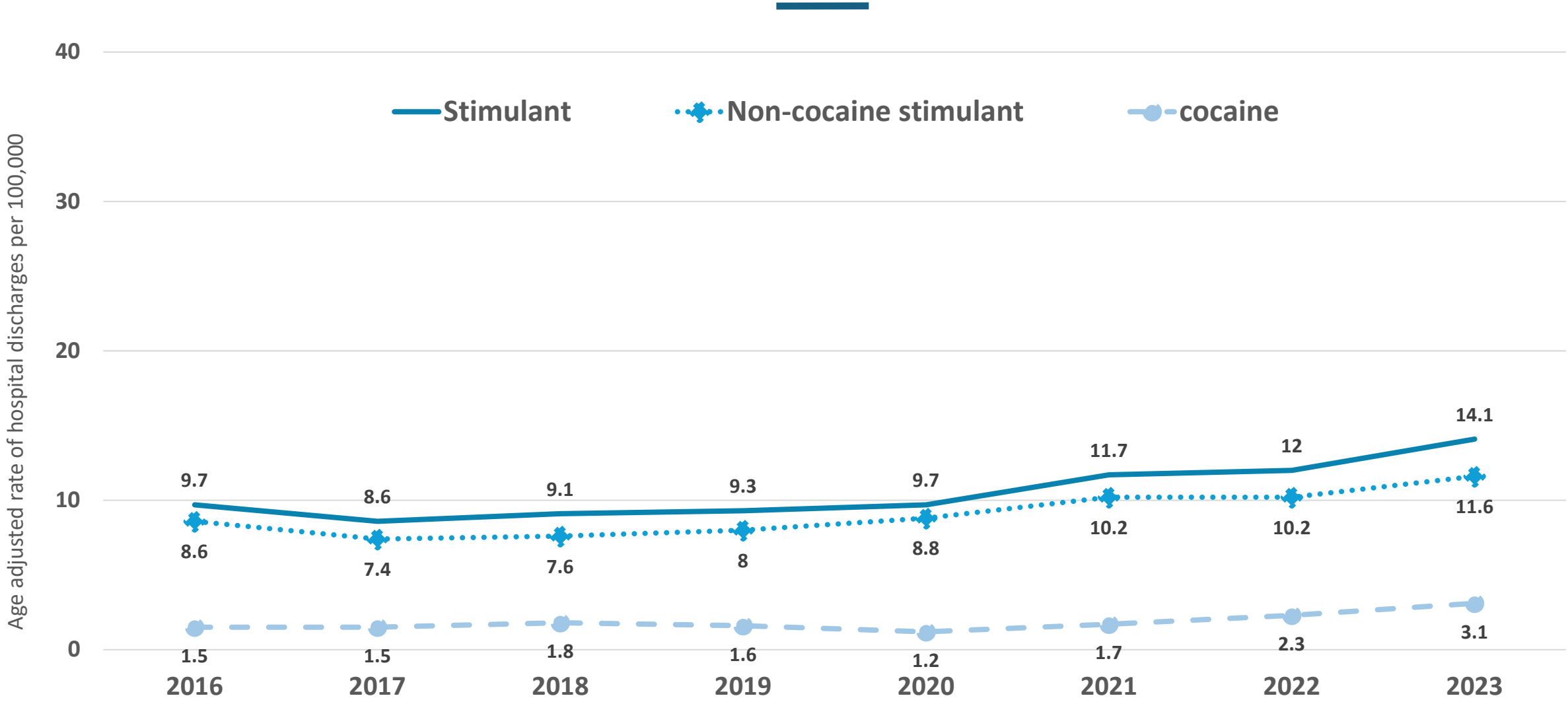
Source: WA DOH death certificates

OD hospitalization rate by drug (2016-2023)



Source: DOH Comprehensive Hospital Abstract Reporting System (CHARS)

OD hospitalization rate and stimulants (2016-2023)



Source: DOH Comprehensive Hospital Abstract Reporting System (CHARS)

treatment of meth use disorder

- behavioral therapies
  - individual or group drug counseling including standard outpatient counseling and intensive outpatient treatment, cognitive-behavioral therapy (CBT), contingency management, & motivational interviewing
- medication therapies
  - injectable naltrexone and oral bupropion
  - mirtazapine
  - psychostimulants
- treat underlying ADHD (10%)
- upstream issues

exposure – public health response

first-hand exposure - methamphetamine users

second-hand exposure from a first-hand user

- health risks from casual secondary exposure to meth residue (surfaces/smoke) in public places is very low as compared to longer-term exposure in spaces where people live and where methamphetamine is/was manufactured or consumed regularly – dermal absorption, hand to mouth ingestion

exposure – public health response

third-hand exposure - methamphetamine-contaminated property by drug use, synthesis or contact with contaminated material

- risk from skin contact, ingestion, and inhalation exposure routes
- non-specific adverse health effects including respiratory irritation, eye irritation, nausea, headaches, behavioral issues, and sleep issues

infants & children most at risk

- behavioral & cognitive effects, sleep, respiratory, eye/skin irritation

exposure – public health response

Methamphetamine Clandestine Lab Cleanup Regulations by State

EPA - Voluntary Guidelines for Methamphetamine and Fentanyl Laboratory Cleanup

Chapter 64.44 RCW Contaminated Properties

WA Drug Lab Clean-up Program

Where to find overdose data?

[Opioid and Overdose Data Dashboard (public)]

Includes all overdose deaths, hospitalizations, and EMS responses filterable by residence, age, sex, and race/ethnicity

[Unintentional Drug Overdose Data Dashboard (SUDORS)]

Includes additional demographic, drug category, and circumstance details on unintentional and undetermined overdose deaths

[Online Injury Data Request Form]

resources

PBS Timeline

UW ADAI Clearinghouse

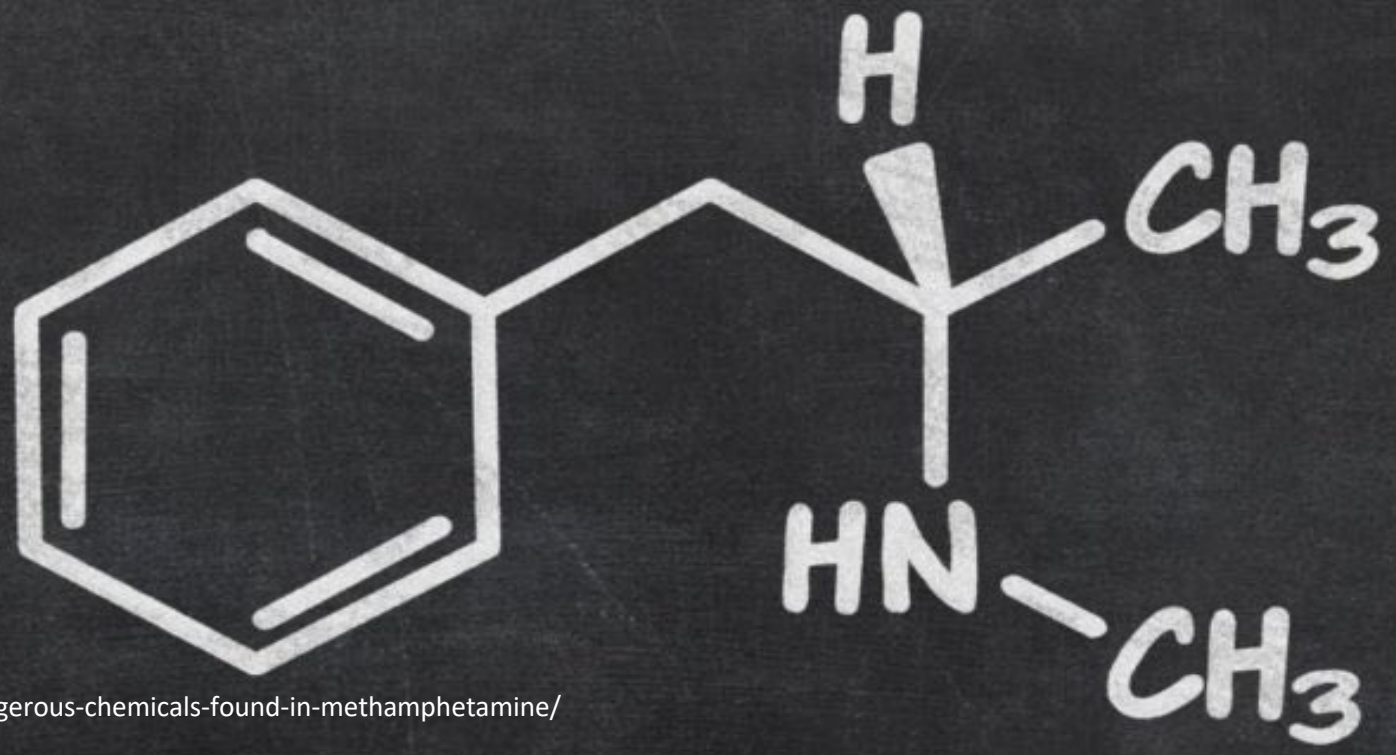
WA DOH Meth Labs

Household Contamination with Methamphetamine: Knowledge and Uncertainties

National Harm Reduction Coalition

Methamphetamine

$C_{10}H_{15}N$



https://www.deconsystems.com.au/dangerous-chemicals-found-in-methamphetamine/