

Colluding Crises: Understanding Stimulant and Fentanyl Overdose Mortality

Phillip O. Coffin, MD, MIA, SFDPH / UCSF

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Disclosure Information



Phillip Coffin, MD MIA

- Direct NIH-funded trial that receives donated tenofovir-emtricitabine from Gilead Sciences

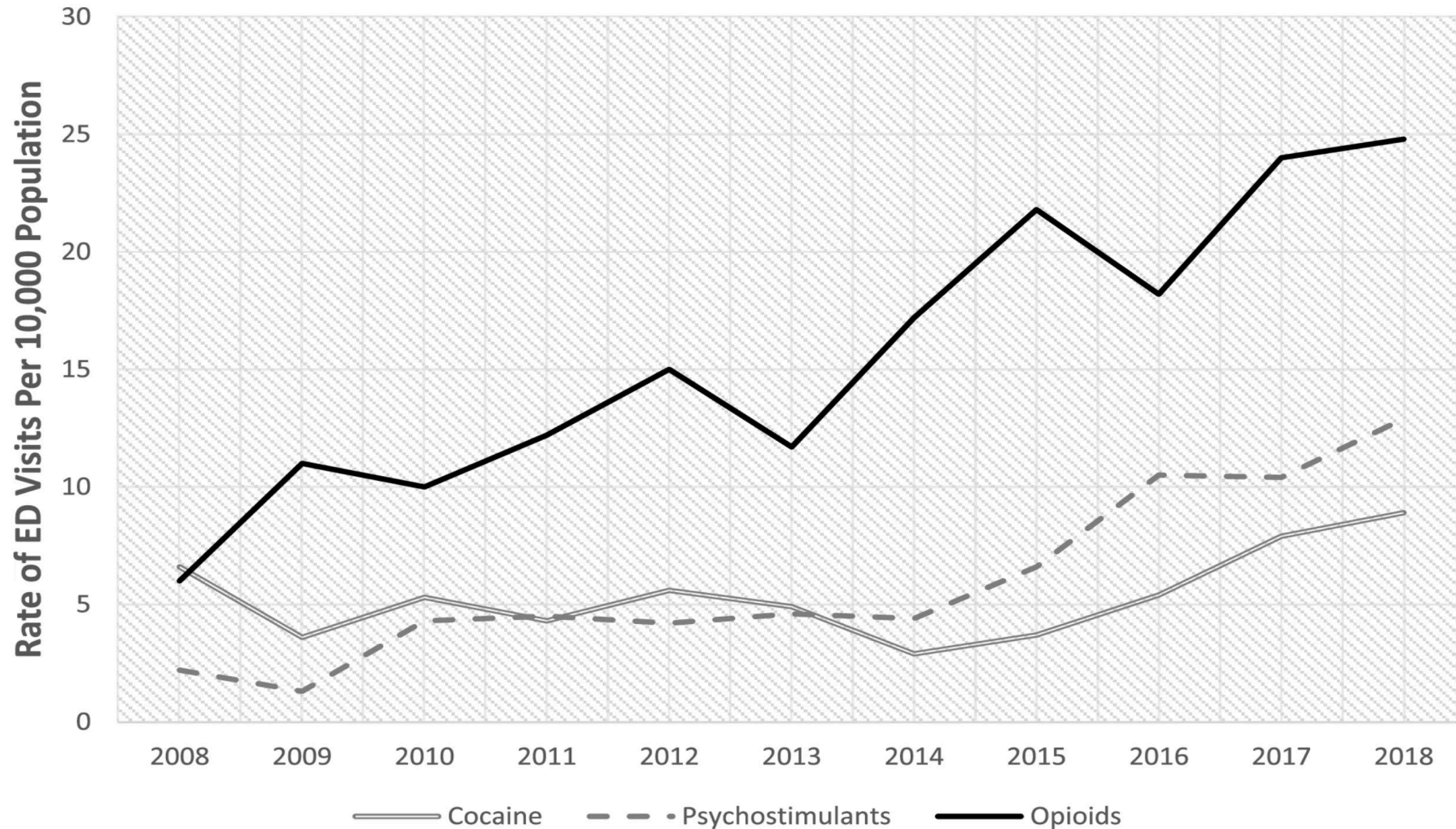
Session Learning Objectives

At the end of the session, you will be able to:

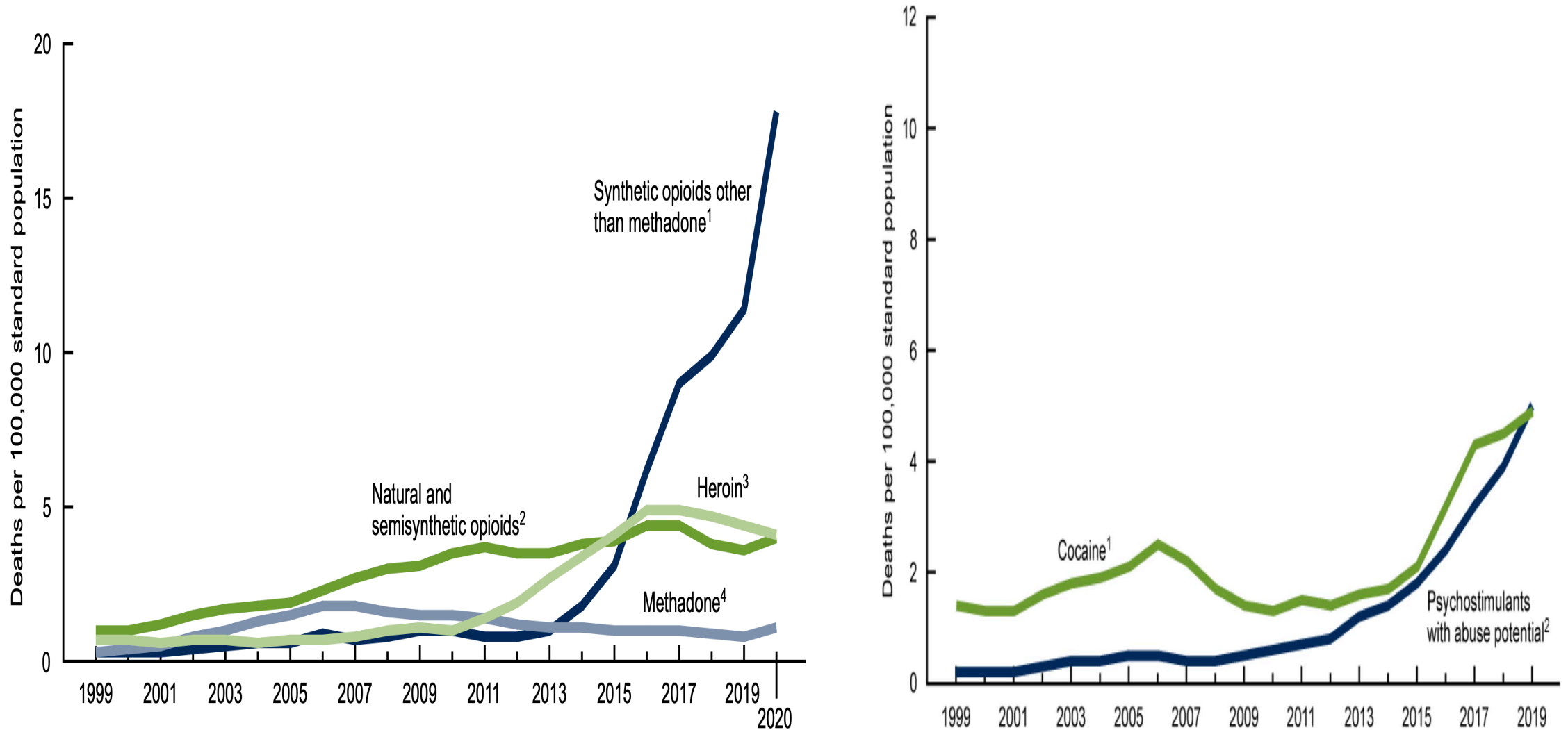
- Describe the current epidemiology of mortality caused by stimulants and fentanyl.
- Distinguish the clinical characteristics of acute opioid and stimulant toxicity.
- Evaluate the potential impact of approaches to addressing mortality due to stimulants and fentanyl.

US ED Visits by Drug Class

(excluding multiple drugs)

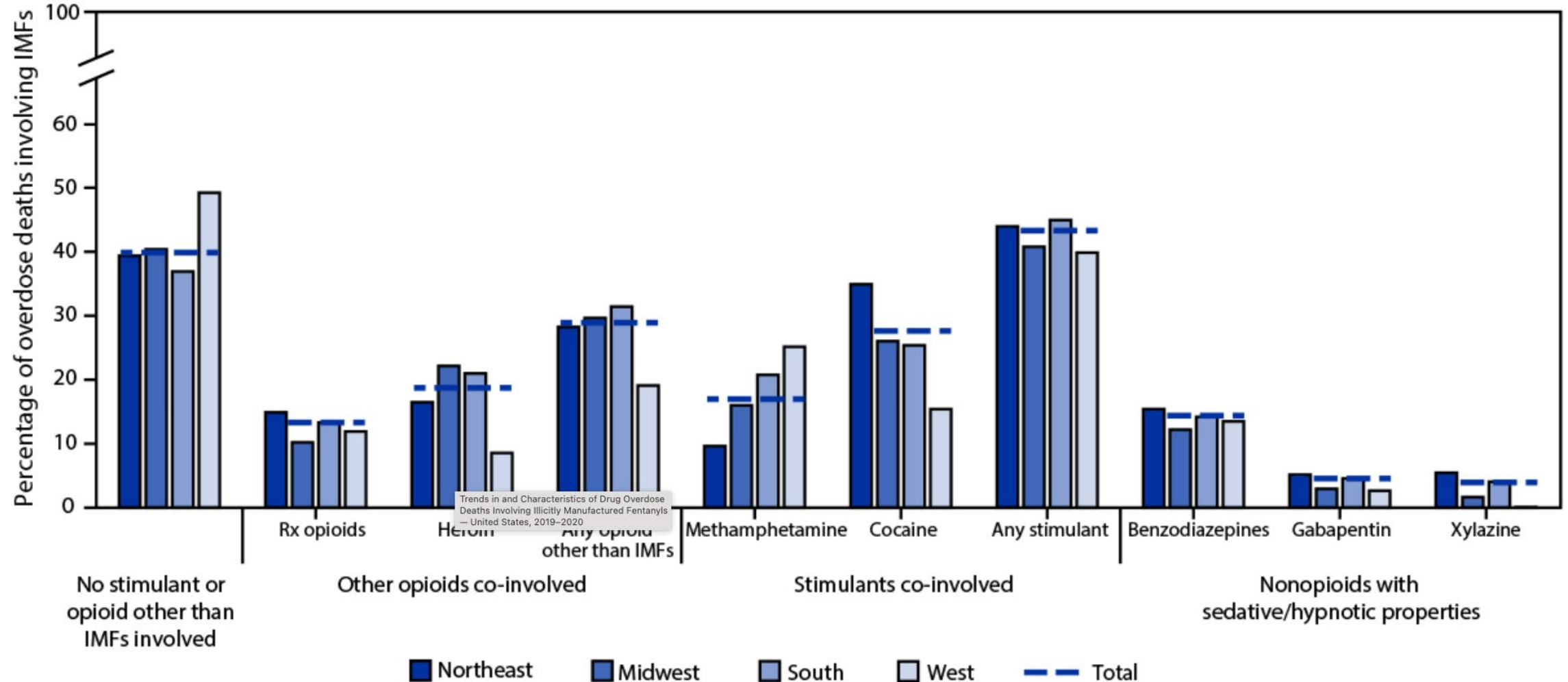


Age-Adjusted U.S. Overdose Death Rate



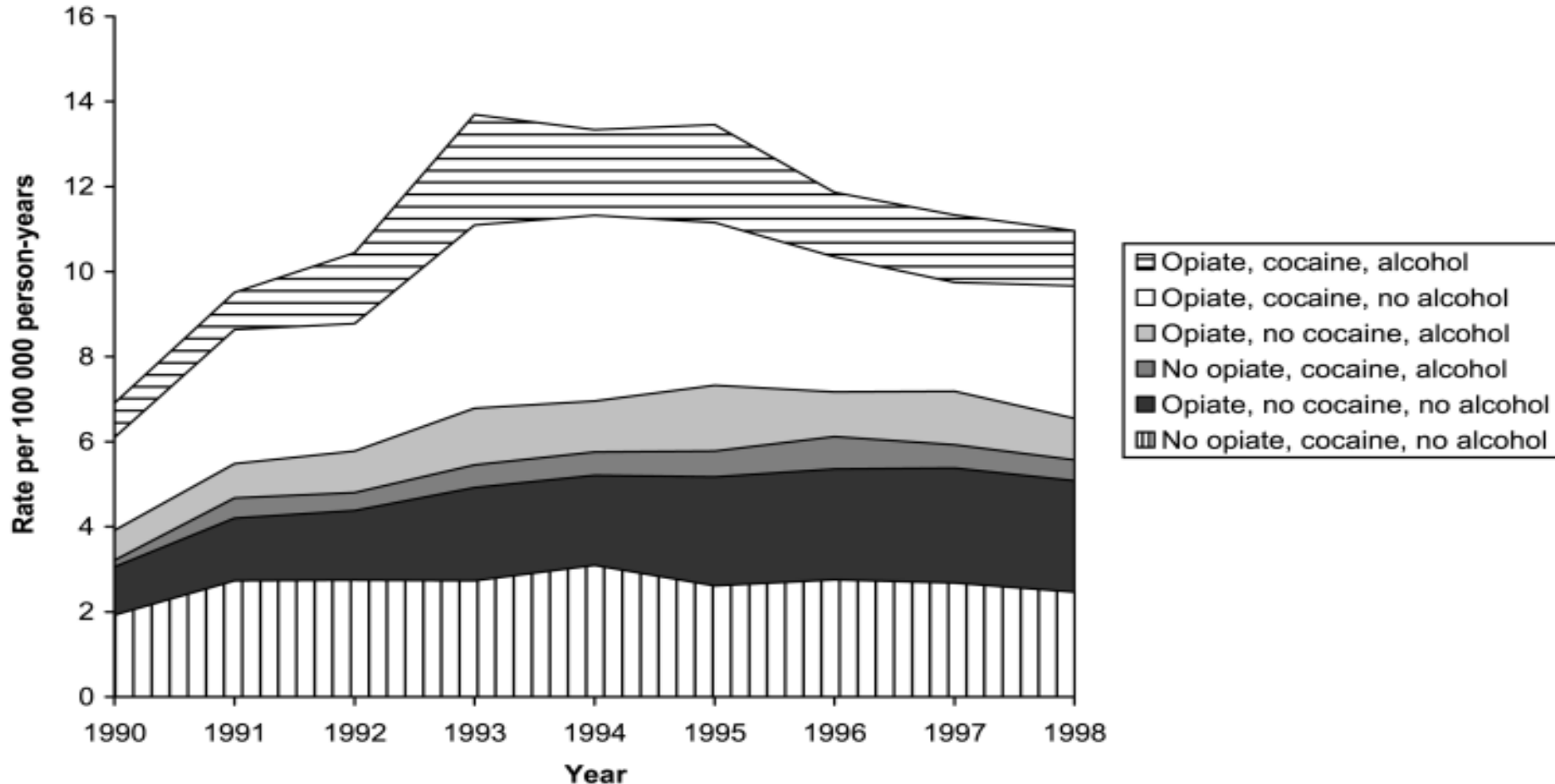
Involvement of Other Drugs in Fentanyl Deaths

(SUDORS, 2020)



Opioids In Combination With Other Drugs In NYC

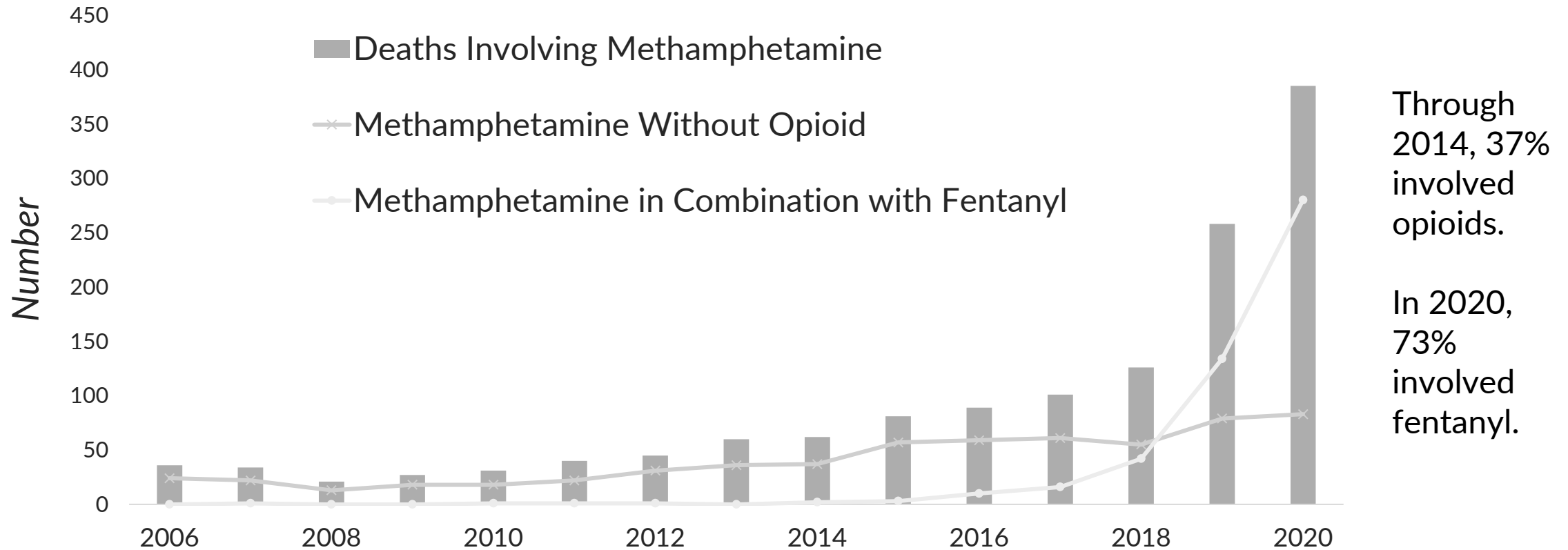
1990s



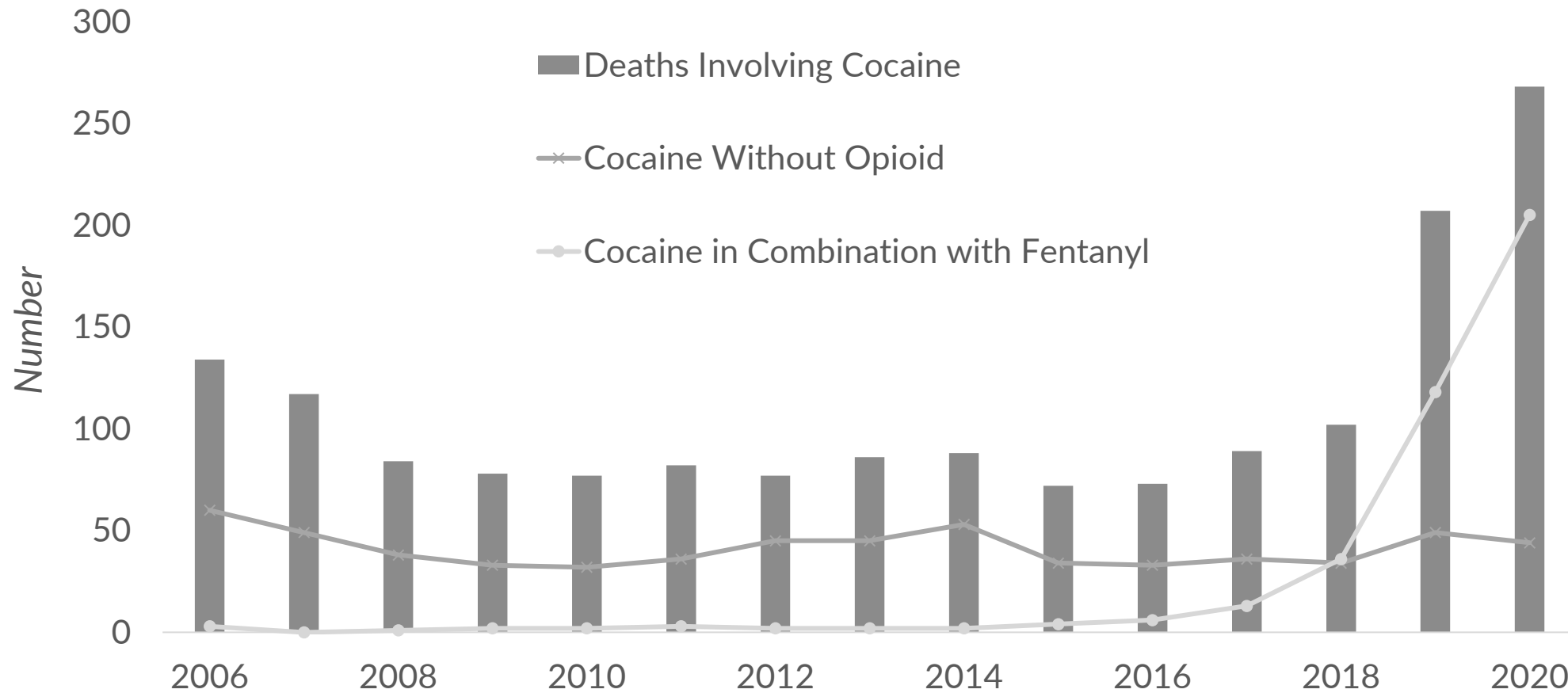
51% of Opioid deaths involved Cocaine

51% of Cocaine deaths involved Opioids

MA Overdose Deaths in San Francisco



Cocaine Overdose Deaths in San Francisco



Through 2014, 54% involved opioids

In 2020, 76% involved fentanyl

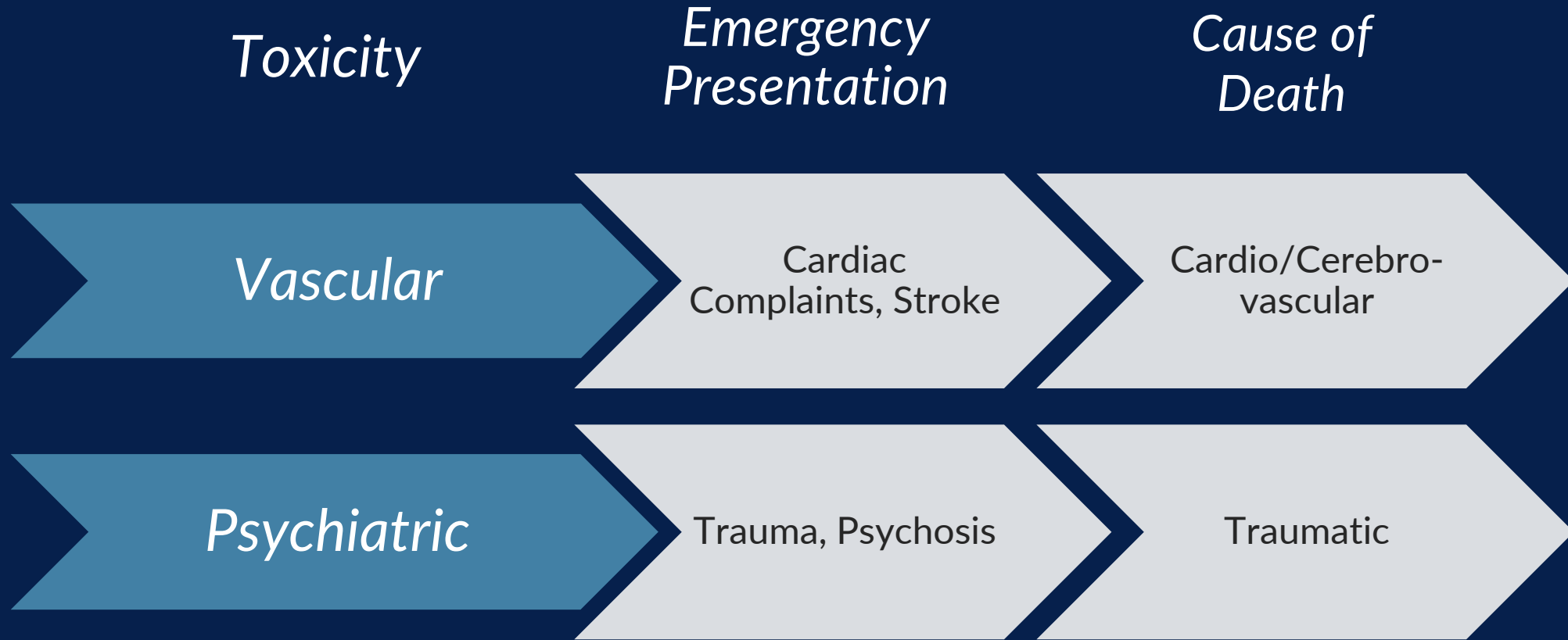
Questions

- What is an “overdose” death?
 - For stimulants
- Are stimulant-fentanyl deaths fundamentally fentanyl deaths?
- How many of these stimulant-fentanyl deaths are due to unintentional fentanyl exposure?
- What is the role of naloxone?

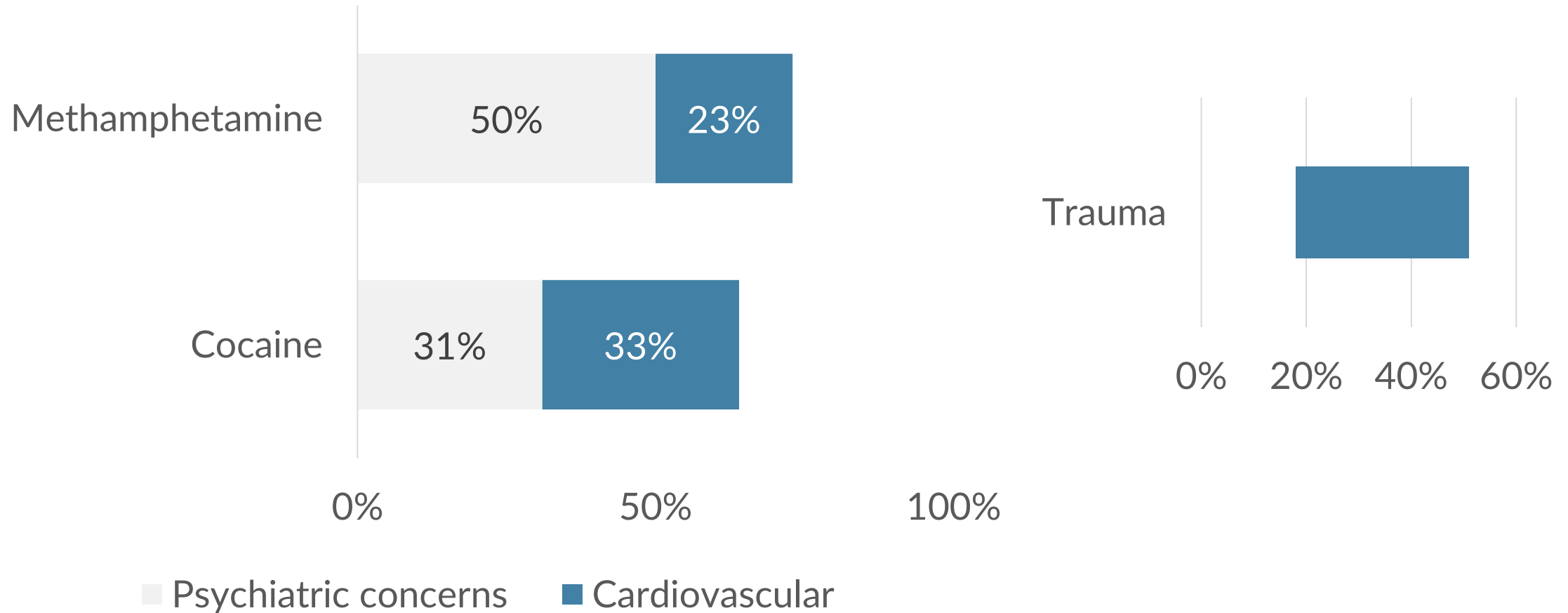
Pathophysiology of Opioid Overdose



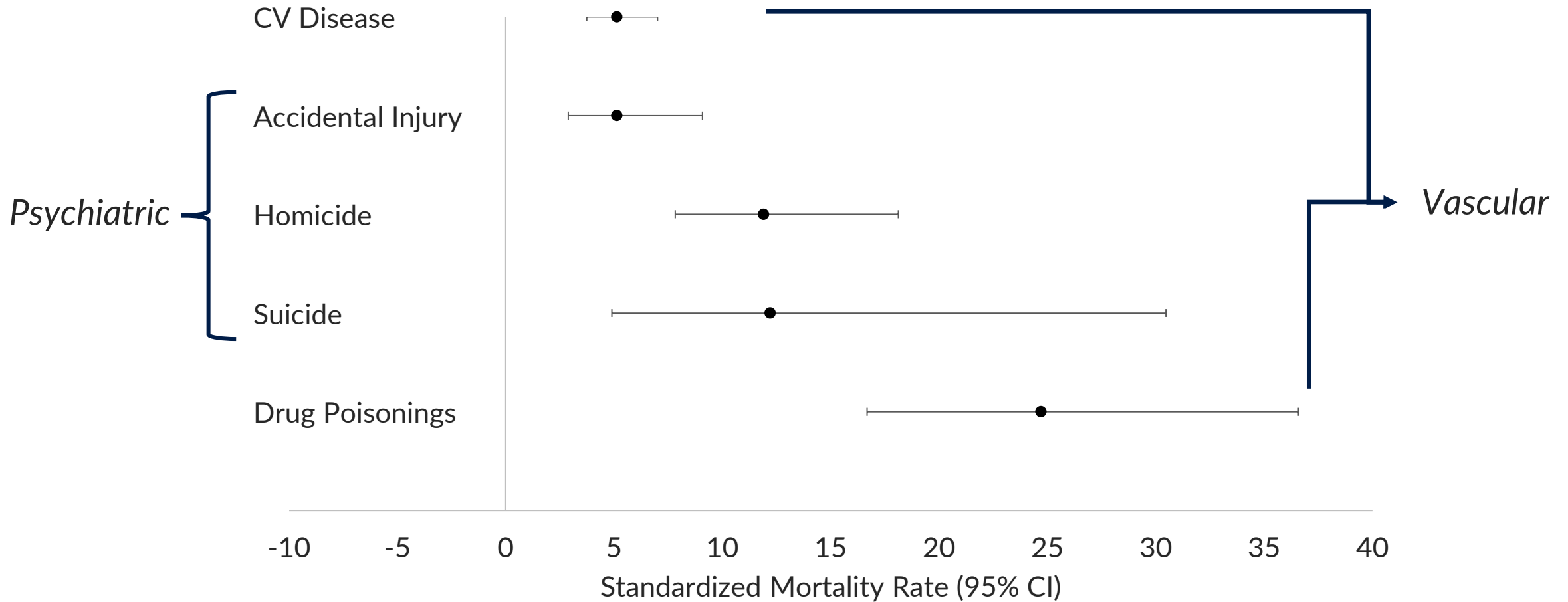
Major Pathways to Stimulant Toxicity



What Leads to Stimulant ED Presentations?



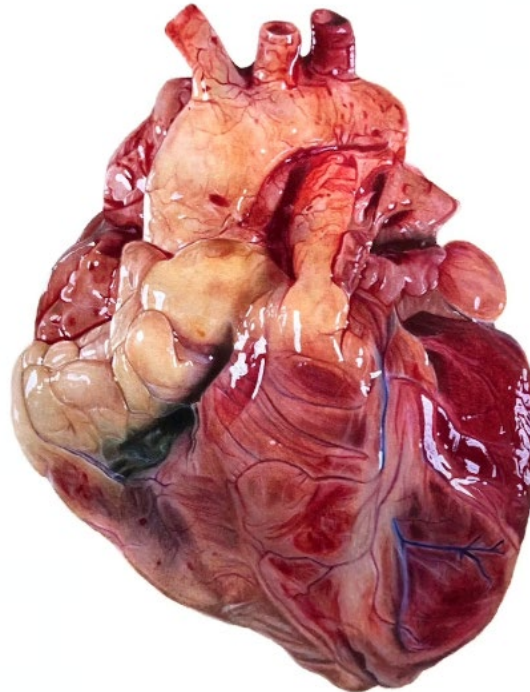
What Leads to Stimulant ED Presentations?



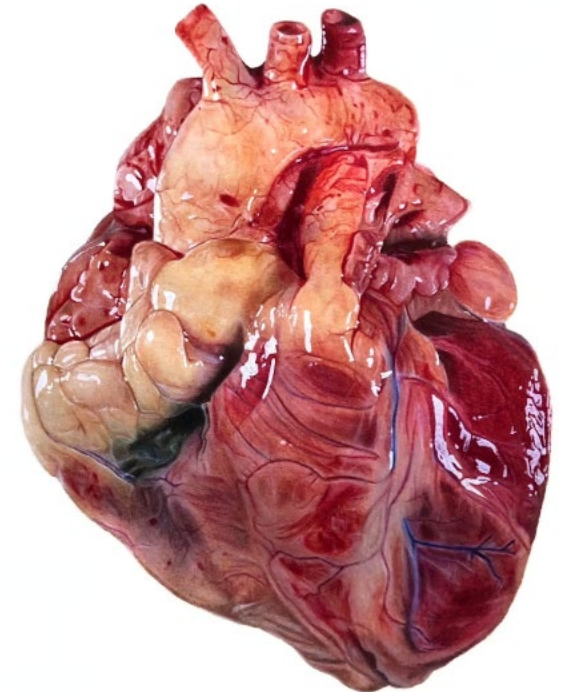
How Does a Medical Examiner Determine Cause Of Death?

- Death scene/history
- Medical record
- Toxicology
- Autopsy

Heart without fatal
ventricular arrhythmia



Heart with fatal
ventricular arrhythmia



Cause of Death Among Stimulant and Opioid Overdose Deaths

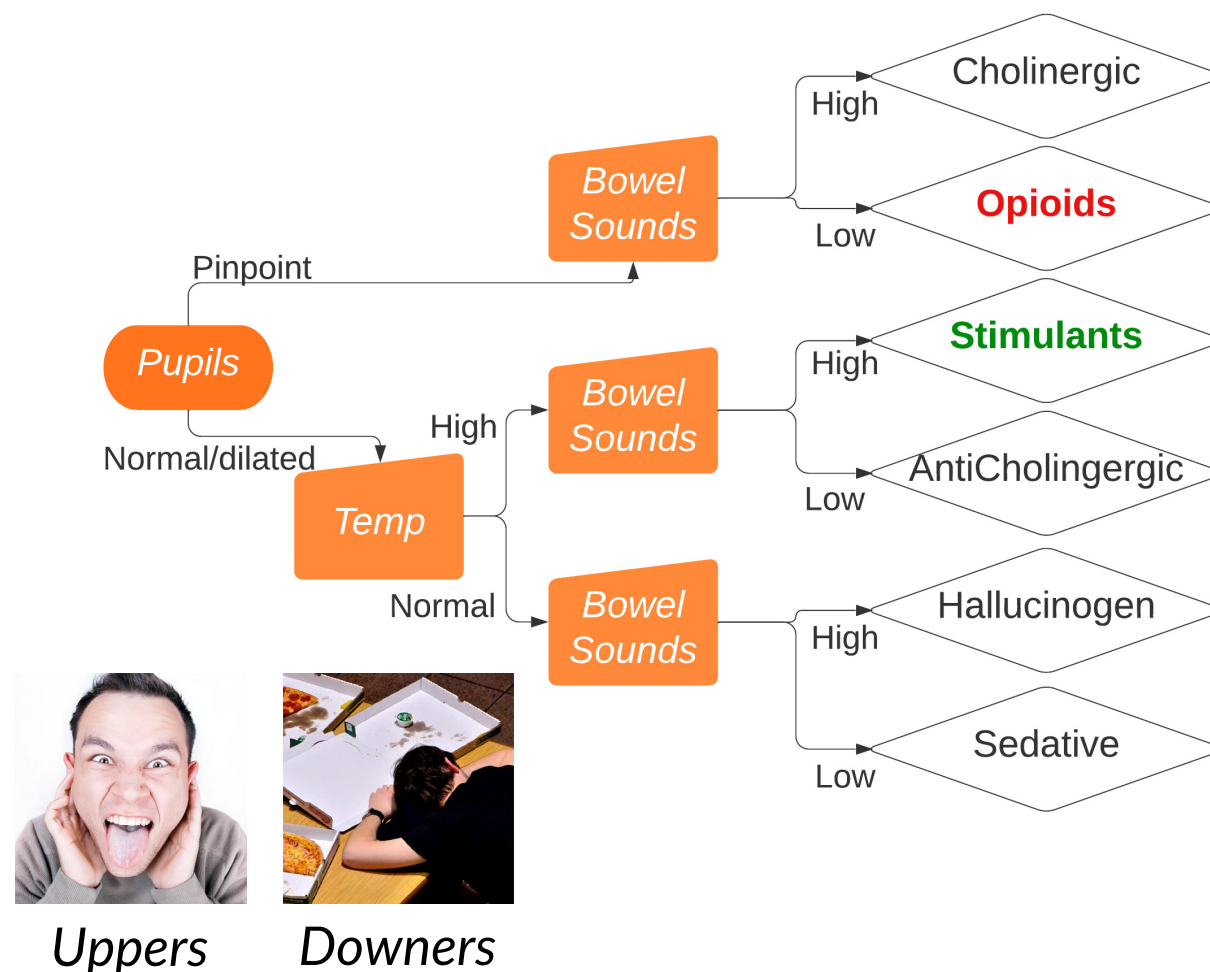
Among 2001 opioid and stimulant deaths in San Francisco from 2005-2015 (pre-fentanyl)

	<i>Cardiac COD</i>	<i>Cerebrovascular COD</i>
Stimulant versus opioid	8% stimulant; 2% opioid	13% stimulant; 0.3% opioid
MA versus cocaine	6% MA; 10% cocaine	15% MA; 12% cocaine

Opioid deaths included opioid/stimulant deaths; results were unchanged when excluding opioid/stimulant deaths.

Stimulants + Fentanyl Deaths: Are these really just fentanyl deaths?

<i>These are fentanyl deaths</i>	<i>Maybe the stimulants play a role</i>
There is no “upper-downer” toxidrome	
Stimulant-opioid decedents (prior to fentanyl) were demographically similar to opioid-only decedents	Fentanyl is a different type of opioid, so might interact differently
Stimulants do not increase the toxicity of morphine in animal models	



Are stimulant deaths really acute?

*Or chronic disease
masquerading as an
acute event?*



A
Cute
Event

Chronic
Condition

Overdose Risk Of Rx Opioids, Heroin, and Fentanyl

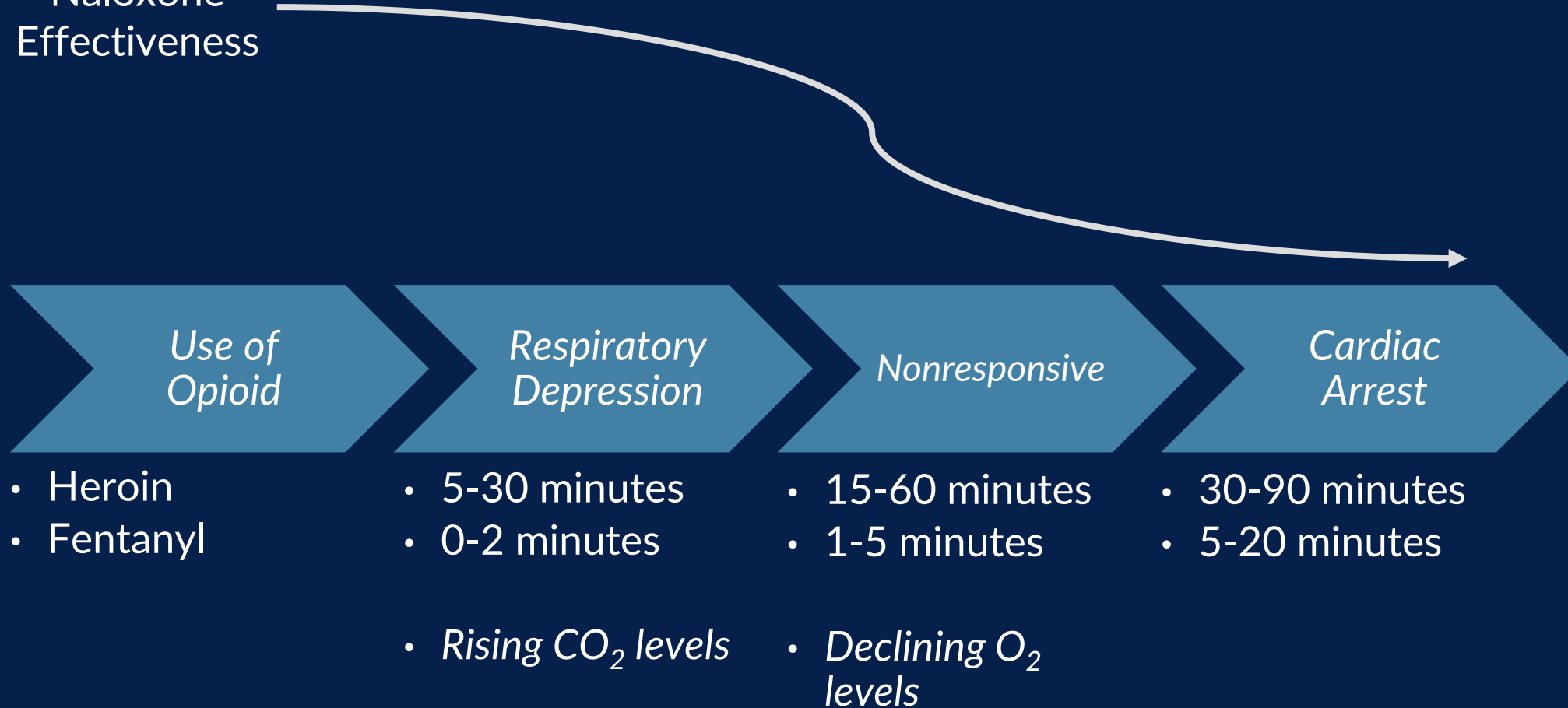
	<i>Rx Opioids</i>	<i>Heroin</i>	<i>Fentanyl</i>
Relative risk of overdose event	1	4	9.2
Relative risk of severe respiratory depression after overdose	1	1	2

High risk of overdose

High risk of death when overdose occurs

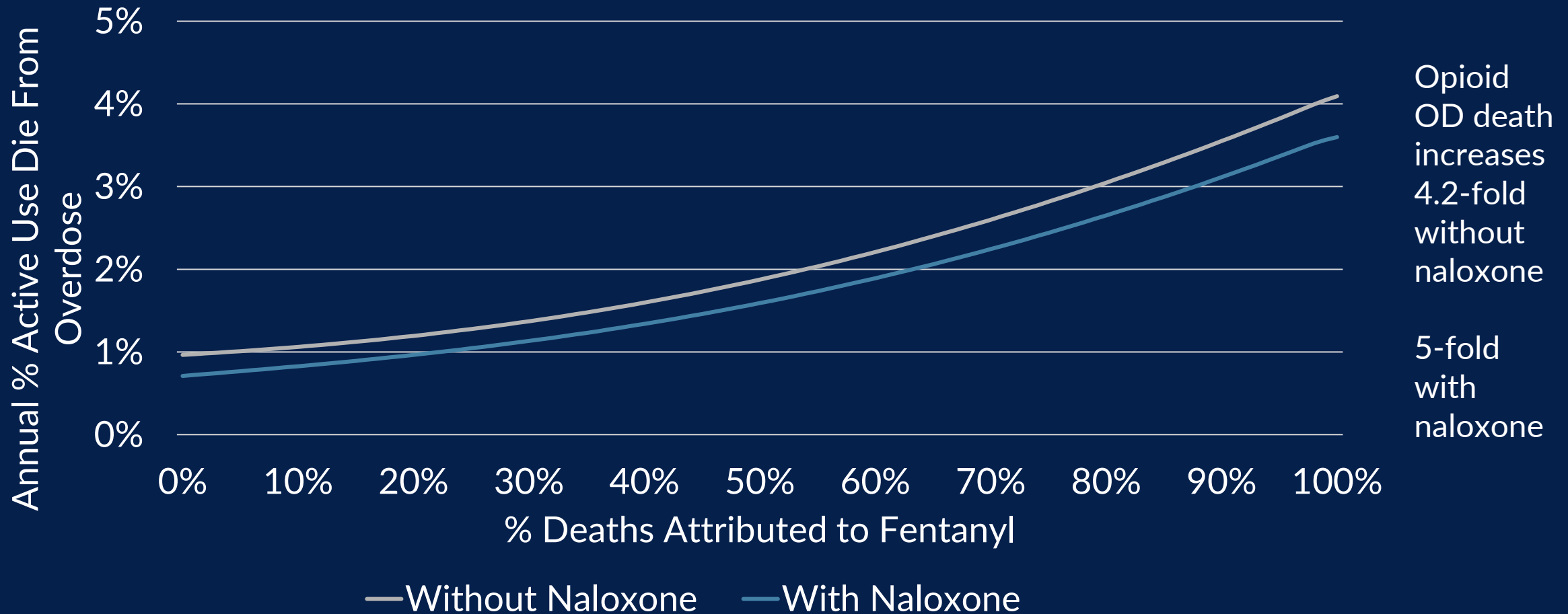
Window for Bystander Response

Naloxone
Effectiveness

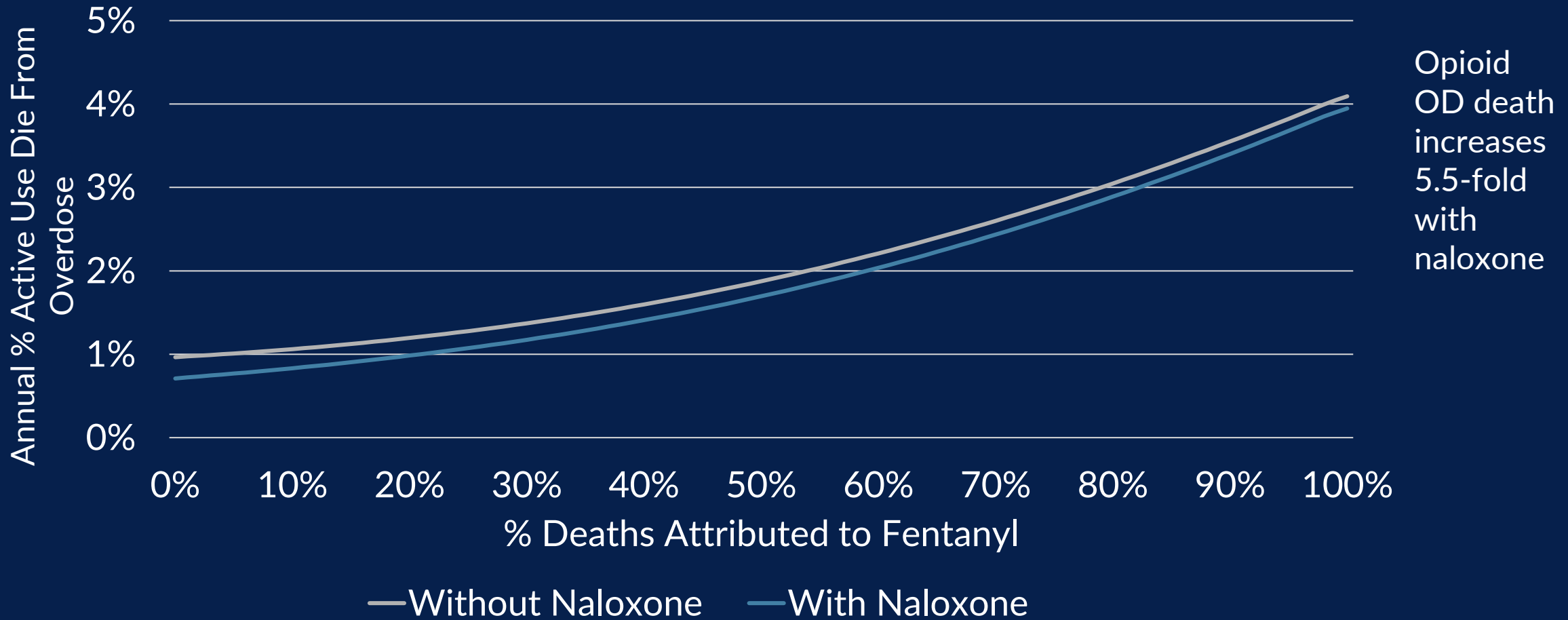


**Times are estimates intended to illustrate magnitude of difference.*

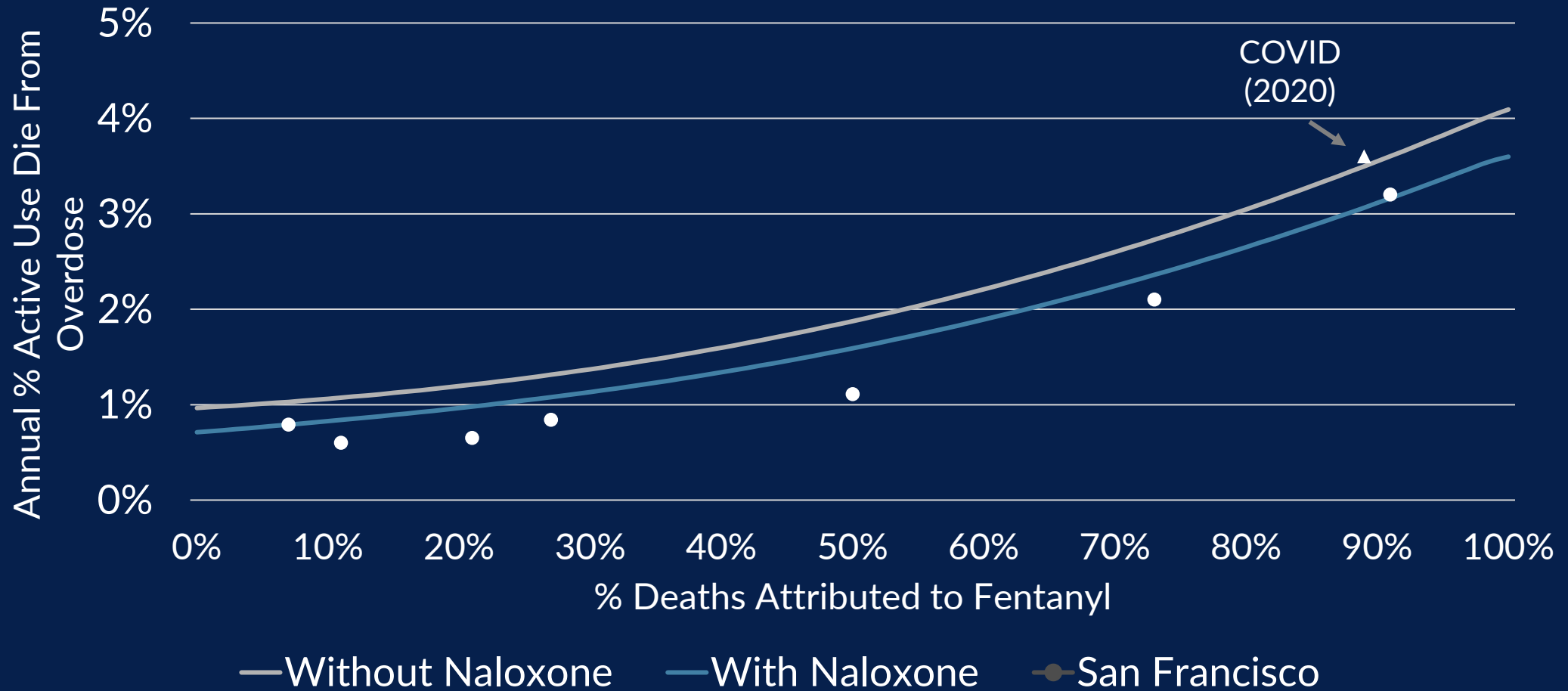
Predicted Opioid Overdose Death Rate by Presence of Fentanyl and 80% Naloxone Coverage



What If Naloxone Was Less Efficacious at Reversing Fentanyl Overdose?



Opioid Overdose Mortality, With Empiric Data From San Francisco



How Often Is Fentanyl Exposure Unintentional?

	Stimulant only (n=140)	Stimulant- fentanyl (n=220)	Fentanyl only (n=34)	Non-fentanyl opioids (n=112)	p-value
	%	%	%	%	
<i>Clinical History of Opioid Use in 3 Years Preceding Death</i>	48%	56%	65%	82%	<0.001

Much lower
than expected

Interventions To Address Opioid And Stimulant Toxicity

<i>Intervention Class</i>	<i>Intervention Sub-Class</i>	<i>Opioid Overdose</i>	<i>Stimulant Toxicity</i>
Pharmacologic	Reversal agent	Naloxone	Benzodiazepines, Chill packs?
	Disorder treatment	Buprenorphine, methadone, XR-NTX	Cumulative use reduction
Behavioral	Behavioral intervention	OD prevention plan	Contingency management
Healthcare	Emergency response	Multiple interventions	
	Medical		Cardiac dz prevention
	Psychiatric		Mental health care
Community	Safe spaces	Drop-in, safe consumption, sobering	
	Safe supply	Multiple opioids	Dextroamphetamine, methylphenidate?
	Drug checking	FTS, FTIR, MS	
	Structural	Social determinants	

Methamphetamine First Assist Pack



CHILL PACK



PURPOSE

Meth Intoxication can cause you to feel **anxious, agitated, fearful** and sometimes, to **hear voices**.

These symptoms can be safely managed outside of a clinic or hospital when you take medication to “chill-out.”

Olanzapine can reduce common symptoms of methamphetamine when used **off-label*** as directed.

*You and your provider can discuss the risks and benefits of continuing these medications.

HOW TO TAKE OLANZAPINE

Olanzapine can help if you

- Feel **anxious** or **agitated**
- Feel **fearful** or **paranoid**
- Hear **voices**
- Cannot **fall sleep**

Place **Olanzapine ODT 5mg** (1 tablet) under your tongue until it fully dissolves. You may take olanzapine **twice a day** until your symptoms improve or you “chill-out” (feel relaxed.)

Side effects with the first dose may include sleepiness or dry mouth**

**For a full list of side effects see NAMI Mental Health Medication Information



Final Takeaways

- Death from stimulant toxicity increased, mostly in combination with fentanyl.
- Stimulants deaths are mostly due to cardiac events and strokes (and maybe psychiatric problems [e.g., suicides, homicides, violent trauma]) – and likely result from chronic, cumulative exposure.
- Stimulants may be merely a marker of risky behavior in opioid-stimulant deaths. However, it remains possible that fentanyl interacts differently than other opioids with stimulants.
- Increased mortality due to fentanyl is explained by heightened overdose risk, and the limited window for response limits the role of any bystander interventions.
- A meaningful proportion of stimulant-fentanyl deaths may be due to unintentional fentanyl exposure.
- Interventions are slowly emerging.
 - Contingency management has proven benefit and is gaining CMS-support!
 - Several medications show promise.
 - Innovative strategies to reduce morbidity include cardiac preventive care, first-assist packs, reduced use as a valid treatment goal, sobering centers and other safe spaces, drug checking.

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