

Benzo-Dope: An Increasingly Prevalent Drug Combination of Significant Toxicological Relevance

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DISCLOSURES

- I have no conflicts of interest to disclose.
- I am a scientist and employee of FRFF / CFSRE, a 501(c)(3) non-profit research and educational facility.
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 - The opinions, findings, conclusions and/or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect those of the Department of Justice.



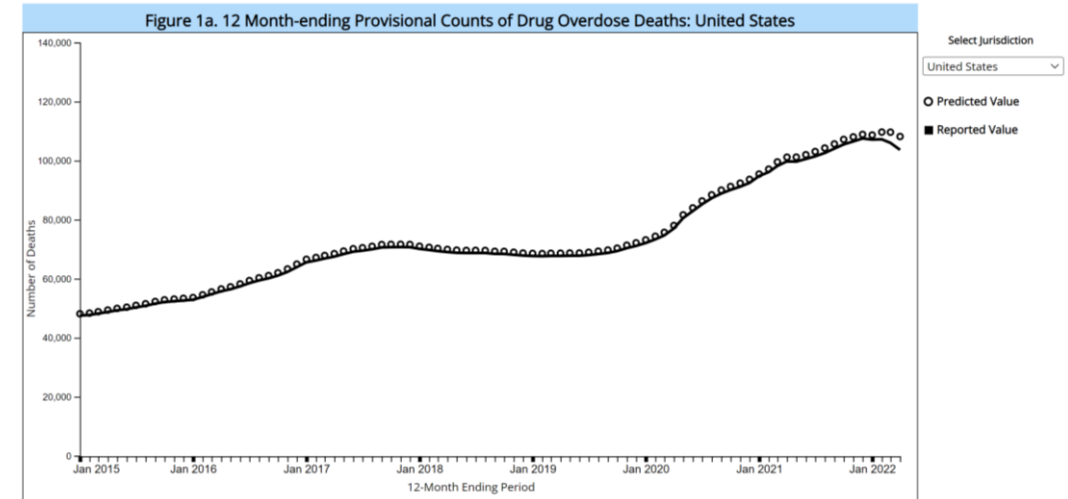
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BACKGROUND & INTRODUCTION

OPIOID CRISIS MEETS POLYDRUG EPIDEMIC

- More than 100,000 people dying per year in the U.S. from drug overdoses (CDC)
- In 2019, nearly half of drug overdose deaths involved multiple drugs (CDC)
- **Poly-drug scenarios:**
 - Opioids and stimulants
 - Stimulants and stimulants
 - **Opioids and benzodiazepines**
 - Opioids and xylazine



Source: CDC, NVSS, Provisional Drug Overdose Death Counts



Source: CDC, Polysubstance Use Facts

CNS DEPRESSANTS

A short, quick discussion about pharmacology

▪ Benzodiazepines

- GABA_A Receptor
- Anxiety relief, euphoria, drowsiness, confusion, etc.

▪ Opioids

- Mu Opioid Receptors (KOR and DOR)
- Analgesia, respiratory depression, euphoria, etc.

▪ Alcohol

- Euphoria, motor incoordination, possible coma and death

▪ Additive in nature when used in combination



Mixing depressants

Examples of depressants: opioids (heroin, morphine, oxycodone, hydrocodone, fentanyl), benzodiazepines

Depressants (also known as downers) can slow down your breathing and increase your risk of several adverse health outcomes. Combining depressants can also directly or indirectly increase your risk of:

- Damage to the brain and other organs
- Overdose
- Death

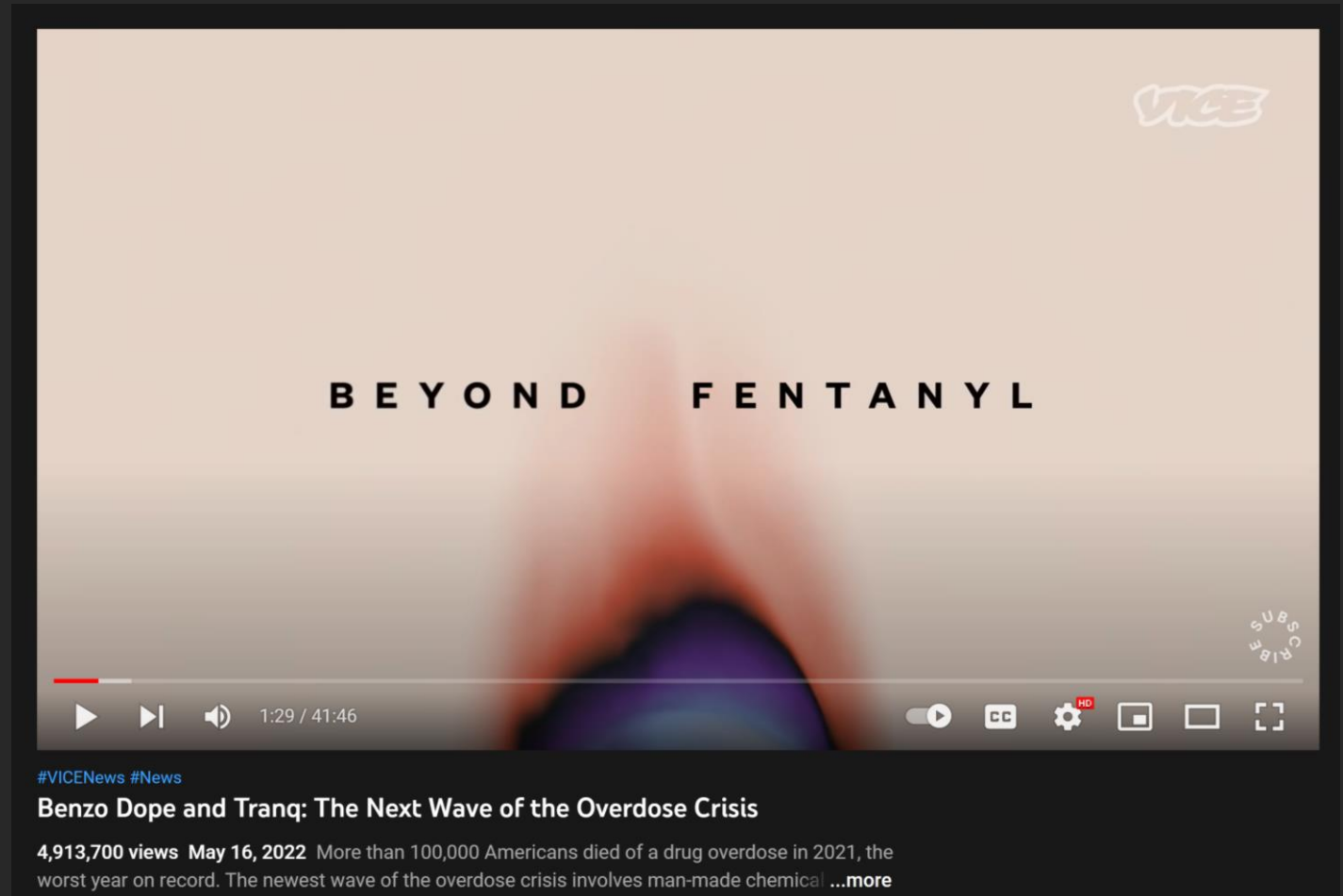
Signs of use/overdose^{5,6} when mixing depressants:

- Slow breathing
- Weak pulse
- Altered mental status or confusion
- Passing out

Source: CDC, Polysubstance Use Facts

BEYOND FENTANYL - VICE NEWS TONIGHT

- Benzo Dope and Tranq: The Next Wave of the Overdose Crisis
 - <https://youtu.be/82QhIOgJy1c>
- Single episode documentary
- Investigations the landscape and outcomes of benzo-dope drug combinations in Canada
 - *“Everything is cut with it [benzos]” in Vancouver*



BENZO-DOPE LANDSCAPE

■ Canada

– Drug Checking Data:

- NPS benzos found in **57%** of expected opioid drug samples (Vancouver Island Drug Checking Project, 2021 Report)
- NPS benzos found in **28%** of expected fentanyl samples (Toronto's Drug Checking Service, September 2022)

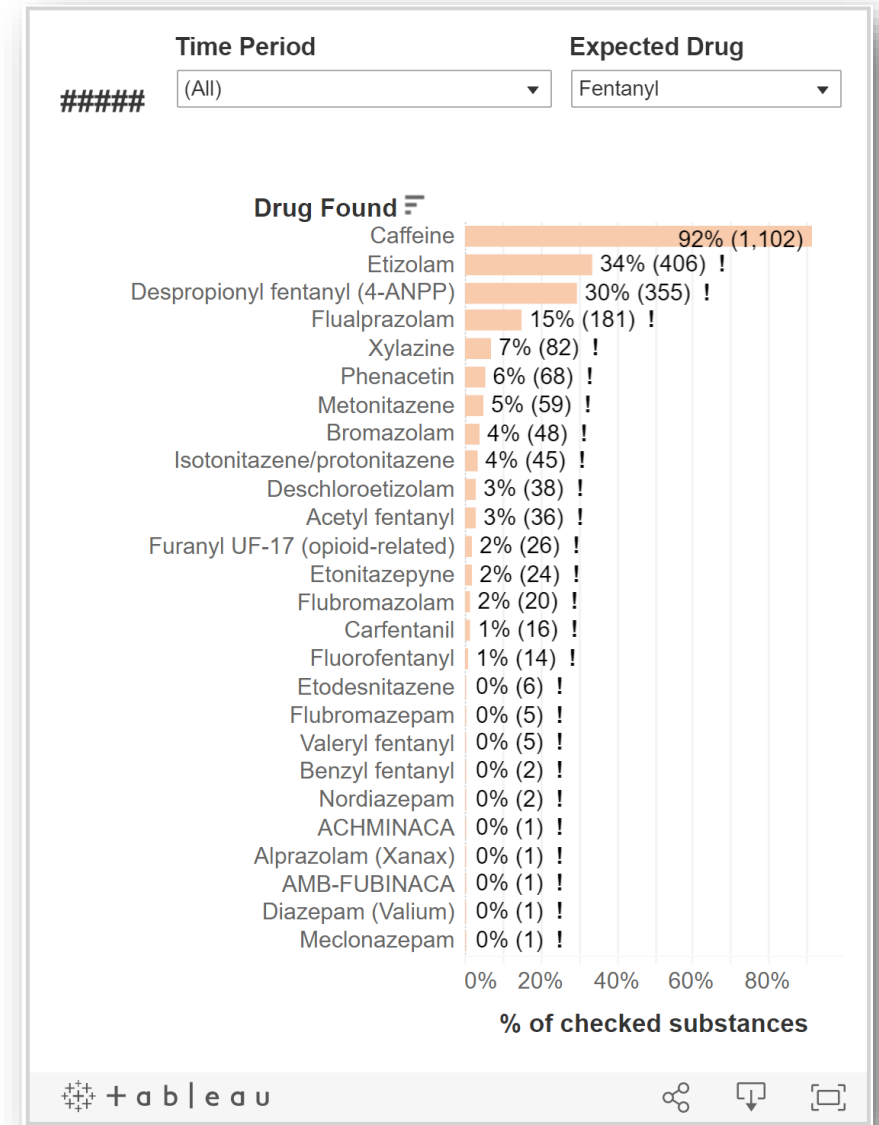
– Medical Examiner Data:

- Benzos positive in **52%** of fatal overdoses in British Columbia (British Columbia Coroner Services, January 2022)

– Toxicology Data:

- Fentanyl co-positive in **84%** of NPS benzo positive cases (submitted to NMS Labs from Canadian agencies)


■ What's happening in the United States ???





Source: Toronto's Drug Checking Service


WHY BENZO-DOPE?

- Anecdotal reports:
 - Benzo-dope gives a better higher
 - Benzo-dope is needed to achieve “nod”
 - Benzo-dope hits quicker
 - Benzo-dope is more addicting
 - Benzos give fentanyl “legs”

 OpiNod · 11 days ago


If your shooting it then it's either tranq dope or just fent not benzo dope.. the benzos aren't water soluble so you wouldn't be getting the benzo effect from shooting it. **Benzo dope is for smoking**

 1  Reply Share Report Save Follow

 **r/opiates** · Posted by u/XxZoe97xX 11 days ago

1 **Goofballs with benzo dope**



Just wondering if anyone has a similar experience to me while doing goofballs with benzo dope instead of regular fent down.

 CanadianRapGod · 1 yr. ago


The coloured down has been very popular in Canada for the past 5-6 years or so. When it first started it had heroin/morphine and fentanyl. The heroin was fazed out and the fatty remained. The other cuts in it are caffiene and sugar alcohols most of the time.

About 2 years ago RC benzos started turning up in batches. I'm not sure if it was a mislabeled batch of fatty or someone intentionally added the benzos. It quickly took off though as everyone was heavily dependent on the fentanyl **so the benzo helped attain a nod not achievable with fatty alone**. I know lots of people that hate the stuff, but plenty who prefer the benzo down. Now fast forward 2 years later about half of all down hitting the streets now has a benzo of some sort.



Xylazine, phenacetin, benzimidazole opioids, and synthetic cannabinoids have been found in batches but not nearly as common as benzodiazepines.

 2  Share Report Save

The second time I did it by accident again. I snorted maybe half a point, started driving home, and then **blacked tf out**. Didn't even realize in the slightest that I was inebriated until it was too late and I was completely blacked out and was driving. I really wish that while on benzos you knew if you were too fucked up to drive because if I had known, I would have pulled into a secluded area to sleep it off.

 Yesfx9611 · 2 mo. ago

Yea **no way they really is benzo dope** I'm a shooter how would the shooters use it Or is there a benzo that you can shoot that I don't know about

 1  Reply Share Report Save Follow



METHODS & DATA ANALYSIS

WORKFLOW & METHODS

- **Sample Source:** Forensic toxicology investigations from agencies across the United States (& Canada)
- **Analysis:** Comprehensive non-targeted acquisition on SCIEX TripleTOF® 5600+ and X500R quadrupole time-of-flight mass spectrometers (LC-QTOF-MS)
- **Data Processing:** Targeted library database containing more than 1,000 traditional drugs, NPS, metabolites, and other relevant analytes
 - 27 NPS benzodiazepines →
 - 26 traditional benzodiazepines

SCOPE OF TESTING

4'Cl-Deschloroalprazolam
Adinazolam
Bromazepam
Bromazolam
Clonazolam
Desalkylgidazepam
Deschloroetizolam
Diclazepam
Etizolam
Flualprazolam
Flubromazepam
Flubromazolam
Flubrotizolam
Fluclozepam
Fluetizolam
Meclonazepam
Metizolam
Phenazepam
Pyrazolam
Etc.

DATA ANALYSIS

- **Tabulation:** Results were consolidated in Excel
- **Data Analysis:** Generated Pivot tables to determine samples with combined fentanyl + NPS benzo results
 - Fentanyl and/or norfentanyl = fentanyl
 - 8-Aminoclonazepam and/or clonazepam = clonazepam
- **Graphics:** Plotted positivity over time as % of total samples analyzed per time period (e.g., quarter)

#	A	B	D	F	G	H	I	J
53280	EX_9605	DE001_36	03/2022AR_038	3/24/2022	62	3/28/2022	2046	Etizolam
53281	EX_9605	DE001_36	03/2022AR_038	3/24/2022	62	3/28/2022	2046	Benzonitrile
53282	EX_9605	DE001_36	03/2022AR_038	3/24/2022	62	3/28/2022	2046	para-Fluorofentanyl
53283	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Amphetamine
53284	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Methamphetamine
53285	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Phenacetin
53286	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Lorazepam
53287	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Xylazine
53288	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Fentanyl
53289	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	4-ANP
53290	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Morphine
53291	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Benzylhexagone
53292	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Norcocaine
53293	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Cocaine
53294	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Cocacethylene
53295	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Flualprazolam
53296	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Naloxone
53297	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Flumazenepam
53298	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Etizolam
53299	EX_9606	DE001_37	03/2022AR_039	3/24/2022	62	3/28/2022	2046	Beta-Hydroxy Fentanyl
53300	EX_9607	DE001_38	03/2022AR_040	3/24/2022	62	3/28/2022	2046	Amphetamine
53301	EX_9607	DE001_38	03/2022AR_040	3/24/2022	62	3/28/2022	2046	Methamphetamine
53302	EX_9607	DE001_38	03/2022AR_040	3/24/2022	62	3/28/2022	2046	Alpha-Hydroxy Fentanyl
53303	EX_9607	DE001_38	03/2022AR_040	3/24/2022	62	3/28/2022	2046	4-ANP
53304	EX_9607	DE001_38	03/2022AR_040	3/24/2022	62	3/28/2022	2046	Flualprazolam
53305	EX_9607	DE001_38	03/2022AR_040	3/24/2022	62	3/28/2022	2046	Naloxone
53306	EX_9607	DE001_38	03/2022AR_040	3/24/2022	62	3/28/2022	2046	Fentanyl
53307	EX_9608	DE001_39	03/2022AR_041	3/24/2022	62	3/28/2022	2046	Methamphetamine
53308	EX_9608	DE001_39	03/2022AR_041	3/24/2022	62	3/28/2022	2046	Flualprazolam
53309	EX_9608	DE001_39	03/2022AR_041	3/24/2022	62	3/28/2022	2046	Naloxone
53310	EX_9608	DE001_39	03/2022AR_041	3/24/2022	62	3/28/2022	2046	Fentanyl
53311	EX_9608	DE001_39	03/2022AR_041	3/24/2022	62	3/28/2022	2046	para-Fluorofentanyl
53312	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	Amphetamine
53313	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	Methamphetamine
53314	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	Chlorpheniramine
53315	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	Norflurazepam
53316	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	Etizolam
53317	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	Benzonitrile
53318	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	8-Aminoclonazepam
53319	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	N-Desethyl Indinavir
53320	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	4-ANP
53321	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	Flumazenepam
53322	EX_9609	DE001_40	03/2022AR_042	3/24/2022	62	3/28/2022	2046	Etizolam

#	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	
1	Years	Quarters	Date	Acquired	Unique ID	Fentanyl	Alprazolam	Diazepam	Trad Benz	Trad Benz	TB+Fent	TB+Fent	Etizolam	Flualprazolam	Clonazepam	Flumazenepam	Flumazenepam	Bromazepam	Adinazolam	Bromazepam
53020	2022	Qtr1	Mar	EX_9552	1				0	0	0	1	0							
53021	2022	Qtr1	Mar	EX_9553	1				0	0	0	1	0	1	1			1	1	
53022	2022	Qtr1	Mar	EX_9554	1				0	0	0	1	0	1	1			1	1	
53023	2022	Qtr1	Mar	EX_9557	1				0	0	0	1	0	1	1			1	1	
53024	2022	Qtr1	Mar	EX_9558	1				0	0	0	1	0	1	1	1				
53025	2022	Qtr1	Mar	EX_9559	1		1	1	2	1	2	1	1	1	1					
53026	2022	Qtr1	Mar	EX_9560	1				0	0	0	1	0	1	1					
53027	2022	Qtr1	Mar	EX_9561	1				0	0	0	1	0	1	1					
53028	2022	Qtr1	Mar	EX_9562	1				0	0	0	1	0	1	1	1				
53029	2022	Qtr1	Mar	EX_9563	1				0	0	0	1	0	1	1					
53030	2022	Qtr1	Mar	EX_9564	1				0	0	0	1	0	1	0					
53031	2022	Qtr1	Mar	EX_9565	1				0	0	0	1	0	1	1	1				
53032	2022	Qtr1	Mar	EX_9566	1				0	0	0	1	0	1	1					
53033	2022	Qtr1	Mar	EX_9567	1				0	0	0	1	0	1	1					
53034	2022	Qtr1	Mar	EX_9568	1				0	0	0	1	0	1	0					
53035	2022	Qtr1	Mar	EX_9569	1			1	1	1	2	1	1	1						
53036	2022	Qtr1	Mar	EX_9570	1				0	0	0	1	1	1	1	1	0	1		
53037	2022	Qtr1	Mar	EX_9573					0	0	0	0	0	0	1					1
53038	2022	Qtr1	Mar	EX_9574					0	0	0	0	0	0	1					1
53039	2022	Qtr1	Mar	EX_9585	1				0	0	0	1	0	1	1	1				
53040	2022	Qtr1	Mar	EX_9586	1				0	0	0	1	0	1	1					
53041	2022	Qtr1	Mar	EX_9587					0	0	0	0	0	1				1		
53042	2022	Qtr1	Mar	EX_9588					0	0	0	0	0	1						1
53043	2022	Qtr1	Mar	EX_9589					0	0	0	0	0	1	1	1				
53044	2022	Qtr1	Mar	EX_9590	1				0	0	0	1	0	0						

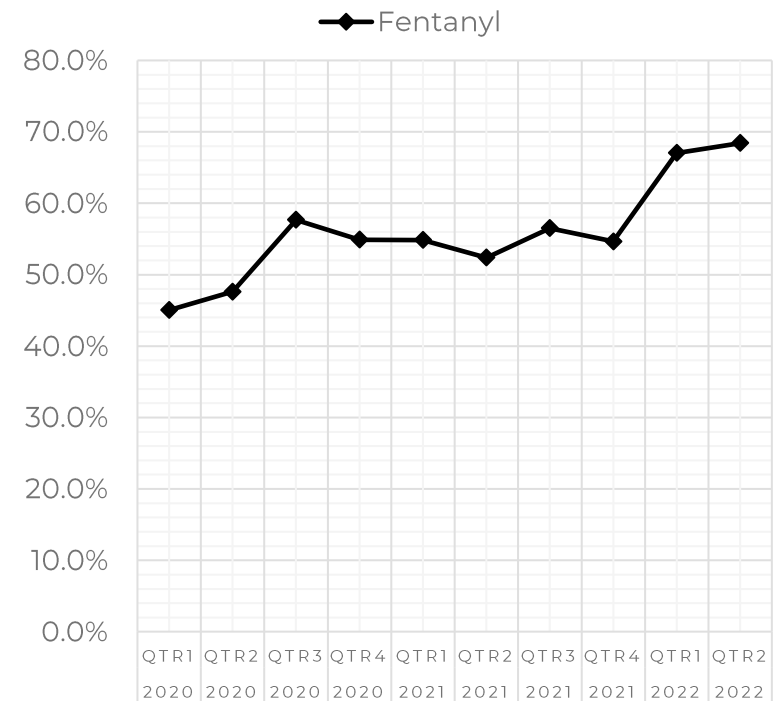
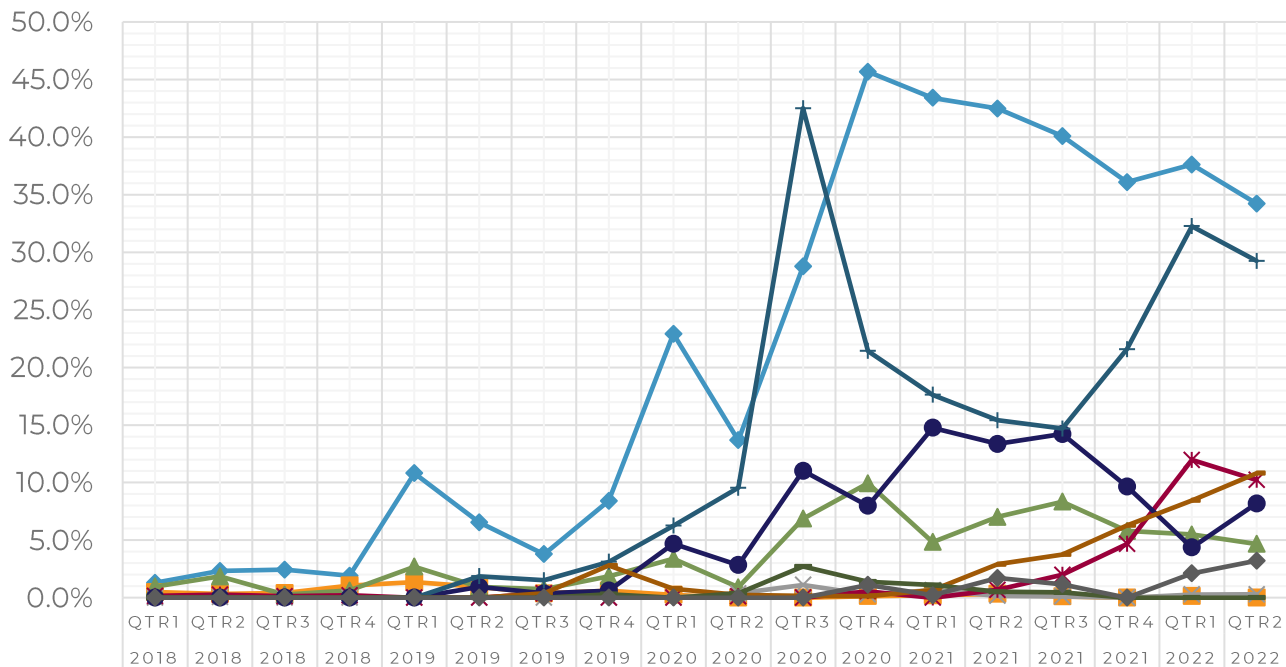
AX	AY	AZ	BA	BB	BC	BD	BE	BF	BG	BH	BI	BJ
Years	Quarters	Fent	Trad Benzos	TB+Fent	NPS Benzos	NPS+Benz	Etiz+Fent	Flualpr+Fent	Clonaz+Fent	Flumazenolam+Fent	Flumazenepam+Fent	Bromaz+Fent
2018	Qtr1	157	107	36	15	6	5	0	0	0	1	0
2018	Qtr2	584	226	113	81	35	26	0	0	4	0	0
2018	Qtr3	347	89	43	20	11	8	0	0	1	1	0
2018	Qtr4	119	46	24	31	21	17	0	0	2	0	0
2019	Qtr1	55	13	6	18	7	6	0	0	0	0	0
2019	Qtr2	39	1	0	11	8	9	1	0	0	0	0
2019	Qtr3	126	13	9	20	12	9	2	0	0	0	1
2019	Qtr4	155	41	24	58	33	27	2	2	3	0	3
2020	Qtr1	175	67	41	123	80	71	13	11	4	0	1
2020	Qtr2	372	96	55	178	102	68	31	13	4	0	0
2020	Qtr3	361	96	77	392	245	107	169	37	17	0	0
2020	Qtr4	393	104	68	396	264	181	67	31	39	0	0
2021	Qtr1	251	63	39	283	195	158	51	31	8	0	1
2021	Qtr2	308	83	51	331	219	165	60	39	20	0	4
2021	Qtr3	484	95	66	476	342	251	85	58	36	15	20
2021	Qtr4	392	78	50	369	281	188	106	35	14	25	23
2022	Qtr1	480	73	56	462	375	226	201	12	18	74	45
2022	Qtr2	236	36	25	234	188	107	85	17	7	24	30



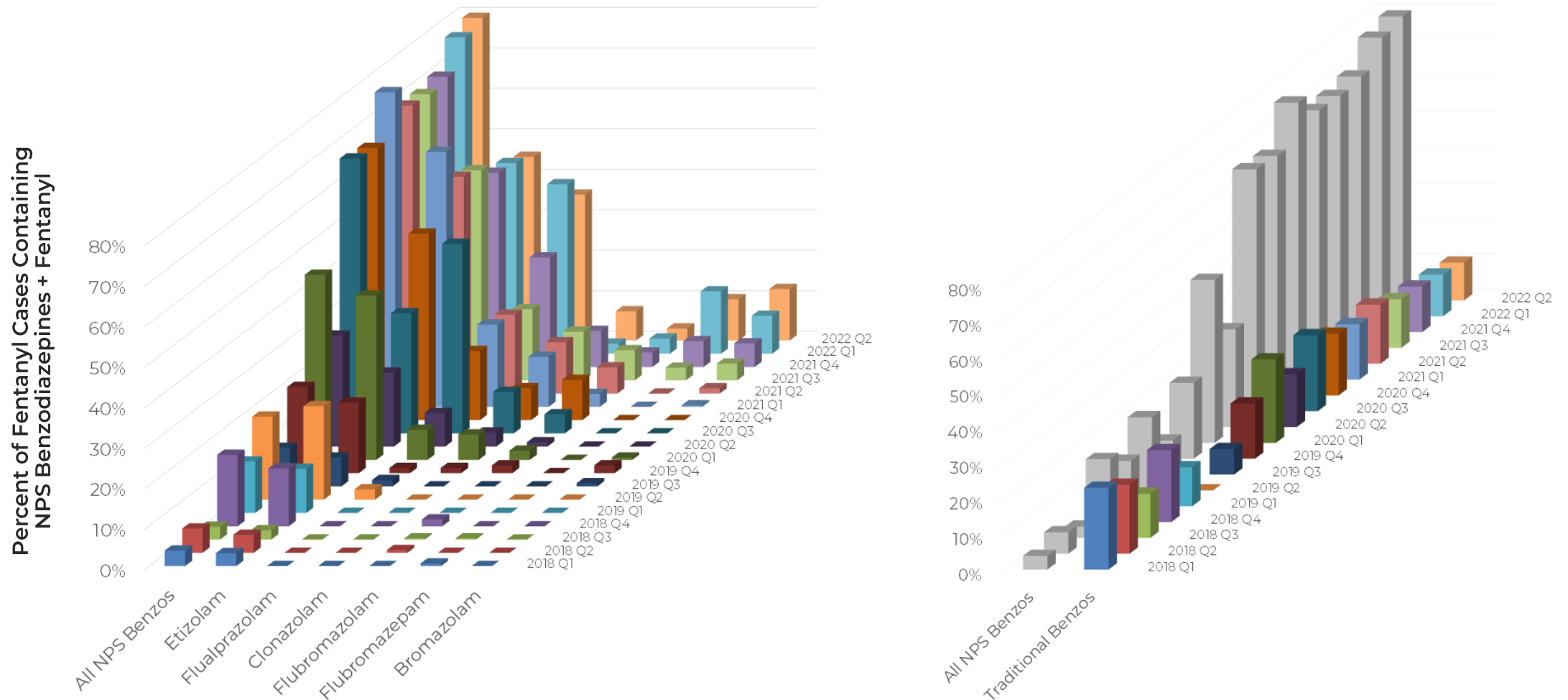
RESULTS & OUTCOMES

SAMPLE SIZE & RESULTS

- The CFSRE analyzed 10,189 samples between Q1 2018 and Q2 2022
 - 4,963 samples positive for fentanyl (2022: n = 710)
 - 5,016+ identifications of NPS benzodiazepines (2022: n = 1,074)
 - *Some samples contain more than one benzodiazepine*



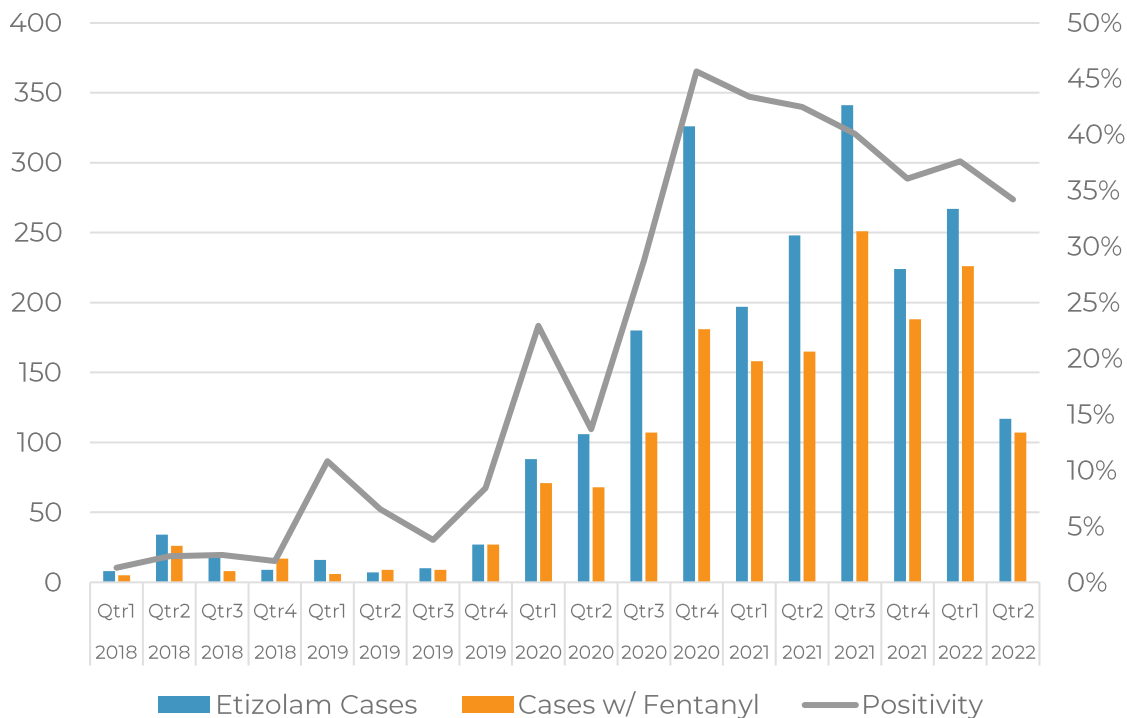
NPS BENZO & FENTANYL CO-POSITIVITY



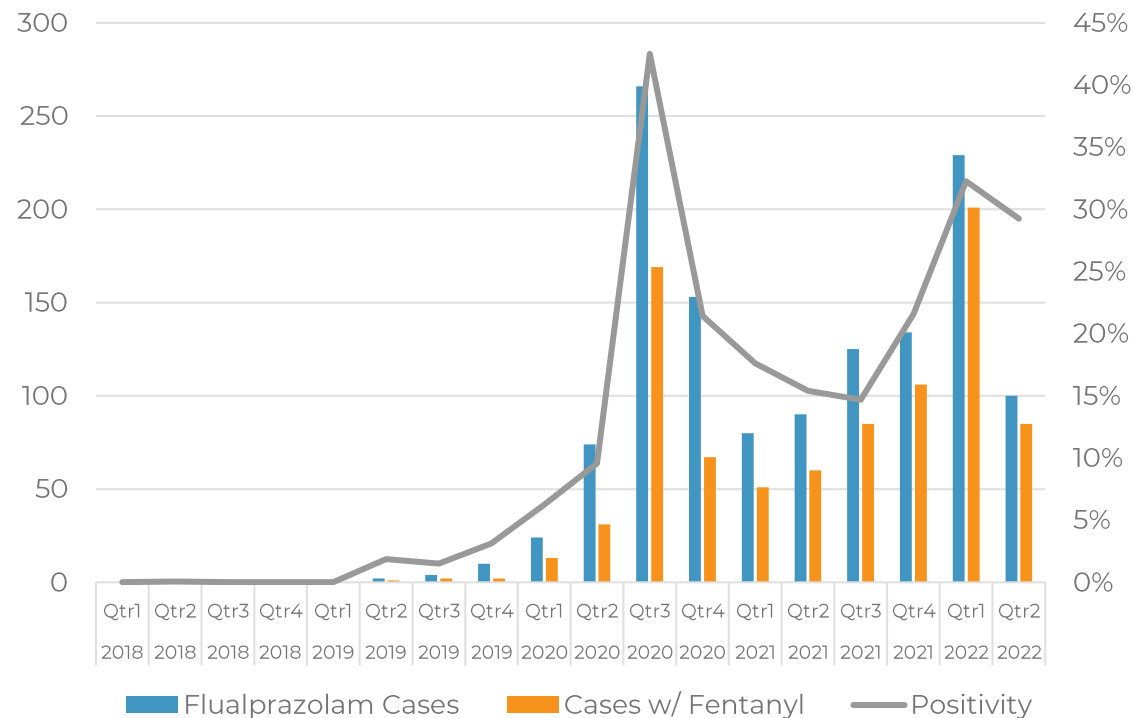
NPS BENZO & FENTANYL CO-POSITIVITY

A deeper look at individual NPS benzodiazepines and their trends

ETIZOLAM



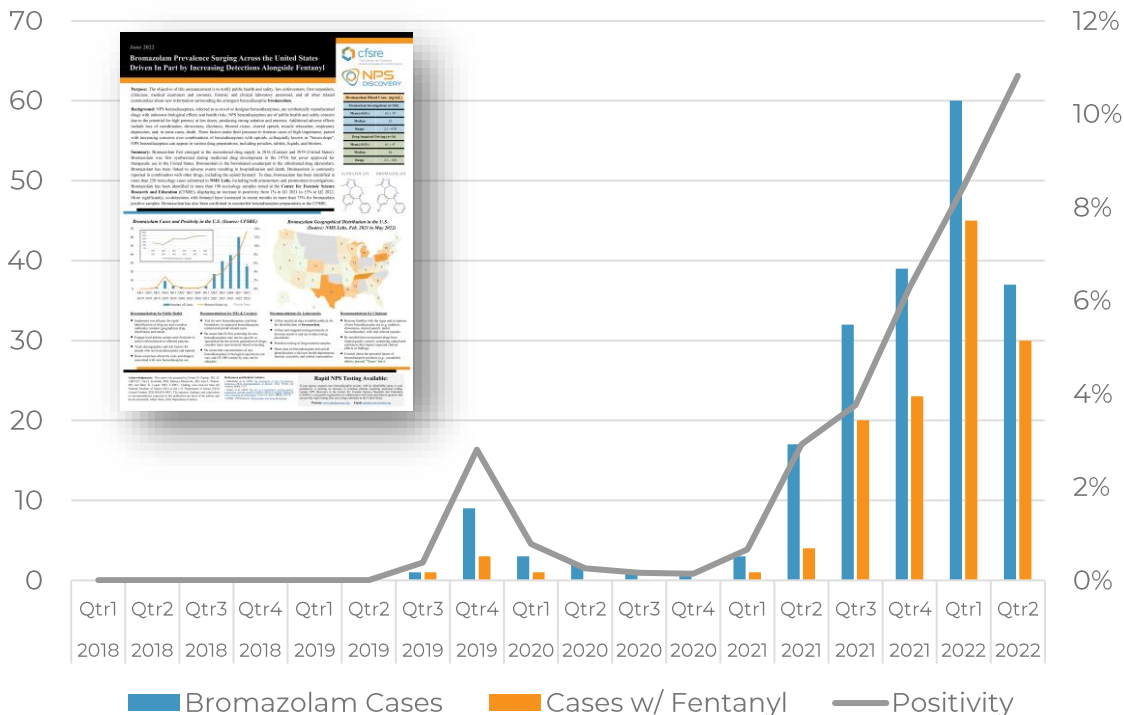
FLUALPRAZOLAM



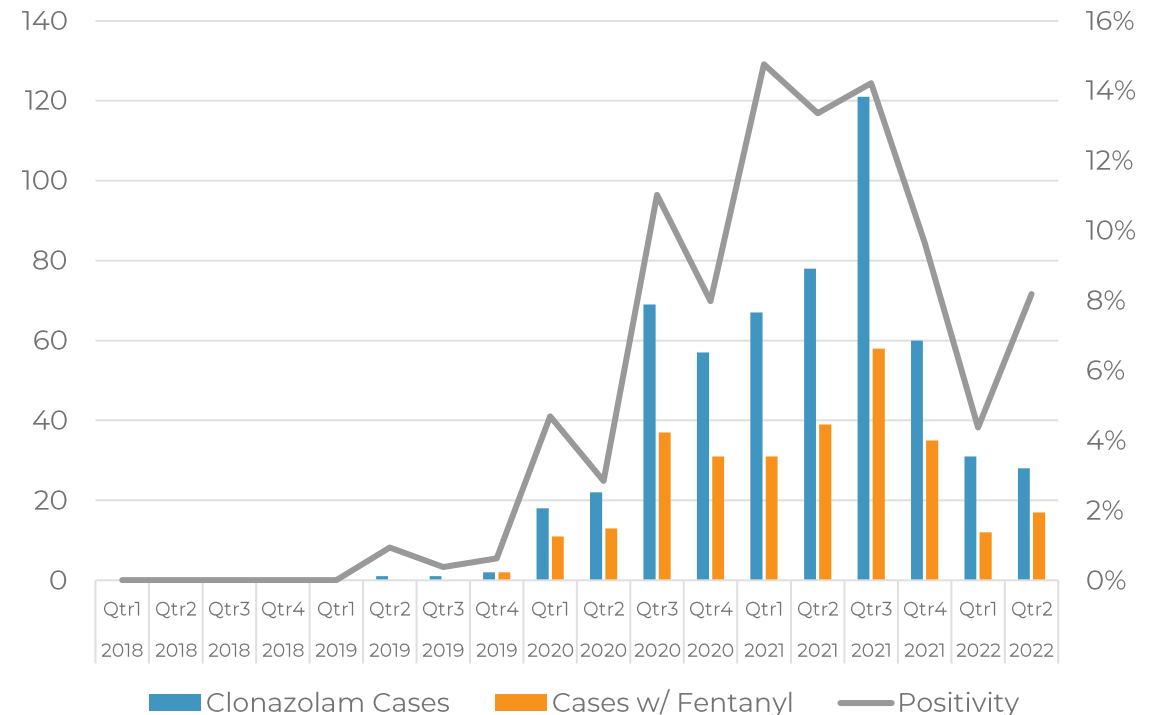
NPS BENZO & FENTANYL CO-POSITIVITY

A deeper look at individual NPS benzodiazepines and their trends

BROMAZOLAM



CLONAZOLAM



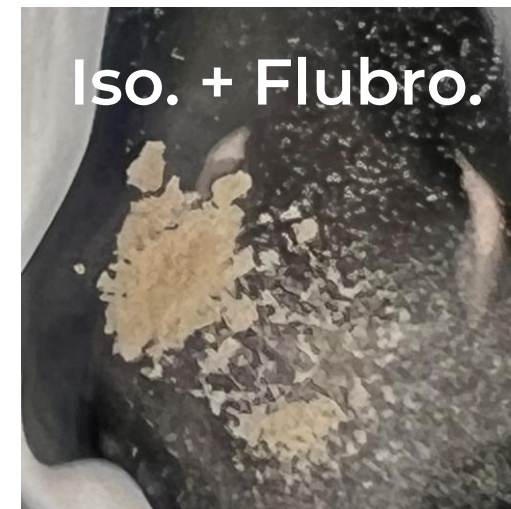
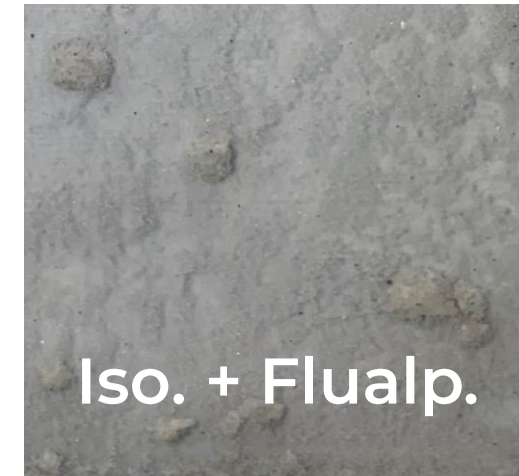
NPS BENZO & NPS OPIOID CO-POSITIVITY

▪ Drug Material Testing (CFSRE):

- Isotonitazene + Flualprazolam (MN)
- Isotonitazene + Flubromazepam (+ Fentanyl) (ME)

▪ Toxicology Testing (CFSRE):

- Isotonitazene + Flualprazolam (WI)
- Metonitazene + Clonazolam + Flualprazolam (IA)
- N-Pyrrolidino Etonitazene + Clonazolam (FL)
- Etodesnitazene + Flubromazepam (Canada)
- 2-Methyl AP-237 + Flubromazolam (OH)
- AP-238 + Clonazolam (CA)
- 2-Methyl AP-237 + Bromazolam (CA)



QUANTITATIVE DATA (NG/ML)

Partnerships between the CFSRE, NMS Labs, toxicology laboratories, and medical examiner and coroner offices

NPS Opioid	NPS Benzo	Other Notable Findings	Case Information
Isotonitazene (1.9)	Etizolam (15)	N/A	Bought “heroin” from Chicago
Isotonitazene (1.8)	Etizolam (30)	THC	Accident / Etizolam toxicity***
Isotonitazene (0.4)	Flualprazolam (4)	N/A	Found slumped over a toilet
Isotonitazene (2.2)	Flualprazolam (10)	N/A	Unknown
Metonitazene (8.7)	Etizolam (6.3)	Tramadol (1,100), THC	Accident / Combined effects of meto., tramadol, and etizolam
Metonitazene (1.4)	Etizolam (54)	pFF (28), Methadone (130), Morphine (36)	Unknown
Metonitazene (3.5)	Pyrazolam (14), 8-Aminoclonazolam	Ethanol (13 mg/dL)	Unknown
N-Pyrrolidino Etonitazene (2.4)	Flualprazolam (6.7 ng/mL)	Fentanyl (14), Morphine (7.5), THC	Homicide / GSWs
N-Pyrrolidino Etonitazene (2.5)	Flualprazolam (9.5)	N/A	Unknown



DISCUSSION & CONCLUSIONS

WE DON'T KNOW WHAT WE DON'T KNOW

How do we know we don't know what we don't know?

WHAT WE KNOW

- Public health risks associated with benzo-dope
- Fentanyl and NPS benzos is most common
 - Likely to continue popularity
- NPS opioids less common but high significance
- Methods to detect benzos and opioids
- Revolving door of NPS benzo
- Turnover in new NPS opioids and NPS benzos
- Naloxone effectiveness on opioids

WHAT WE DON'T KNOW

- **The extent of the problem**
- Prevalence and popularity
- Quantitative significance
 - When is the NPS benzo contributing vs. significant?
- How to interpretation more complex cases
 - Pathologists and toxicologists
- Concurrent vs. sequential use
 - Drug material testing



CONCLUSIONS

- **Benzo-dope** toxicology and drug material cases are increasing in positivity and prevalence
 - NPS benzodiazepines and traditional opioids
 - NPS benzodiazepines and NPS opioids
- Significant risk to **public health**
 - True understanding of human impact is unknown
 - Downstream effects on toxicology labs
- **Recommendation:**
 - Labs should test for NPS benzodiazepines routinely and quantify when possible



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■ CFSRE / NPS Discovery

- Barry Logan
- Mandi Mohr
- Melissa Fogarty
- Sara Walton
- Josh DeBord
- Judith Rodriguez-Salas
- Grace Cieri
- Lindsey Domonoski
- Alyssa Reyes
- Natasha Cunningham

■ NMS Labs

- Donna Papsun

■ National Institute of Justice

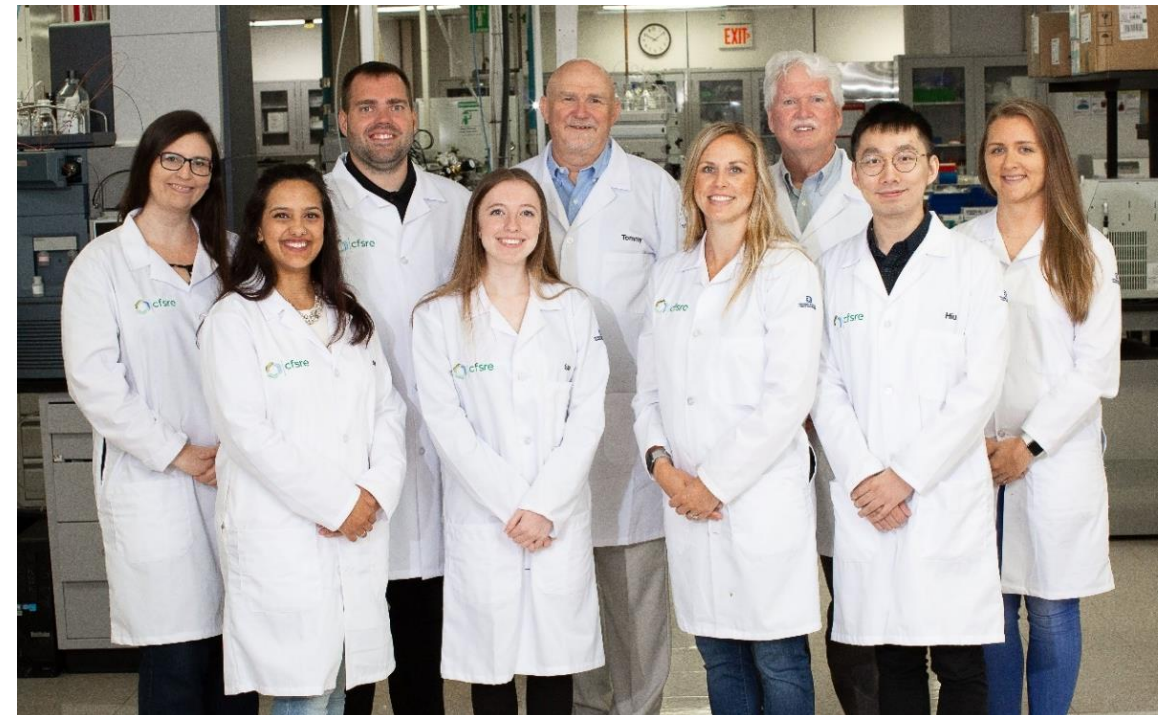
■ Various Partners

- Forensic
- Clinical
- Medical Examiner
- Coroner
- Crime Lab
- Public Health
- Public Safety
- Etc.



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Thank you!

Questions?

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