



The Trouble with Kratom: Postmortem Challenges and Interpretation

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Disclaimer

- I am a paid employee of NMS Labs, a commercial provider of toxicology and other forensic testing services.

About me (because I'll forget)

- Education
- Pharma
- Forensic toxicology

Medicolegal Death Investigations

What is it?

- Investigation to determine the cause and manner of death

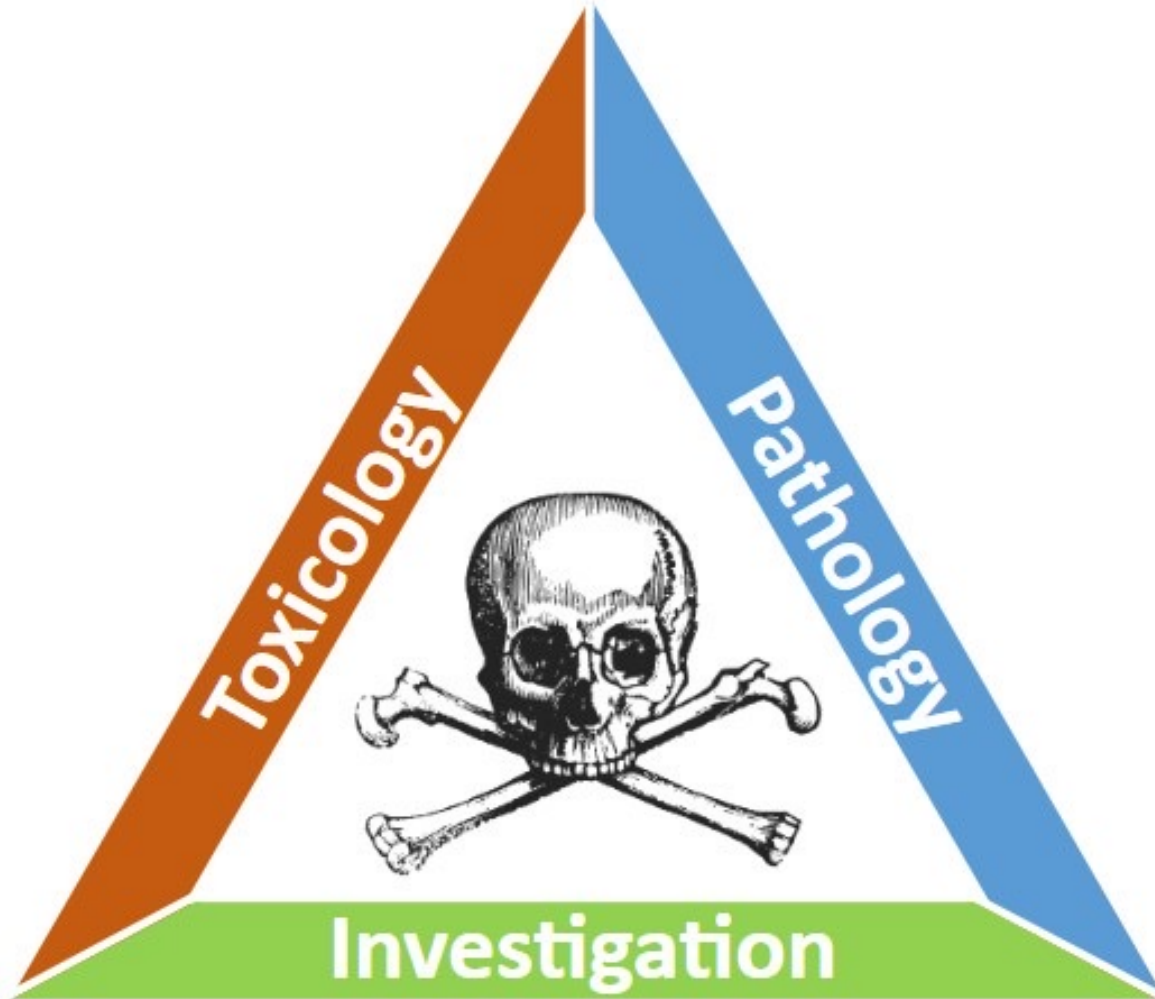
What types of deaths?

- Unnatural
- Unexpected
- Violent
- In-custody
- Children
- Threats to public health

Why is it important?

- Medical
 - The 'hows' and 'whys'
 - Answers for family, friends, community
- Legal
 - Convict the guilty
 - Protect the innocent
 - Civil litigation, malpractice, insurance
- Public Health
 - Epidemiology
 - Surveillance
 - Prevention (injury, violence, drug)

Medicolegal Death Investigations



Investigation

- Starts with a body
- History and circumstances
- Witnesses
- Evidence

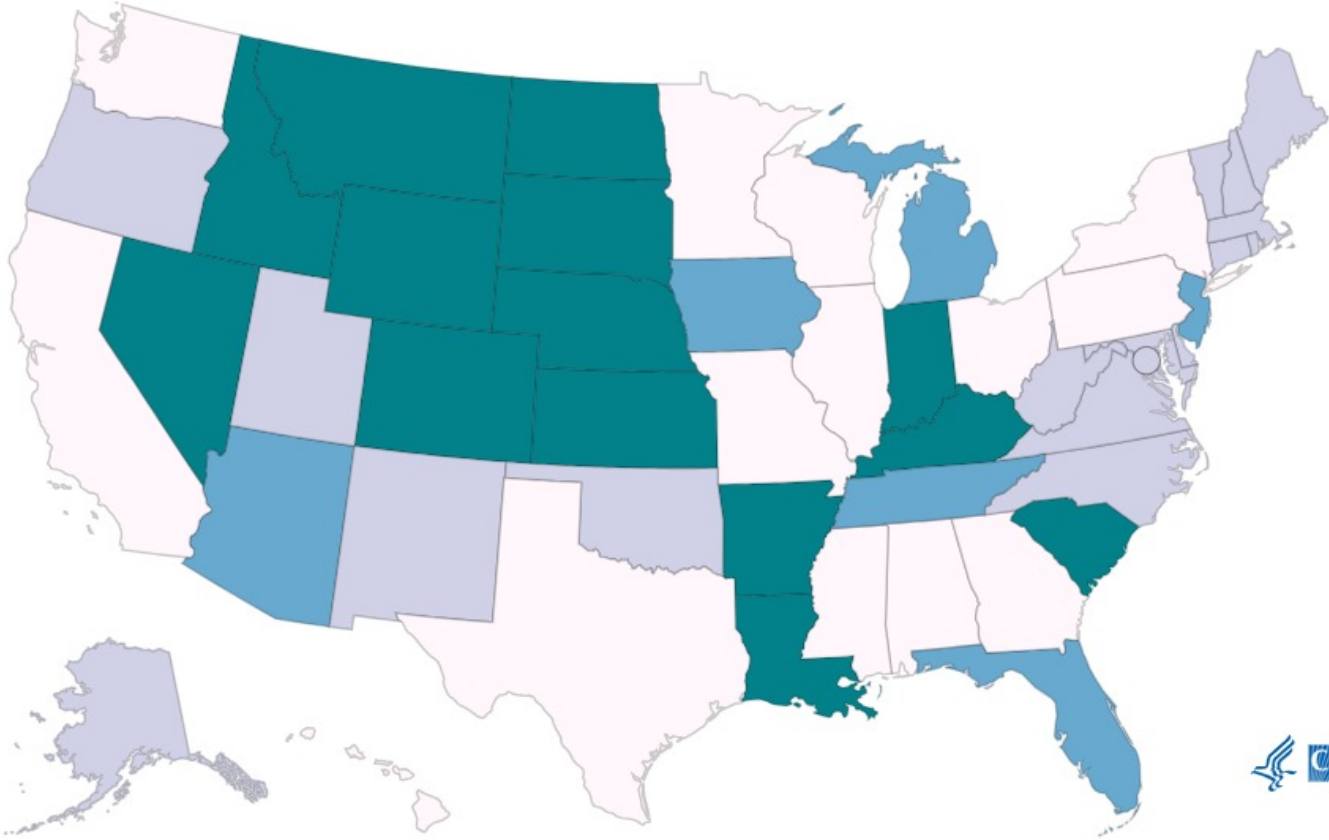
Pathology

- External examination
- Internal examination

Toxicology

- Postmortem specimens
- Antemortem specimens
- Physical evidence

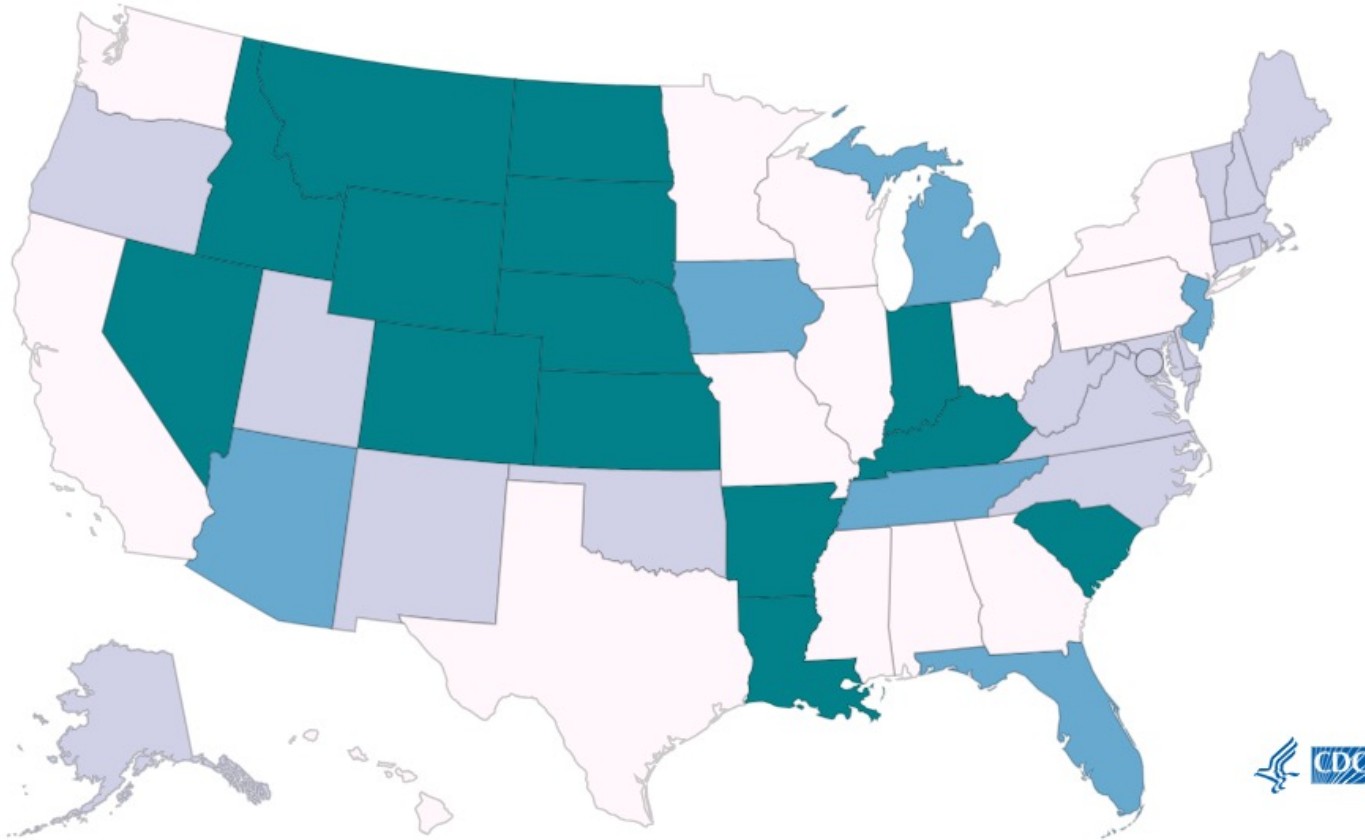
Death Investigation Systems



- County-based mixture of medical examiner and coroner offices
- Centralized state medical examiner office
- County/district-based medical examiner offices
- County/district-based coroner offices



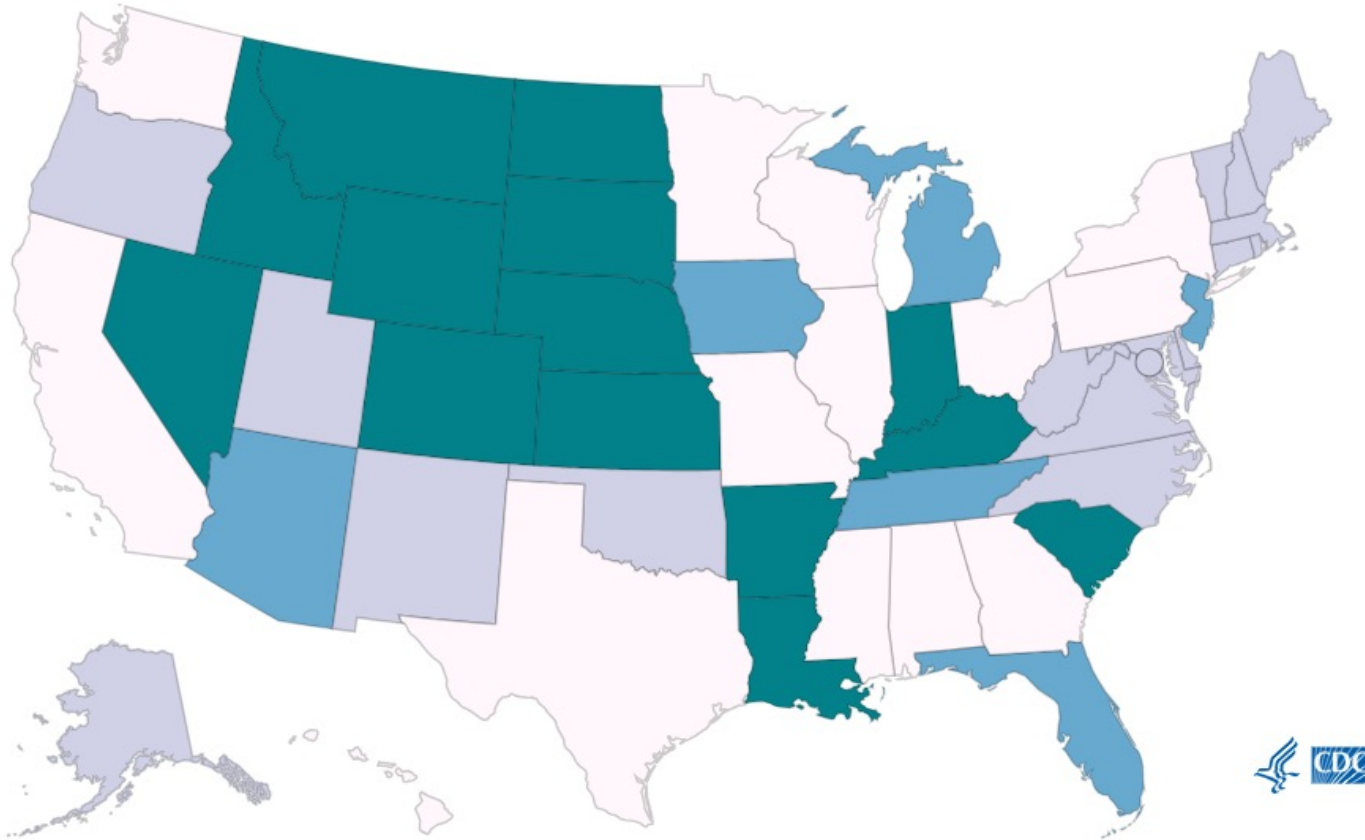
Not Created Equal



Coroners

- Most elected
- Some appointed
- Minimal requirements
 - Pulse & high school diploma
 - Usually no medical experience
 - Other full-time jobs
- Training
 - Less than half require any at all
 - Range from 4 to 40 hours
- Review all evidence and determine COD and MOD

Not Created Equal



Medical Examiners

- Appointed
- Requirements
 - Usually have medical experience
 - May have a full-time job
- Training
 - Range from 4 to 40 hours
- Scene investigation
- External examinations
- Review all evidence and determine COD and MOD

And the Point of all this?

Who decides a drug is involved in the death?

- Coroner
- Medical Examiner
- Forensic Pathologist

Toxicology Training

- None to minimal

Cause and manner of death

- Are opinions based on facts on hand
- Reasonably degree of certainty, i.e. >50%

And the Point of all this?

How is it decided which drugs are involved in an OD death?

- No consensus, even amongst fully-trained forensic pathologists

<u>Compound</u>	<u>Result</u>	<u>Units</u>	<u>Matrix Source</u>
4-ANPP	Positive	ng/mL	001 - Femoral Blood
Caffeine	Positive	mcg/mL	001 - Femoral Blood
Cotinine	Positive	ng/mL	001 - Femoral Blood
Nicotine	Positive	ng/mL	001 - Femoral Blood
Morphine - Free	13	ng/mL	001 - Femoral Blood
Norfluoxetine	190	ng/mL	001 - Femoral Blood
Citalopram / Escitalopram	1000	ng/mL	001 - Femoral Blood
Amphetamine	19	ng/mL	001 - Femoral Blood
Methamphetamine	10	ng/mL	001 - Femoral Blood
Fentanyl	13	ng/mL	001 - Femoral Blood
Norfentanyl	1.0	ng/mL	001 - Femoral Blood
Mitragynine	39	ng/mL	001 - Femoral Blood

“Lumpers”



Combine everything
and call it a day

“Lumpers”



Combine like drugs,
e.g. CNS depressants

“Splitters”

“Heavy hitters”

e.g. fentanyl and meth

“Splitters”

Illicits

e.g. fentanyl and meth

What about kratom?

Legality in their state?

Personal opinion?

Why does this Matter?

- Medical

- The 'hows' and 'whys'
- Provide answers to family, friends, community

- Public Health

- Epidemiology
- Surveillance
- Prevention



Public Health (federal level)

- Data comes from death certificates
- How is it listed?
 - Immediate to COD (Part I of DC)
 - Contributing to COD (Part II of DC)
- What is listed?
 - Kratom vs mitragynine
 - Misspellings are common

Analytical Challenges

Forensic Standards

- Screen and confirmation

Screening

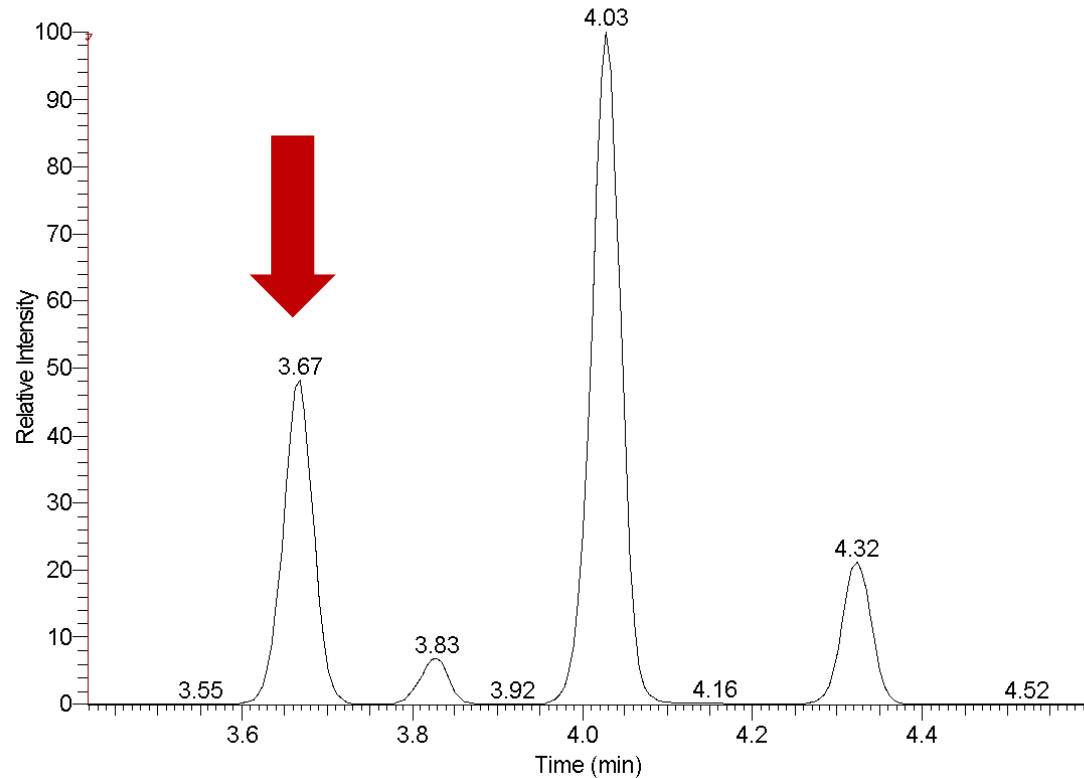
- Targeted – LC-MS

Confirmation

- Separate diastereomers

Stability...it's' not good

- Time, temperature, pH
- 7-OH is a no-go



Postmortem Data

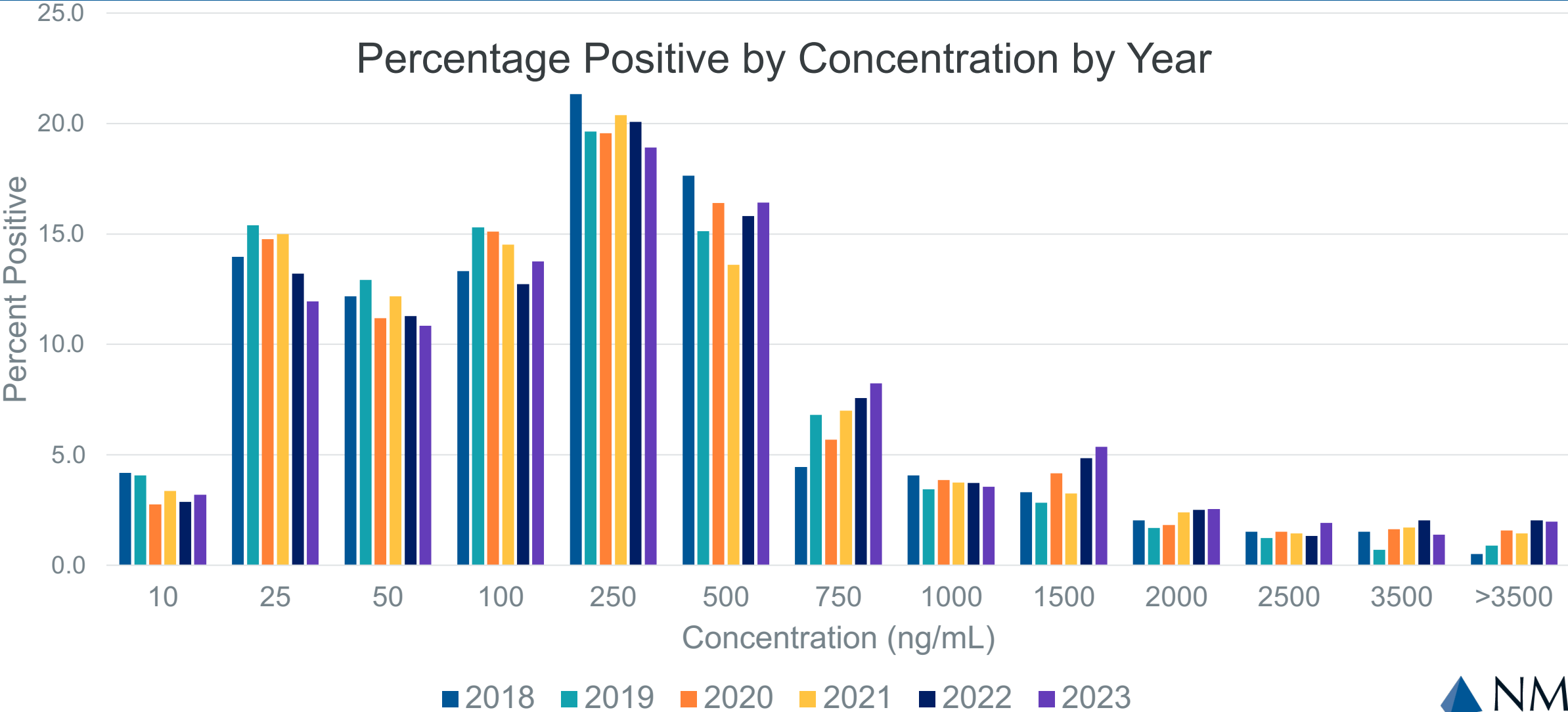
	2018	2019	2020	2021	2022	2023
N	785	1125	1704	1869	1878	1883
Mean (ng/mL)	353	329	412	404	466	474
Median (ng/mL)	120	110	130	120	150	160
Range (ng/mL)	5.9 - 7000	5.3 - 8900	5.0 - 11000	5.5 - 8000	5.5 - 9900	5 - 12000
Positivity Rate	1.24%	1.67%	1.88%	1.75%	1.76%	N/A

- Wide ranges
- Low positivity
 - Requires targeted screening (NMS Basic vs Expanded panels)
- Test what we're sent

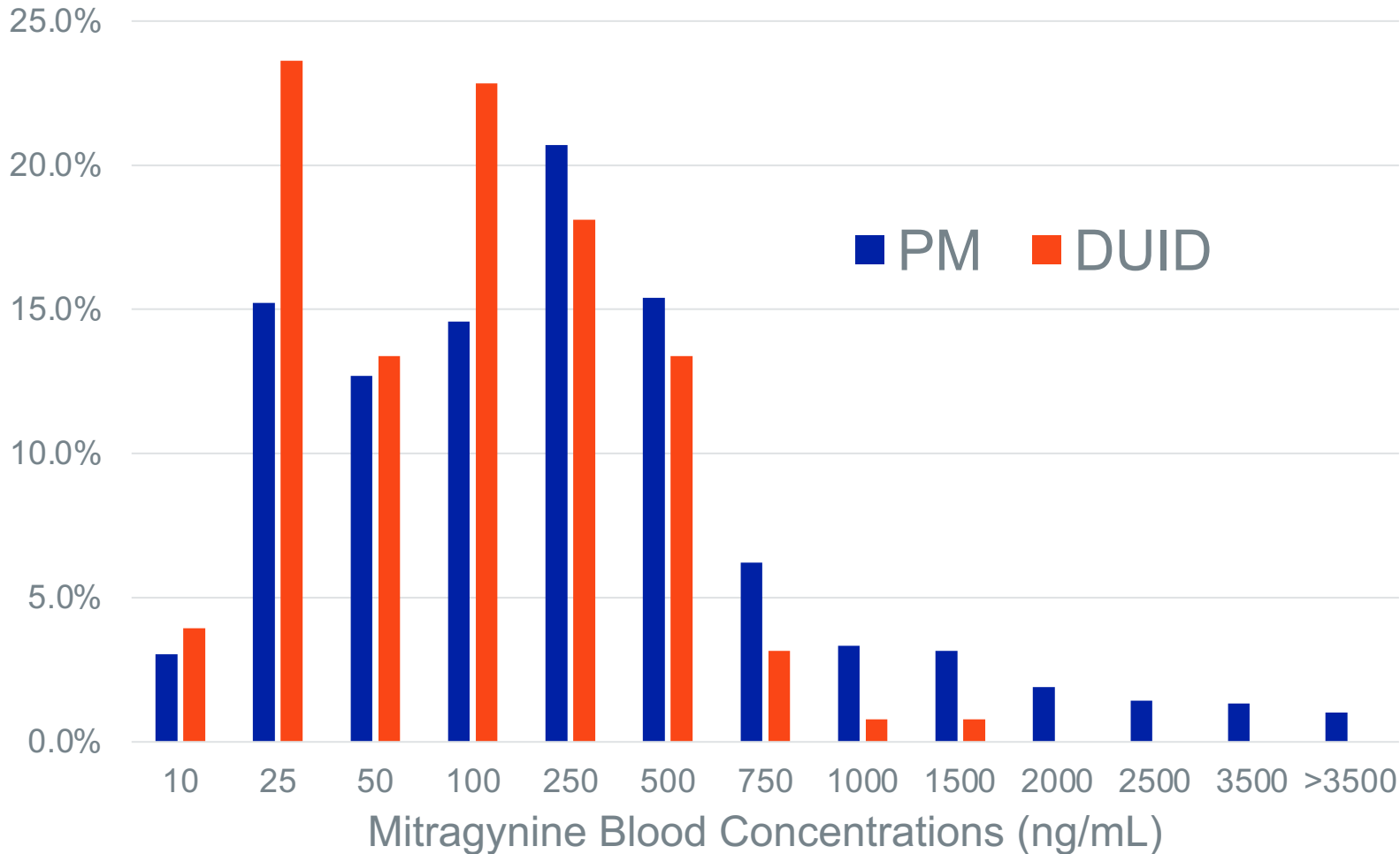
Updated from: "Forensic Implications of Kratom." *Current Addiction Reports* 2023, 10(2): 1-10.

Postmortem Data

Percentage Positive by Concentration by Year



Lessons from Drivers



“When you stop driving, you start dying” – Me

Considerable overlap up to ~500 ng/mL

My starting thresholds:

- ~50 – “Therapeutic”
- >500 – Contributing
- >1000 – COD

“Forensic Implications of Kratom.” *Current Addiction Reports* 2023, 10(2): 1-10.

Potentially Fatal Mitragynine Concentrations

	2018	2019	2020	2021	2022	2023
N > 1000 ng/mL	70	83	183	192	239	248
% of Total	8.9%	7.3%	10.7%	10.2%	12.7%	13.2%

Using 1000 ng/mL as a threshold

- Absolute # and % is increasing
- Rising with popularity and availability (?)
- Likely misuse, not necessarily abuse (?)

Conventional “Wisdom”

“Kratom is 100% safe”

“No one has ever died”

“Not a drug or an opiate”

Kind regards,
Kratom advocates

“Mitragynine isn’t an opiate, but if it is, it’s a partial agonist”

“No one has ever died, but if they have, it’s because of other CNS depressants”

Kind regards,
More kratom advocates

Mitragynine-only Deaths in NC

Mitragynine	n	ng/mL			Frequent other drugs	Cause of death
		Mean	Median	Range		
Mitragynine-only	12	2450	2000	730 – 5900	---	Mitragynine
+ therapeutic Rx/OTC (no illicit/opioids/EtOH)	11	3590	3200	1700 – 6800	SSRI, gabapentin	Mitragynine (1 seizure)
+ illicit/opioids/EtOH	41	1040	980	500 – 3800	Fentanyl, cocaine	Most are multi-drug

- Limitations: Small sample size (n=64)
- Considerable overlap between bins, as expected
- 9 men, 3 women: 18 – 51 years old (mean 35, median 33)

Mitragynine-only Cases (not even alcohol)

Sex	Age	Mitragynine (ng/mL)
F	30	2000
F	32	2900
F	50	970
M	18	730
M	25	1000
M	27	5900
M	27	1300
M	35	1000
M	38	5200
M	41	2000
M	46	4000
M	51	2400

- Collapsed after exiting bathroom
- Picked up by friend's mom, acting "weird"

- Worked by EMS; and clothes covered in powder
- No med or drug history

- Unresponsive on floor of home
- Went to sleep, found deceased
- No submersion or airway obstruction

- History of worsening chronic pain

- Used kratom

Mitragynine-"only" Cases (therapeutic Rx/OTC, no EtOH)

Sex	Age	Mitragynine (ng/mL)	Other drugs (ng/mL)
34	F	1700	Amp/Cital/Diphen <250
25	M	2100	Sert/NorSert 530/630
27	M	3200	Ven/ODM-Ven 1300/310
29	M	5500	Gabapentin 5500
31	M	2000	Citalopram 650
34	M	5400	Citalopram 440
35	M	3900	Gaba 24000
39	M	2700	Dextromethorphan 490
42	M	6800	Gabapentin 6400
49	M	2900	Alprazolam 31
--	--	3300	Sert/NorSert 450/930

- Depression, anxiety, ADD
- Recent stress
- In parking lot slumped over steering wheel
- Found dead on couch
- Recently started uncontrolled seizure disorder
- Kratom blister pack = seizure packs on scene

Postmortem Thoughts

Always Evolving

- More cases, more data
- Investigator education

Harm may be low, but not harmless

- Dose makes the poison, yada yada yada

Cases

- Often lack foam cones
- Many seem sudden
- Cardiac component (?)

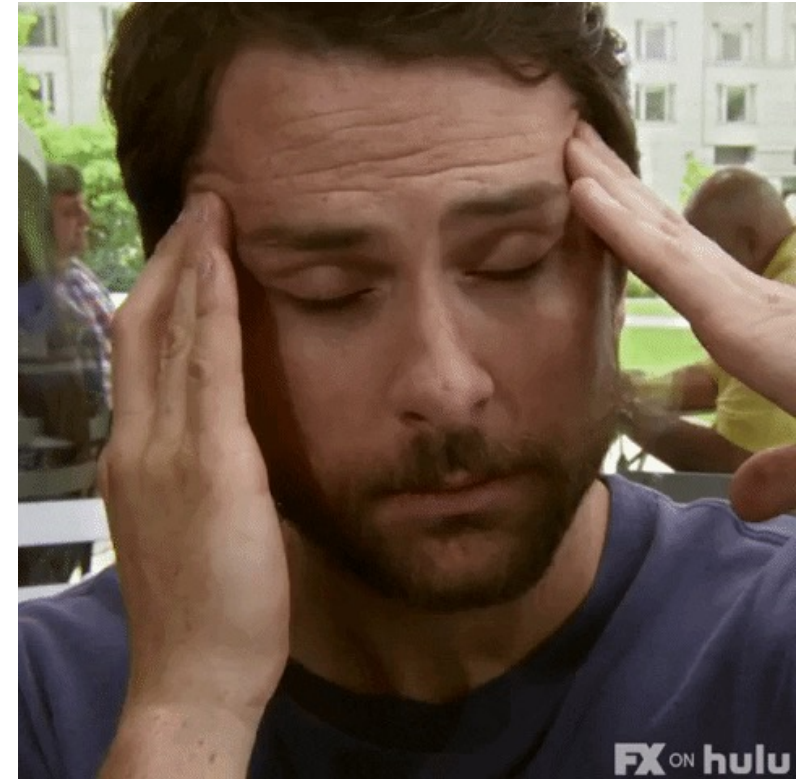
Postmortem Thoughts

Kratom in general

- Under-represented due to testing
- Concentrations lower due to stability

Implicating kratom in deaths

- Look at our coroner and ME systems
 - Not all are qualified
 - Not all are trained
- No consensus
 - Lumpers and splitters
 - Some still don't know what it is



Postmortem Thoughts

What is needed:

Pharmacology

- Mechanism of action
- Isomers and alkaloids

Clinical

- Concentrations
- Effects and events

Toxicology

- Postmortem redistribution
- Stability



Acknowledgements

Donna Papsun (NMS Labs)

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- Gracious use of data/tables
- Presenting at AAFS next week



THANKS!
Nice comments
or
Easy questions?
Just ask.