



**RÄTTSMEDICINALVERKET**  
NATIONAL BOARD OF FORENSIC MEDICINE

# **A global review of NPS toxidromes**

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# Some NPS related toxidromes

# Opioid toxidrome

- coma, respiratory depression, shock, pulmonary edema, unresponsiveness, bradycardia, hypotension, hypothermia

# Sympathomimetic toxidrome

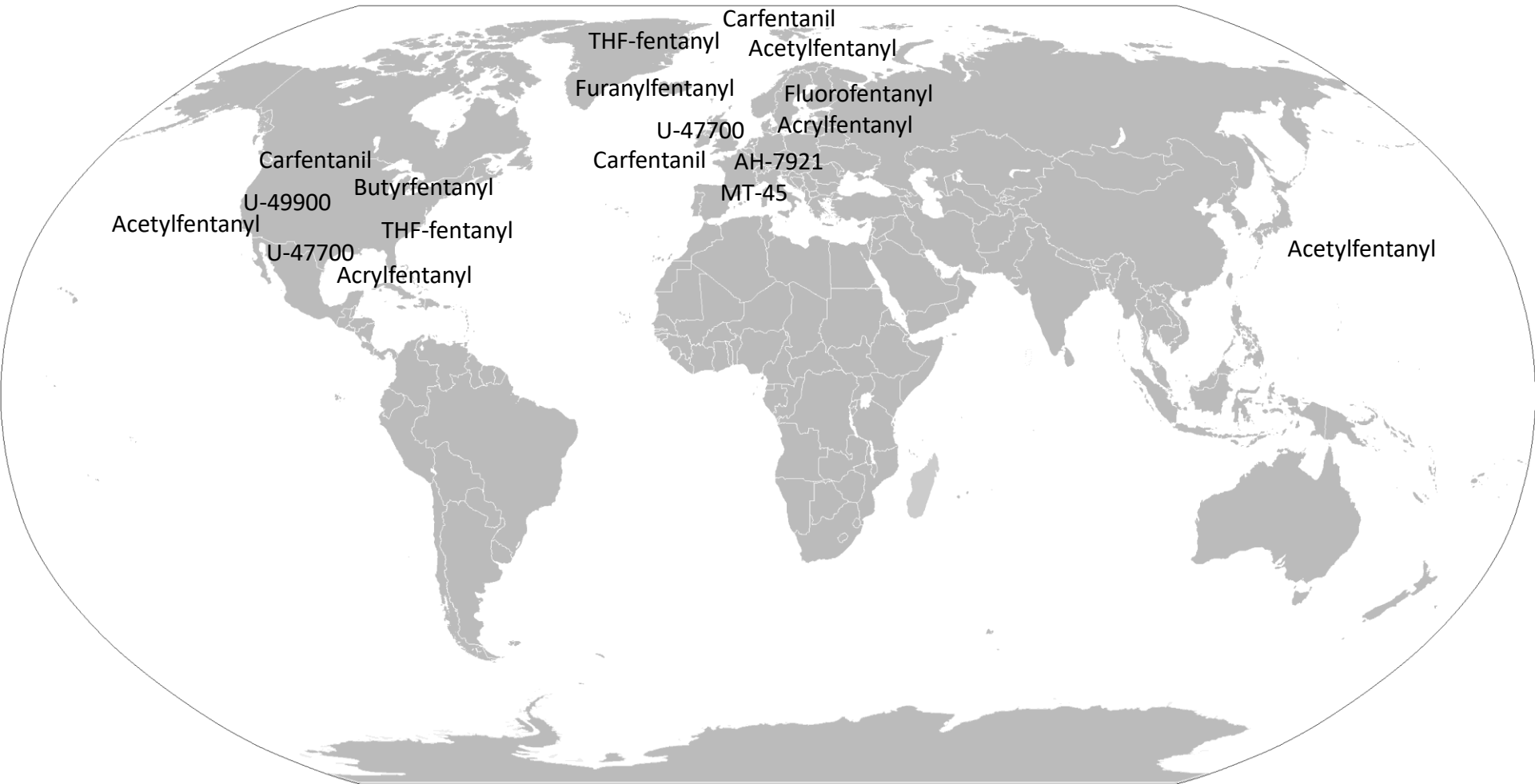
- Anxiety, paranoia, delusions, hyperactivity, hyperpyrexia, seizures, hypertension, tachycardia,

# Hallucinogenic toxidrome

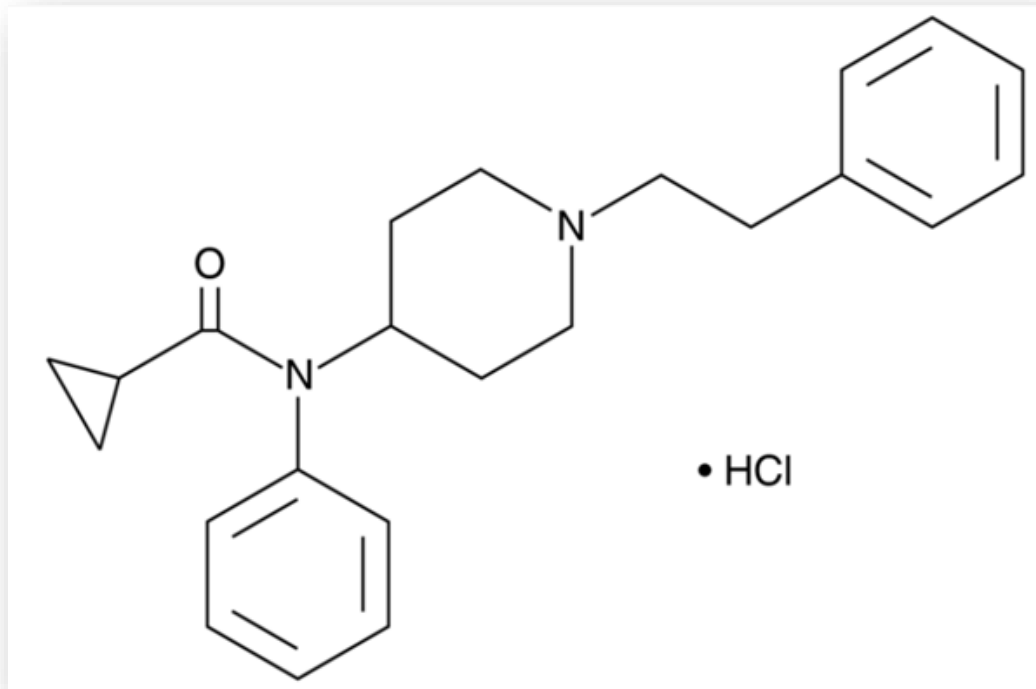
- Disorientation, hallucinations, psychotic episodes, paranoia, anxiety, memory disruption, hypertension, tachycardia, tachypnea

# Sedative toxidrome

- Sedation, disorientation, ataxia, coma, hypoventilation, apnea, hypotension, hypothermia
- coma, respiratory depression, shock, pulmonary edema, unresponsiveness, bradycardia, hypotension, hypothermia



# Deaths associated with cyclopropylfentanyl in Sweden



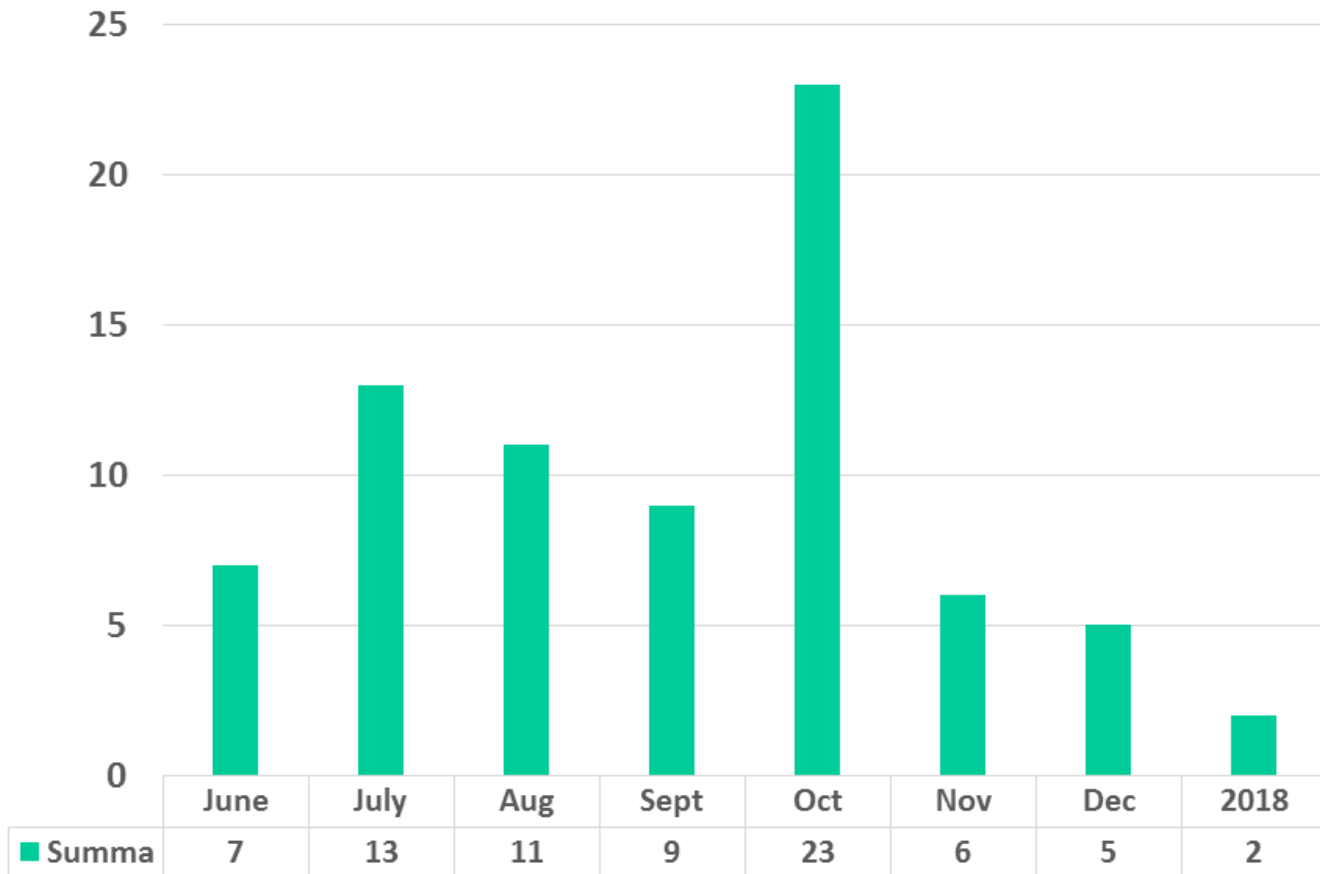




# Cyclopropylfentanyl

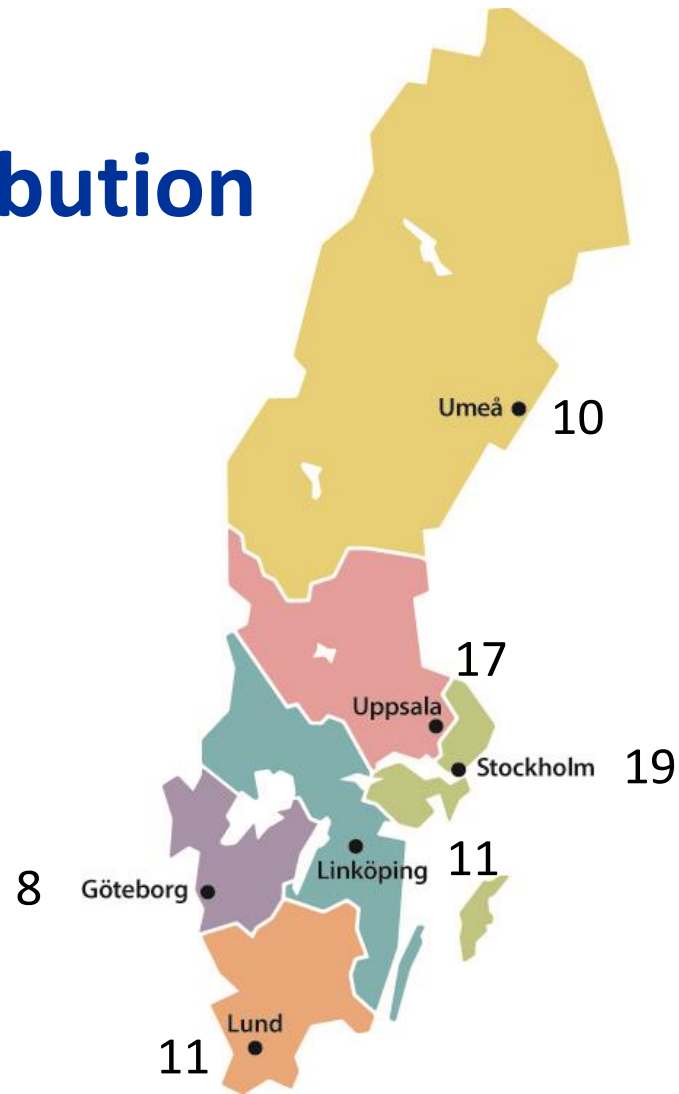
|      | Cases (males) |
|------|---------------|
| 2017 | 74 (68)       |
| 2018 | 2 (2)         |

# Timeline (day of autopsy)

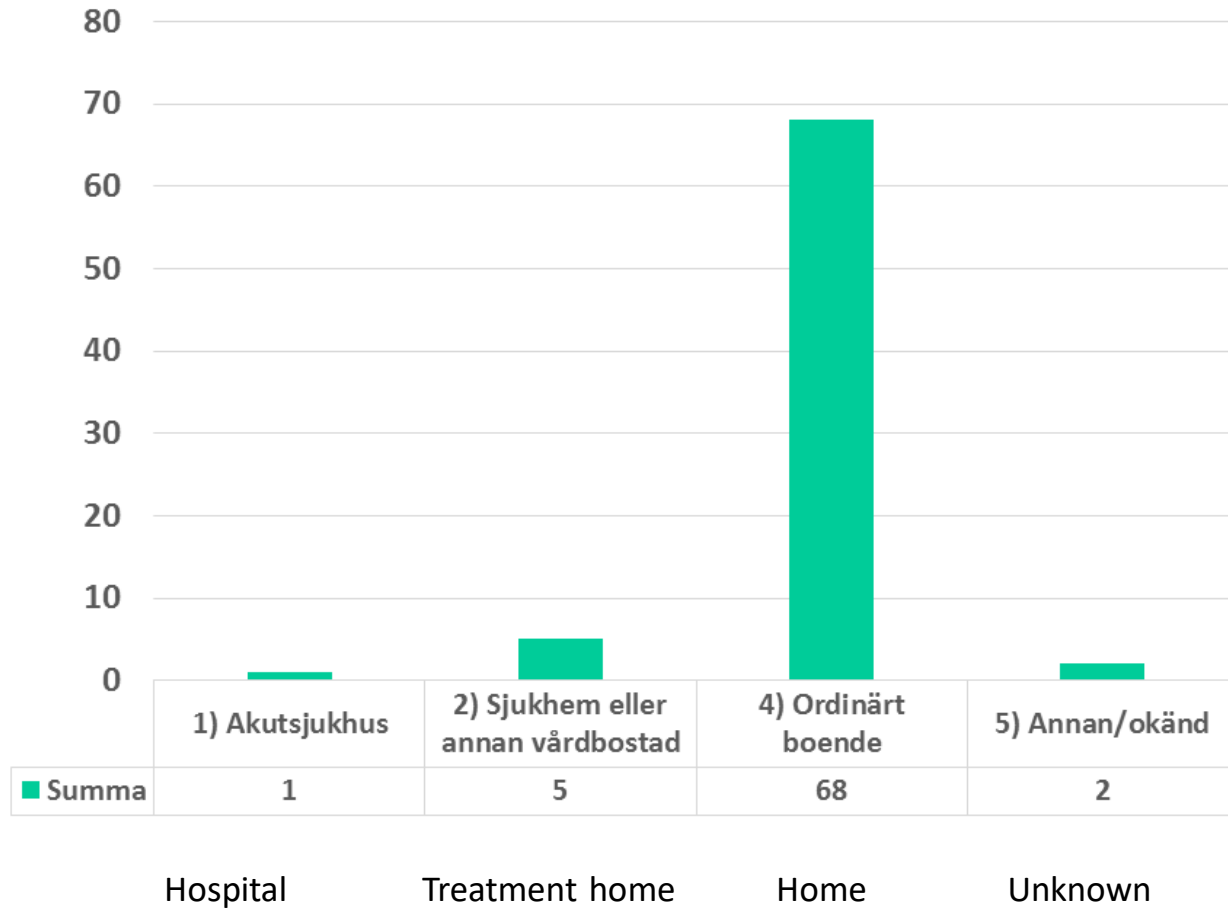




# Geographic distribution

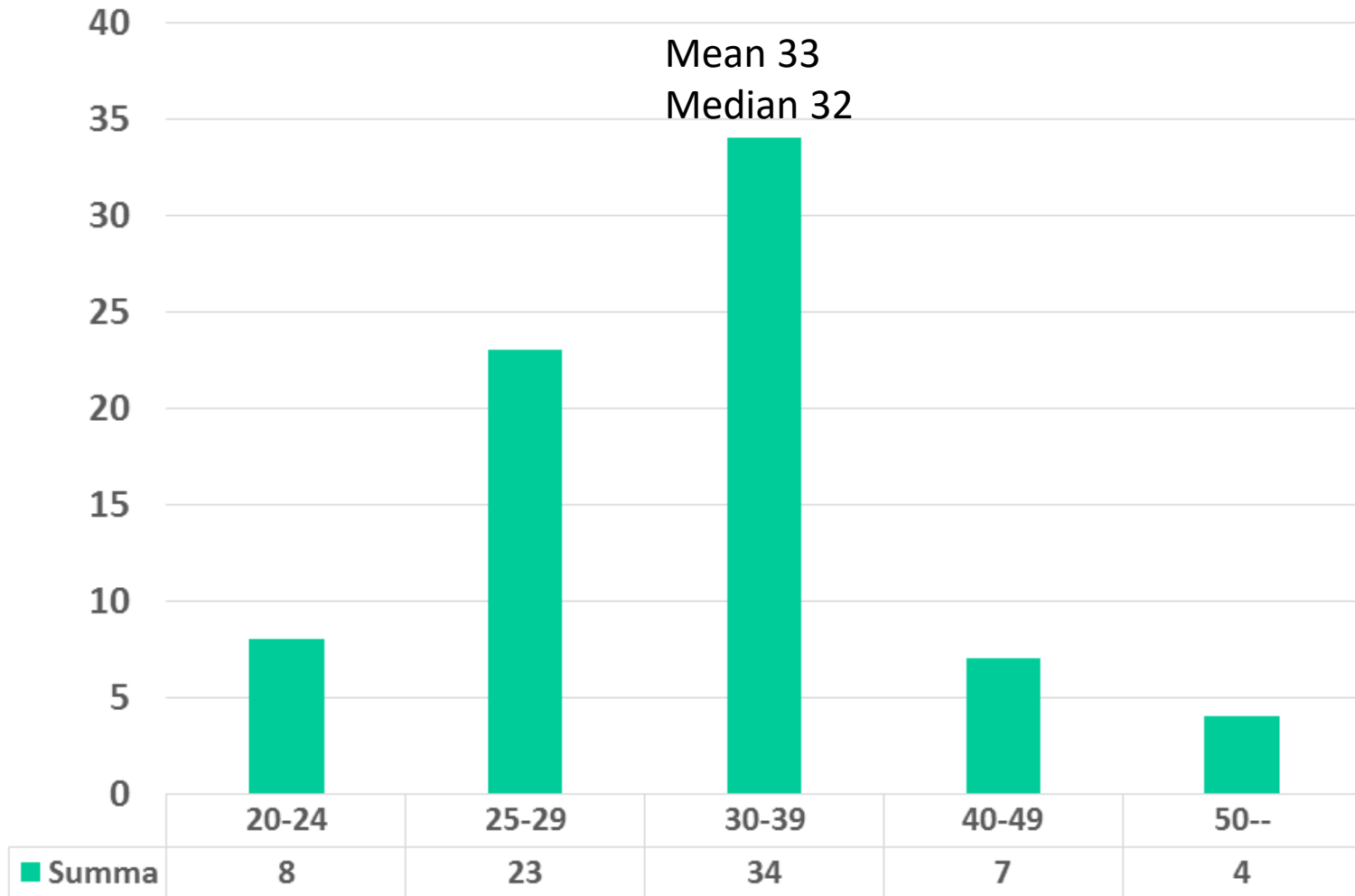


# Place of death

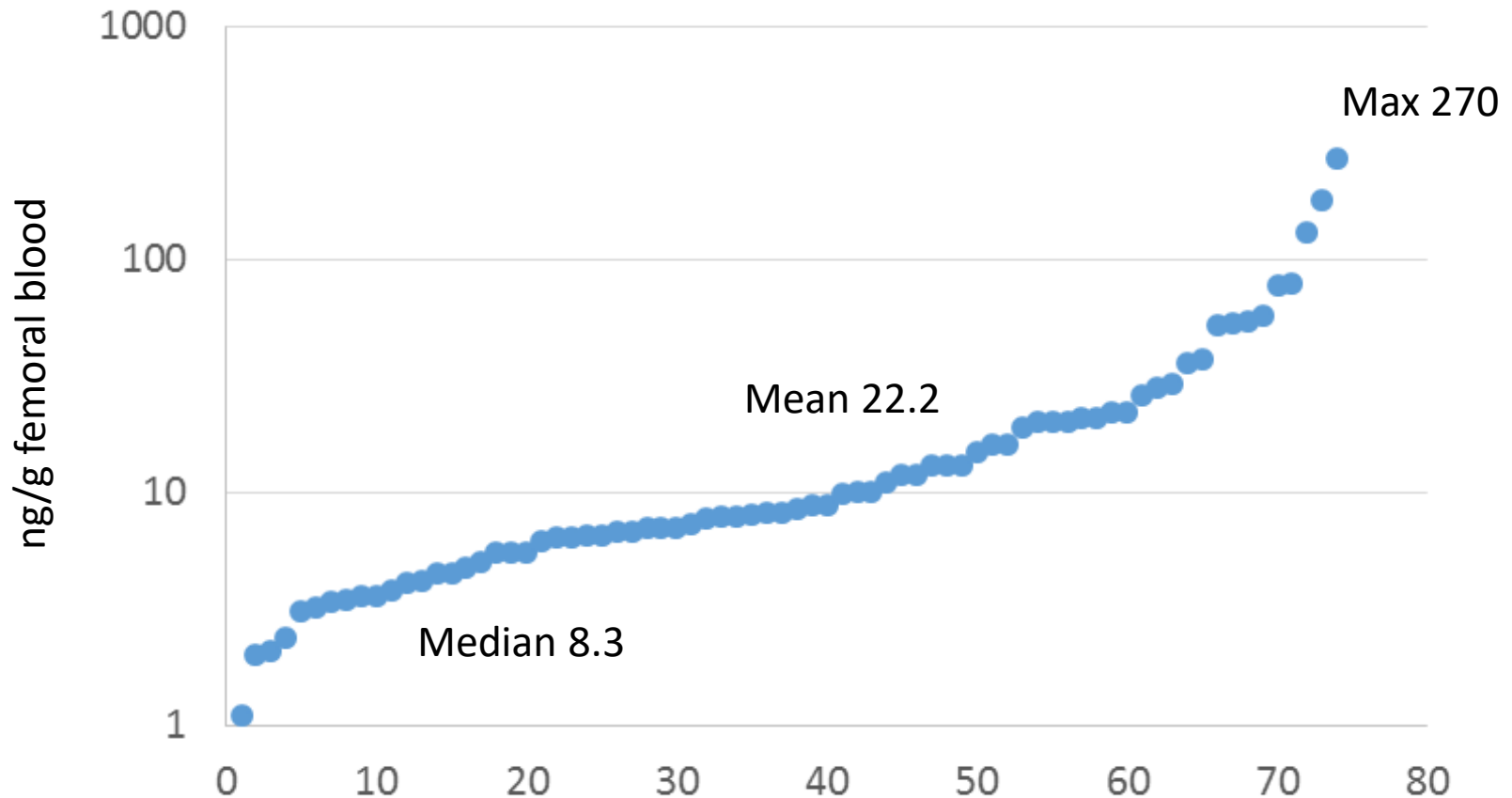




# Age distribution



# Concentrations (N=74)



## Other drugs present

| Drug           | Antal | Range ( $\mu\text{g/g}$ ) |
|----------------|-------|---------------------------|
| Norfludiazepam | 35    | 0.02 – 4.8                |
| THC            | 22    | 0.0005-0.16               |
| Alprazolam     | 20    | 0.002-0.19                |
| Pregabalin     | 20    | 0.97 - 26                 |
| Ethanol        | 17    | 0.12-2.07 (promille)      |
| Amphetamine    | 16    | 0.04 – 6.7                |

## Deaths MoD and CoD

|      | Cases | N  | ICD9 | MoD      | CoD          |
|------|-------|----|------|----------|--------------|
| 2017 | 74    | 23 | E859 | Accident | Intoxication |
|      |       | 33 | E866 | Accident | Intoxication |
|      |       | 14 | E980 | Unclear  | Intoxication |
|      |       | 2  | E950 | Suicide  | Intoxication |
|      |       | 1  | E911 | Accident | Aspiration*  |
|      |       | 1  | E953 | Suicide  | Asfyxia      |

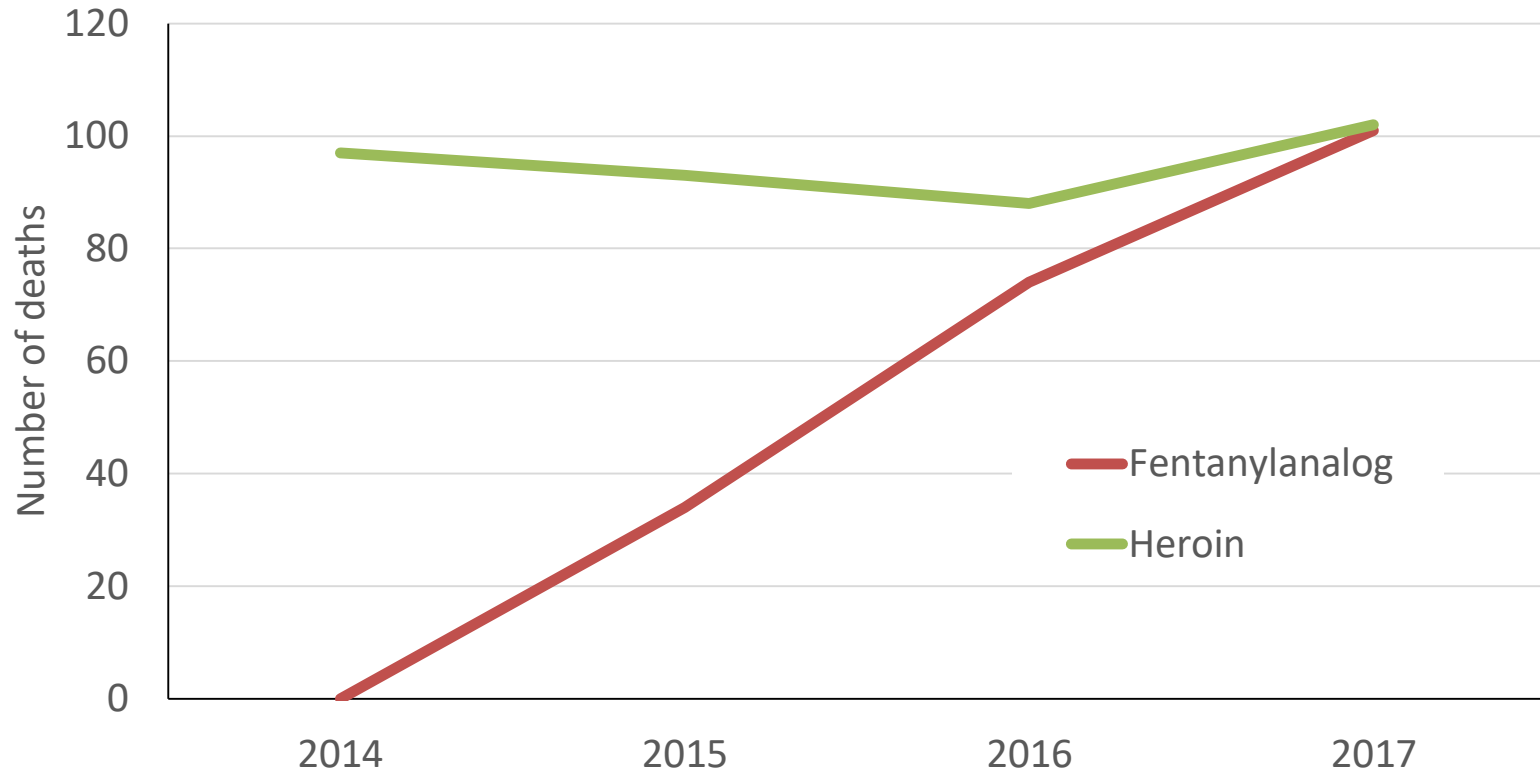
\* Due to CPF-nasal spray (cyclopropylfentanyl 26 ng/g)



# Administration ways

- Difficult to find out
- Counted cases that mention nasal sprays at the scene or that the persons were seen using a nasal spray
- **23 cases**

# Fentanyl analogs and heroin Sweden



## Summary opioids

- They are potent on their own but often taken in combination with other drugs that may add to the negative effects, most decedents took the drug alone. New administration ways may add to the risk of fatal intoxication.



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# Synthetic cannabinoids

# Scientific papers of SCRA related deaths

- USA, Sweden, Norway, Germany, Japan, Poland

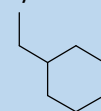
## Reported medical complications

- AM: chest pain, trouble breathing, low pulse, cardiac arrest and asystole
- PM: enlarged heart, arteriolar wall hypertrophy, ischemic cardiac disease, heart fibrosis, myocardial cell death, pulmonary edema

(fluoro/cyano)  
alkyl chain

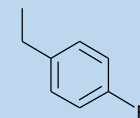


methylene-  
cyclohexyl



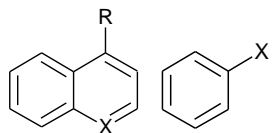
MDMB-CHMICA  
AB-CHMINACA  
ADB-CHMINACA

fluoro-benzyl



AB-FUBINACA  
ADB-FUBINACA

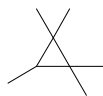
aromatic



JWH-018  
JWH-073  
JWH-022  
JWH-122  
JWH-210  
AM2201  
MAM2201

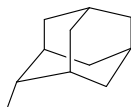
5F-PB-22  
NNEI  
THJ-2201  
AM-694  
AM-1220  
AM-2232

tetramethyl-  
cyclopropyl



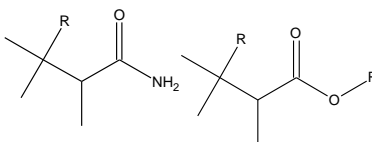
XLR-11  
UR-144

adamantyl



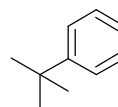
AKB48  
STS-135

valinamide/valinate

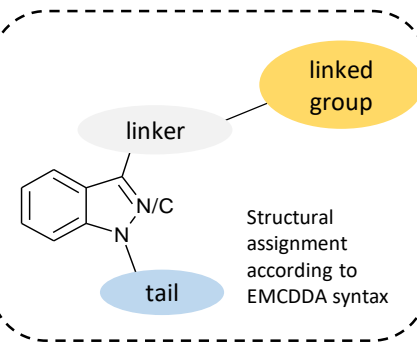


AB-PINACA  
5F-ADB  
5F-AMB  
5F-ADB-PINACA  
ADB-PINACA

cumyl



CUMYL-  
4CN-  
BINACA






# Deaths associated with CUMYL-4CN-BINACA

RESEARCH ARTICLE

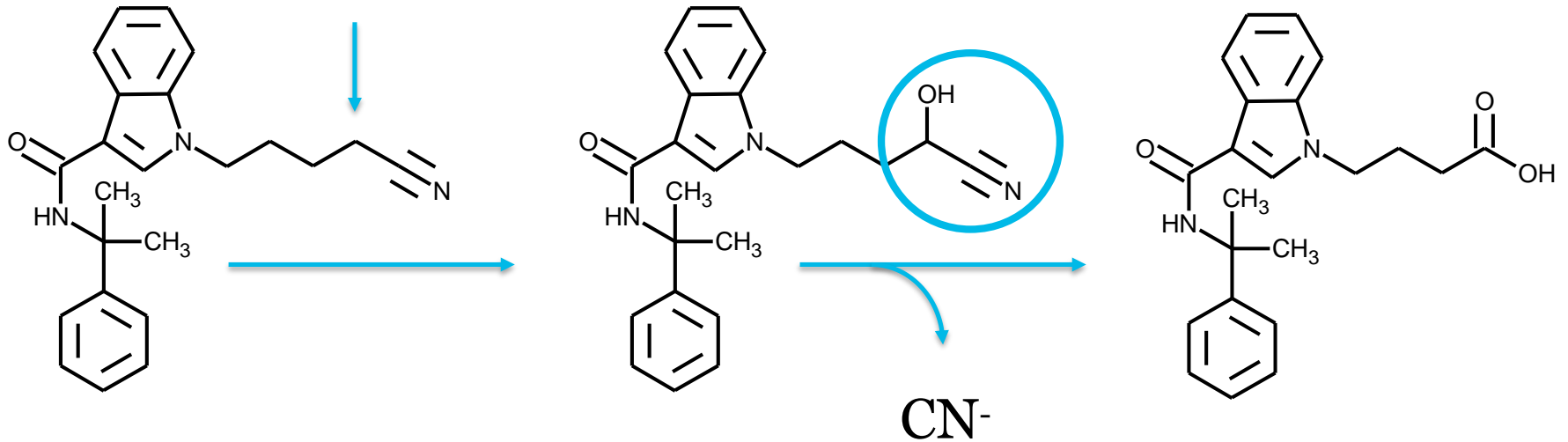
WILEY

**Metabolism study for CUMYL-4CN-BINACA in human hepatocytes and authentic urine specimens: Free cyanide is formed during the main metabolic pathway**

Anna Åstrand<sup>1</sup> | Svante Vikingsson<sup>1,2</sup> | Daniel Lindstedt<sup>1</sup> | Gunilla Thelander<sup>1</sup> |  
Henrik Gréen<sup>1,2</sup> | Robert Kronstrand<sup>1,2</sup>  | Ariane Wohlfarth<sup>1,2</sup> 



# Decyanation carboxylic acid



# Summary of 4CN Cumyl cases

Case Gender Age History

1 M 36 Uncounscious directly after smoking. Taken to hospital.

2 M 61 Found dead after smoking at a home for addiction treatment.

3 M 61 Found dead in his bed.

4 M 38 Dead at home. Treated with methadon due to pain.

5 M 29 Found dead in his parents home. Earlier suicid attempts

6 M 41 Found in the bath. Arrived from addiction treatment some days earlier.

7 M 35 Known drug abuser. Found dead in his friends apartment.

8 F 29 Drug addict, in Subutex program. Found dead at home.

## Case 4CN-Cumyl BINACA

- White powder analyzed by NFC
- A man smoked cannabis together with a friend (Oct 17<sup>th</sup>), collapsed directly after intake of "cannabinoid". At hospital in respirator, *declared* dead Oct 19<sup>th</sup> at 12:22. Blood and urine samples taken Oct 19<sup>th</sup> at 15:30
- Toxicological analysis: 0.00016 µg Cumyl-4CN-BINACA /g blood and 0.02 µg THC-acid /ml urine
- Cause of death: Cerebral infarction due to circulation and respiratory arrest caused by intake of Cumyl-4CN-BINACA
- Manner of death: accident

## Summary of 4CN Cumyl cases

| Case | Cumyl ng/g | Other findings µg/g  | CoD  | MoD      |
|------|------------|--|--|----------|
| 1    | 0.16       | 0.02 THC-acid in urine   | Cerebral infarction,<br>Cumyl contributing | accident |
| 2    | 8.3        | 0.16 quetia 0.06 olanza 0.07 dm olanza<br>0.22 aripip 0.04 dh aripip<br>0.06 biper 0.1 ali | Intox Cumyl                                | accident |
| 3    | 1.0        | -  | Intox Cumyl                                | accident |
| 4    | 1.2        | 0.02 alp 0.06 dia 0.05 norda<br>0.19 meth 0.03 mirt 0.02 dm mirt<br>16 preg 7.1 klorzox    | Intox Cumyl                                | accident |
| 5    | 0.10       | 0.03 dia 0.06 norda 0.01 7amflu 0.26 meth<br>1.3 sert 1.3 dmsert 6.1 preg                  | Intox methadon<br>and sertraline           | suicid   |
| 6    | 0.22       | 0.10 α-PHP   | Drowning                                   | unclear  |
| 7    | 2.4        | 7.6 preg   | Intox Cumyl                                | accident |
| 8    | 0.5        | 6.1 ng bup 11 ng norbup 0.82 gaba  | Intox Cumyl                                | accident |

# Concentration comparison

## Postmortem

| Case | Cumyl ng/g |
|------|------------|
| 1    | 0.16       |
| 2    | 8.3        |
| 3    | 1.0        |
| 4    | 1.2        |
| 5    | 0.1        |
| 6    | 0.22       |
| 7    | 2.4        |
| 8    | 0.5        |

## Living persons

| Police case        | Cumyl ng/g |
|--------------------|------------|
| Traffic case       | 6.1        |
| "                  | 0.3        |
| "                  | 0.2        |
| "                  | 0.3        |
| Petty-drug-offence | 2.9        |
| "                  | 4.6        |
| "                  | 1.0        |
| suspicion drugged  | 0.4        |



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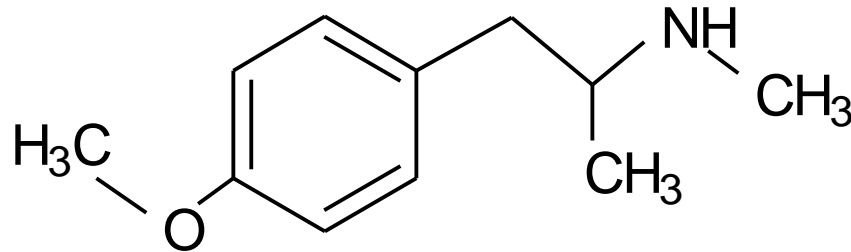
# Synthetic cathinones/phenylethylamines

# Synthetic cathinones/phenylethylamines

- Japan, USA, Italy, Sweden, Poland, The Netherlands, Great Britain, France, Norway, Israel, Denmark,

# PMMA

- paramethoxymethamphetamine





# Preamble



169mg PMMA

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### Drugs monitor issues warning for dangerous Superman 'ecstasy' pills

Society |     December 19, 2014



Copyright, NFI 2014

The Dutch **Trimbos** drug addiction clinic has issued a warning about a dangerous type of ecstasy pill currently in circulation in the Netherlands.

The warning comes just weeks after several tourists died in Amsterdam after taking heroin they believed to be cocaine.

The Trimbos institute says the dangerous pills are pink and feature the Superman logo. They contain a very high dose of a chemical known as PMMA, rather than MDMA which is the main component of ecstasy.

Tests have found drugs with possible links to the [deaths of four men](#) did contain the dangerous ingredient PMMA.

More than 400 red triangular pills with a Superman logo were found by Suffolk police near Norwich Road in Ipswich on Sunday.

The pills - similar to ecstasy - are believed to have led to the recent deaths of two young men in Ipswich, on Christmas Eve and New Year's Day respectively. The death of a third man in Rendlesham, Suffolk, is also under investigation.

The [death of a fourth man in Telford](#), Shropshire, is also being linked to the drugs. Two men have been admitted to hospital in Suffolk, possibly as a result of taking the drug.

On Wednesday, Suffolk police said it had tested the pills and found PMMA - a stronger and more dangerous active ingredient than that usually found in ecstasy.

# Demographics

| Case | Gender | Age | Length | Weight | History   |
|------|--------|-----|--------|--------|---|
| 1    | M      | 25  | 170    | 66     | Found dead after intake of EtOH, cocaine and ecstasy.                 |
| 2    | F      | 18  | 165    | 70     | Found unconscious outdoors. CPR                                       |
| 3    | M      | 24  | 176    | 60     | Becomes ill at friends after intake of ecstasy. CPR                   |
| 4    | M      | 22  | 177    | 77     | Arrives at hospital with hyperthermia and seizures after PMMA intake. |
| 5    | M      | 18  | 175    | 63     | Found unconscious in caravan after PMMA, MDMA, and AMP intake.        |
| 6    | M      | 22  | 184    | 65     | Trouble breathing at party.   |
| 7    | F      | 23  | 157    | 41     | Found dead outdoors in water.   |

# Autopsy findings

| Case | Findings  | CoD                       | MoD |
|------|---|---------------------------|-----|
| 1    | Pulmonary congestion and edema<br>Brain edema                         | Intoxication              | Acc |
| 2    | Pulmonary congestion and edema<br>Brain edema                         | Intoxication              | Acc |
| 3    | Severe pulmonary edema and congestion<br>Anoxic heart injury          | Intoxication              | Acc |
| 4    | Pulmonary edema<br>Liver necrosis                                     | Intoxication              | Acc |
| 5    | Pulmonary congestion, brain edema<br>Anoxic heart and kidney injuries | Intoxication              | Acc |
| 6    | Pulmonary congestion, anoxic heart injury                             | Intoxication              | Acc |
| 7    | Unremarkable  | Intoxication/<br>drowning | nd  |

# PM tox findings

| Case | PMMA | PMA  | EtOH | DoA                                      | Medications                              |
|------|------|------|------|--|--|
| 1    | 4.2  | 0.21 | 0.98 | 0.26 BE, 0.17 AMP,                       | -  |
| 2    | 4.9  | 0.33 | -    | 0.004 THC, 0.25 AMP, 0.16 MDMA, 0.02 MDA | -  |
| 3    | 7.1  | 0.59 | 0.47 | 0.002 THC, 0.43 AMP, 0.12 MDMA           | Amiodaron                                |
| 4    | 0.03 | 0.02 | -    | 0.09 AMP                                 | 8.2 levetiracetam, 0.09 MIDA, 0.14 MOR   |
| 5    | 3.6  | 0.28 | -    | 0.19 AMP, 0.02 MDMA                      | 0.06 DIA, 0.19 HYD, 0.02 7ACLO, 0.7 LIDO |
| 6    | 4.1  | 0.39 | 0.18 | 0.004 THC, 0.19 AMP                      | 0.03 DIA                                 |
| 7    | 3.3  | 0.20 | -    | 0.001 THC, 0.12 AMP, 0.02 BE             | -  |

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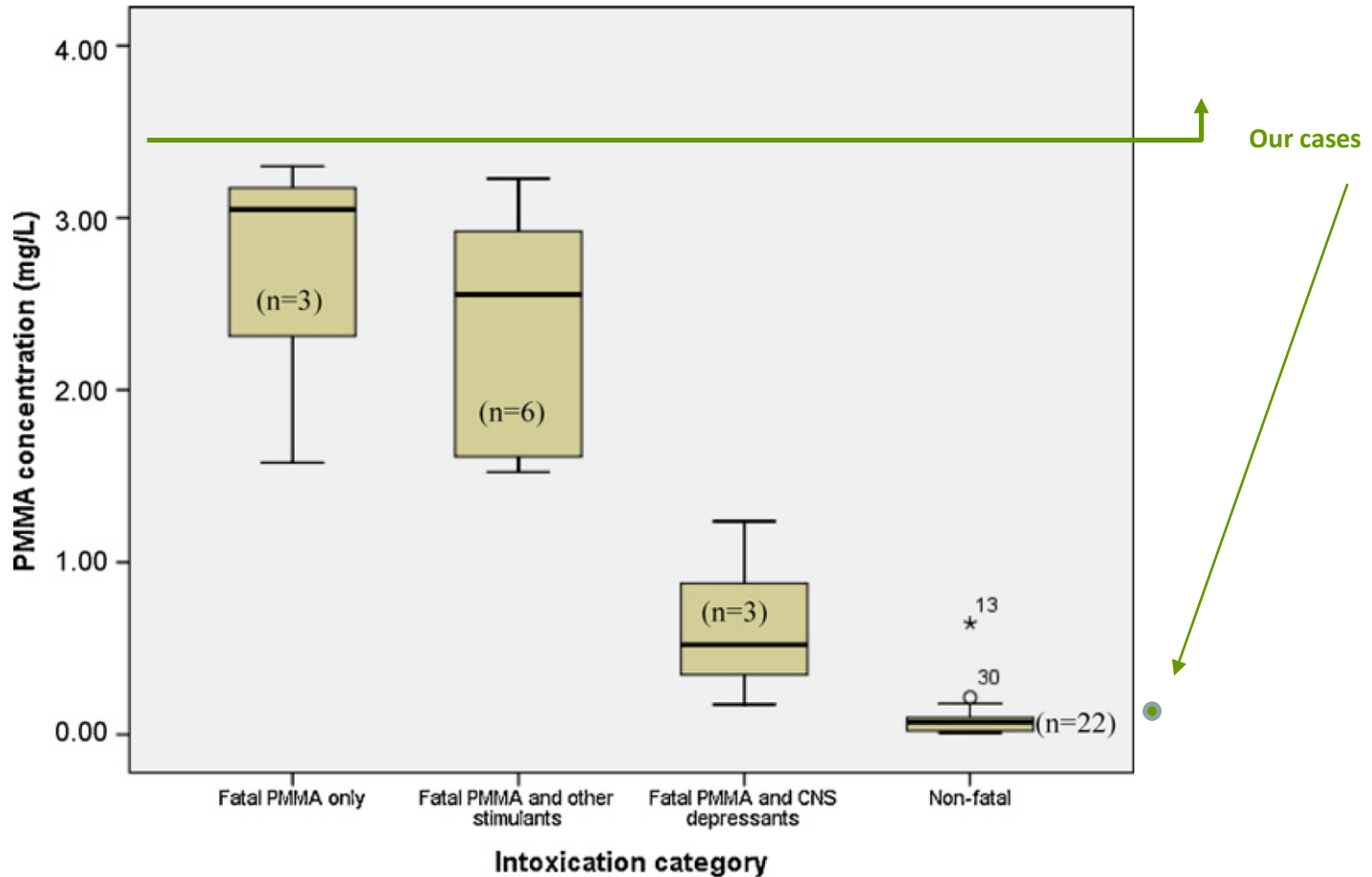
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| 7    | 3.3  | 0.20 | -    | 0.001 THC, 0.12 AMP, 0.02 BE             | -  |



# Published tox data



# Summary PMMA

- Isolated cluster
  - Media reaction
  - No additional deaths
- Published data helped interpretation
  - High PMMA concentrations
  - AM and PM findings consistent with PMMA intake and toxicity

# Conclusions

- Opioids are the major threat
- Synthetic cannabinoids have unpredictable symptoms that vary between compound and subject
- NPS seem to be more dangerous than their traditional corresponding drug



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**Thank you for listening**

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