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SERVICES**
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Post Mortem Toxicology: Challenges in Detecting New Substances

Hazel Torrance, Head of Forensic Toxicology

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Introduction

Dr Hazel Torrance

Head of the Forensic Toxicology Service

- Worked at Department of Forensic Medicine and Science, University of Glasgow since 2001.
- Before transferring to SPA Forensic Services in December 2022.
- In charge of the Post Mortem Toxicology Service since 2008.



Forensic Services at the Moorepark Laboratory (Govan)

Post Mortem Toxicology

- ~3900 Cases a year
- Covering 90% of Scotland
 - 10% Homicides/Fatal Road Traffic/Deaths in Custody
 - 45% Drug Related Deaths
 - 45% Natural/Suicide



Challenges in Forensic Toxicology

1. Biological Specimens
2. Range of Analytes and Chemical Nature (Emergence of new drugs)
3. Availability of Reference Material
4. Development and Validation of new Test Methods – Regulation/Accreditation



We need to understand the challenges, to overcome and provide robust data for policy makers to base their decisions on.

Challenges – 1. Biological Specimens

- Examples of Ante Mortem:

- Whole Blood
- Serum, Plasma
- Urine
- Oral Fluid
- Hair
- Meconium
- Breast Milk
- Sweat
- Nail Clippings
- Cerebrospinal Fluid

- Examples of Post Mortem:

- Blood
- Urine
- Vitreous Humour
- Bile
- Gastric Contents
- Hair
- Nail Clippings
- Bone
- Maggots
- Organs/Tissue (liver, brain, lung, muscle)

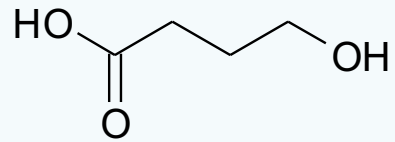


Challenges – 1. Biological Specimens

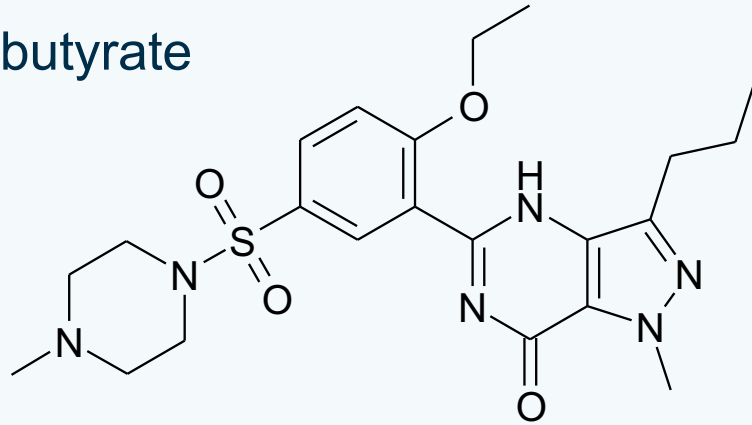


Need to extract drugs from biological matrix to reduce problems with inaccurate quantitation and interference on instruments.

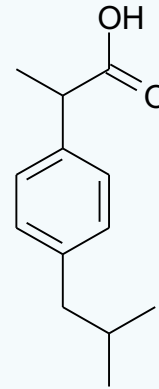
Challenges: 2. Chemical Nature of Analytes



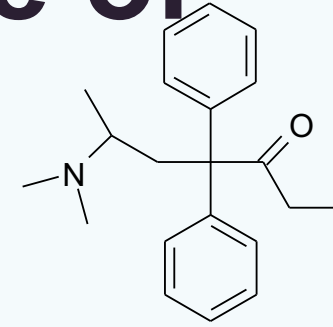
Small: gamma-hydroxybutyrate
MWt 104.1



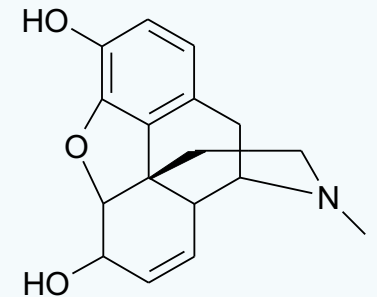
Large: sildenafil (Viagra)
MWt 474.6



Acidic: ibuprofen



Basic: methadone



Amphoteric: morphine

Challenges: 2. Range of Analytes

Over-the-Counter Medicines
e.g. paracetamol, ibuprofen

Controlled Prescription Drugs
e.g. methadone, oxycodone, gabapentin

Controlled Drugs
e.g. heroin, ecstasy

Drug Metabolites
e.g. 6-monoacetylmorphine

Herbal Drugs
e.g. psilocybin (magic mushrooms)

Poisons
e.g. arsenic, cyanide

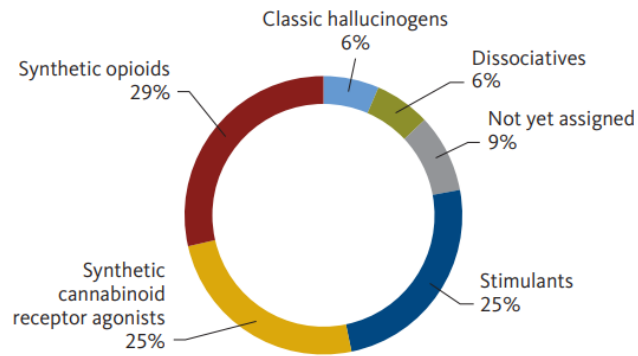
Novel Psychoactive Substances
e.g. Mephedrone, SCRAs

Volatile Substances / Inhalant Drugs
e.g. ethanol (alcohol), alkyl nitrites (poppers)

Toxic Metals / Trace Elements
e.g. lead, mercury, copper, iron

Challenges: 2. Range of Analytes

Classification by effect



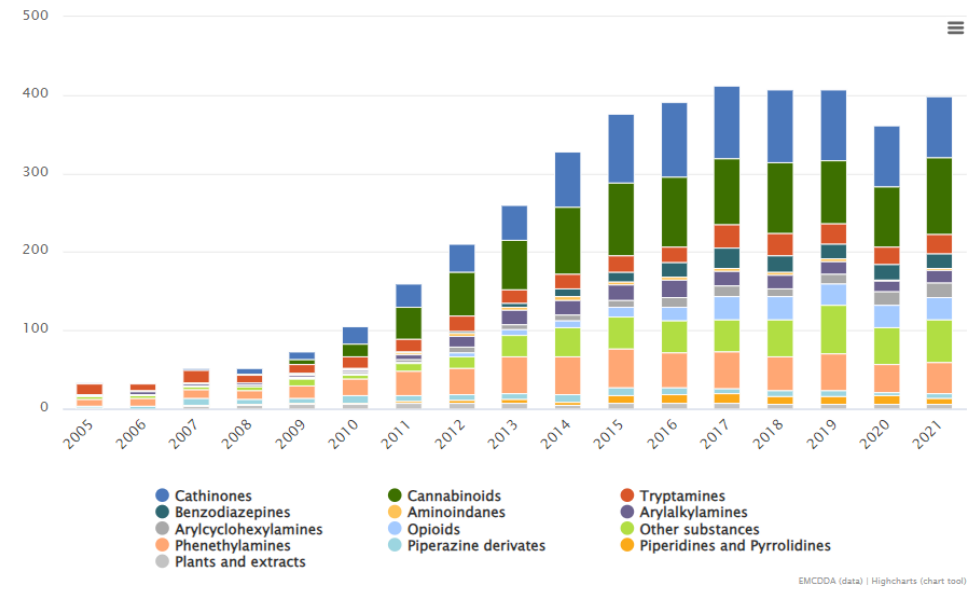
Source: UNODC early warning advisory on new psychoactive substances.

UNODC World Drug Report



Classification by chemistry

Figure. Number of new psychoactive substances reported each year following their first detection in the European Union, by category, 2005–2021



EMCDDA European Drug Report 2023

Challenges: .2. Range of Analytes

- **Benzodiazepines** are one of the largest classes of prescribed drugs worldwide:

diazepam, oxazepam, temazepam, midazolam, lorprazolam, flurazepam, nimetazepam, estazolam, chlordiazepoxide, lorazepam, alprazolam, bromazepam, clonazepam, brotizolam, flunitrazepam, clobazam, prazepam, medazepam, triazolam, nitrazepam, clorazepate, brontizolam, ketazolam, lormetazepam, flutoprazepam, camazepam, metaclazepam, tetrazepam, clotiazepam, cinolazepam, cloxazolam, delorazepam, doxefazepam, ethyl loflazepate, halazepam, haloxazolam, mexazolam, oxazolam, pinazepam, quazepam, tetrazepam, tofisopam, demoxepam.....

Challenges: 2. Range of Analytes

- Don't forget their metabolites:

desmethyldiazepam, chlordiazepoxide lactam, norclobazam, α -hydroxyalprazolam, desalkylflurazepam, α -hydroxytriazolam, α -hydroxyethylflurazepam, α -hydroxytriazolam, 7-aminoclonazepam, 7-aminoflunitrazepam, desmethylflunitrazepam, 7-amino-3-hydroxyflunitrazepam, 3-hydroxyflunitrazepam, 4-hydroxymidazolam, 1-hydroxymidazolam, hydroxybromazepam, lorprazolam-N-oxide, acetamidoloprazolam, hydroxylorprazolam.....etc

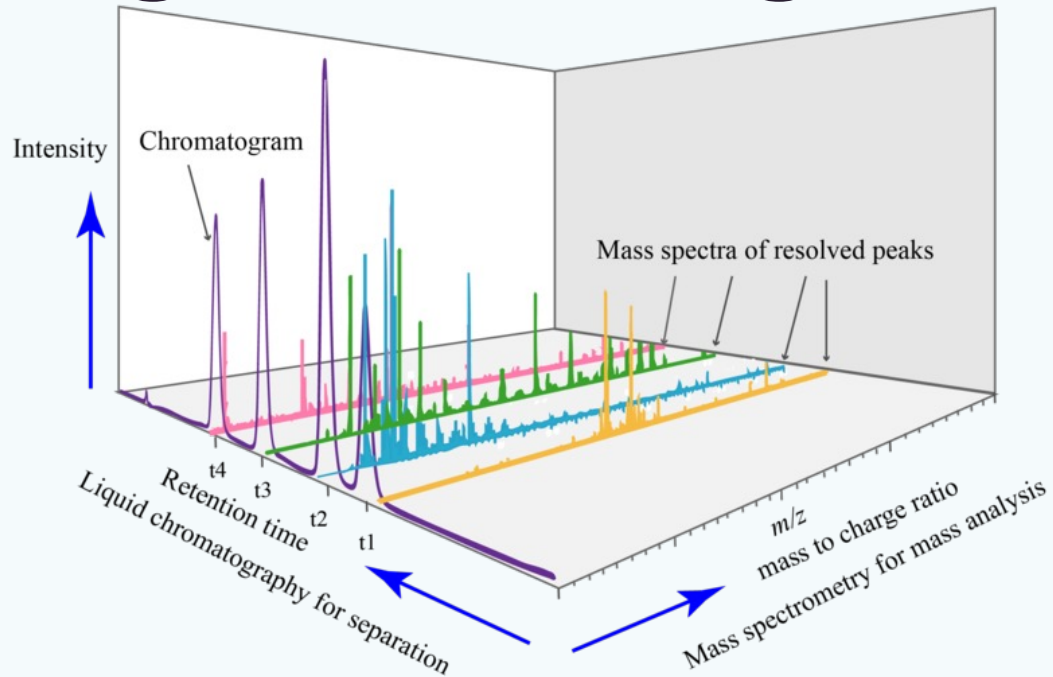
Challenges: 2. Range of Analytes

- AND the ever expanding illicitly available list:

phenazepam, 3-hydroxyphenazepam, flubromazolam, metizolam, fonazepam, bromazolam, adinazolam, alprazolam triazolobenophenone derivative, etizolam, pyrazolam, deschloroetizolam, flunitrazolam, 4-chlorodiazepam, clonazolam, diclazepam, flubromazepam, meclonazepam, nitrazolam, clonitrazolam, nifoxipam, desalkylgidazepam.....

And that's just the ones that we know about.

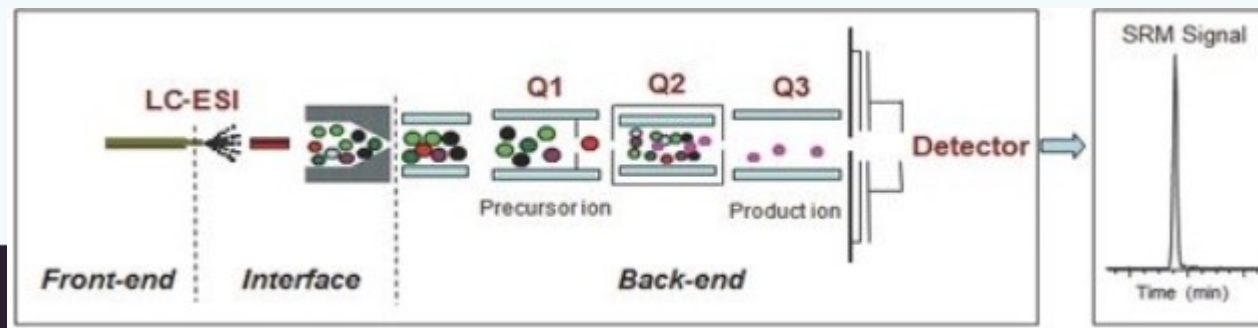
Challenges: 2. Range of Analytes



Separate
Mixture

and

Detect
Drugs



Challenges: 3. Availability of Reference Material

- Importance of Reference Materials (RM)
- Pure powders or solutions of drugs and/or metabolites
- Suitable internal standards
- Not always available e.g. NPS
- Expensive



This week's new reference materials

Take a look at the new additions

NEW PRODUCTS EVERY WEEK!

Supelco. www.sigmaaldrich.com

Certified Reference Material - Certificate of Analysis
Gabapentin, Primary Measurement Standard

Product No.: G-007-1ML
Lot No.: FN08132008
Description of CRM: Gabapentin in Methanol (Solution)
Expiration Date: October 2025 See Stability Section
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Stability Section
Chemical formula: C₉H₁₇NO₂
CAS No.: 60142-96-3

NC1CCC(CC1)C(=O)O

Analyte	Certified Concentration ± associated uncertainty U , $u = k \cdot u$ ($k = 2$)
Gabapentin	1.00 ± 0.01 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 3.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 3.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use. Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB  
Darren Ellsworth, Quality Assurance Manager

May 17, 2021
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A, Round Rock, TX, 78665, USA.
Tel: 800-948-7837 / 512-238-9974; www.cerilliant.com
Sigma-Aldrich Production GmbH is a subsidiary of Merck KGaA, Darmstadt, Germany.

G-007-1ML
Revision 00

Certificate Page 1 of 8

Challenges: 4. Regulation/Accreditation

There are no off the shelf test methods. Each laboratory **MUST** complete their own:

- Development
- Validation
- Sign-off
- Accreditation

*Includes adding drugs to an established method.



ISO/IEC 17025

Testing and calibration laboratories

ISO/IEC 17025 enables laboratories to demonstrate that they operate competently and generate valid results, thereby promoting confidence in their work both nationally and around the world.

LAB 51

Edition 2 January 2023

UKAS accreditation of laboratories performing analysis of toxicology samples



Forensic Science
Regulator

Challenges: Post Mortem Toxicology

- There is no legislation which impacts on the scope of our testing.
- We need to test for as wide a range of drugs as possible, and quantify all that we can, to answer:
 - What drugs may have contributed to this death?
 - If not an acute intoxication of drugs, what drugs may have been affecting their behaviour or functioning?
e.g. Hallucinogens, Anti-Epileptics
- Are we missing something? Unknown drugs?

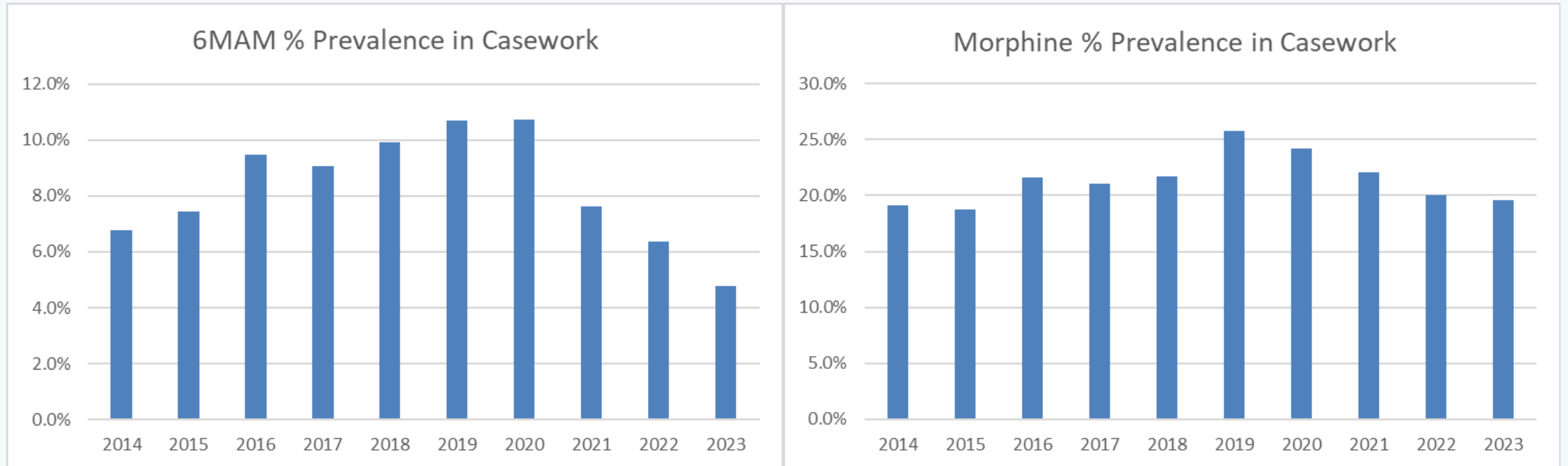
What we see in Post Mortem Toxicology

What drugs do we see in deaths?

- Alcohol
- Morphine (mixture of prescribed, heroin and metabolite of codeine)
- Methadone
- Diazepam
- Bromazolam
- Etizolam
- Codeine (mixture of prescribed and heroin)
- Mirtazapine
- Paracetamol
- Cocaine
- Pregabalin
- Gabapentin

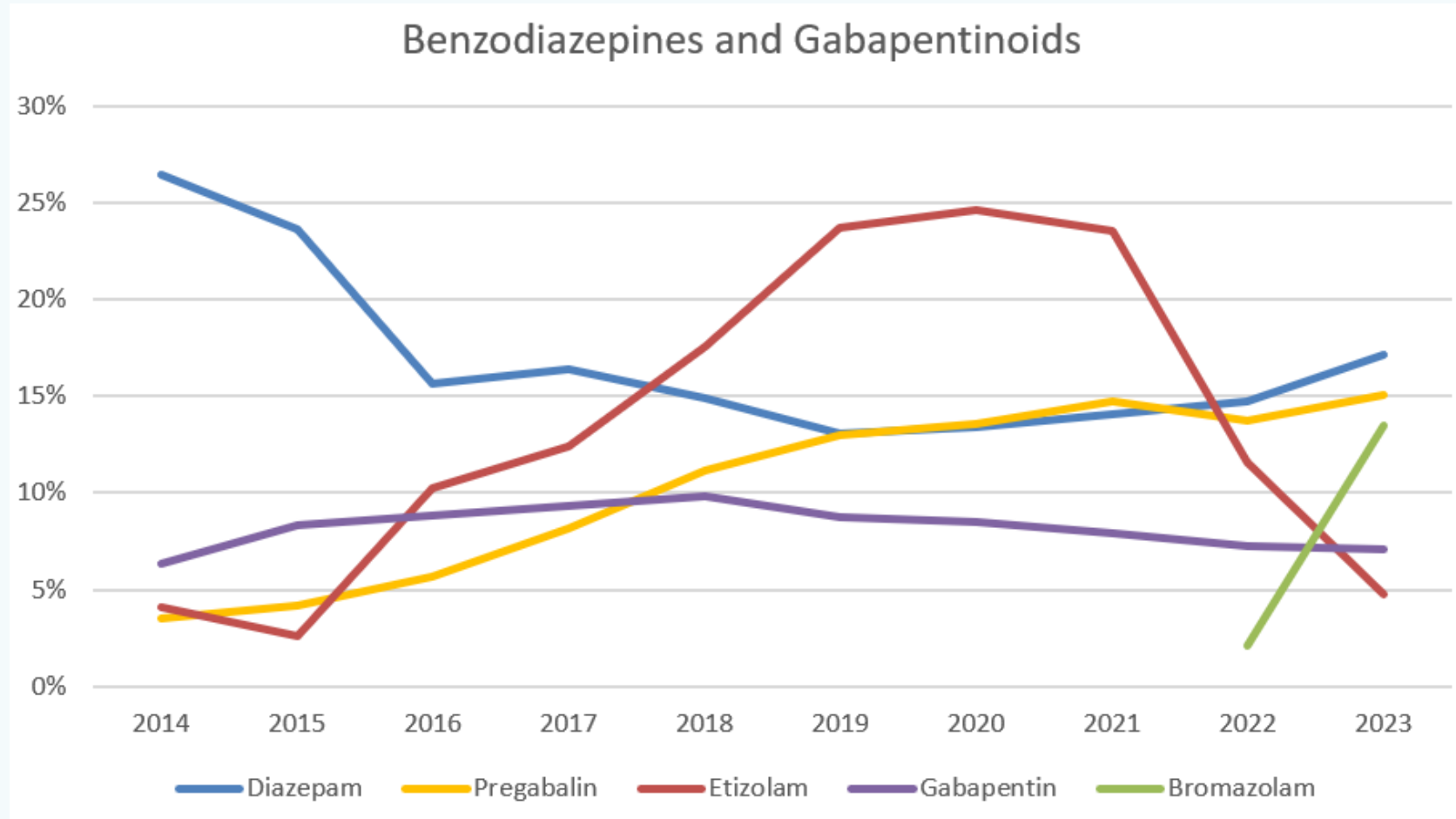
Mostly
Respiratory Depressants

Service Data 2014-2023: 6MAM/Morphine

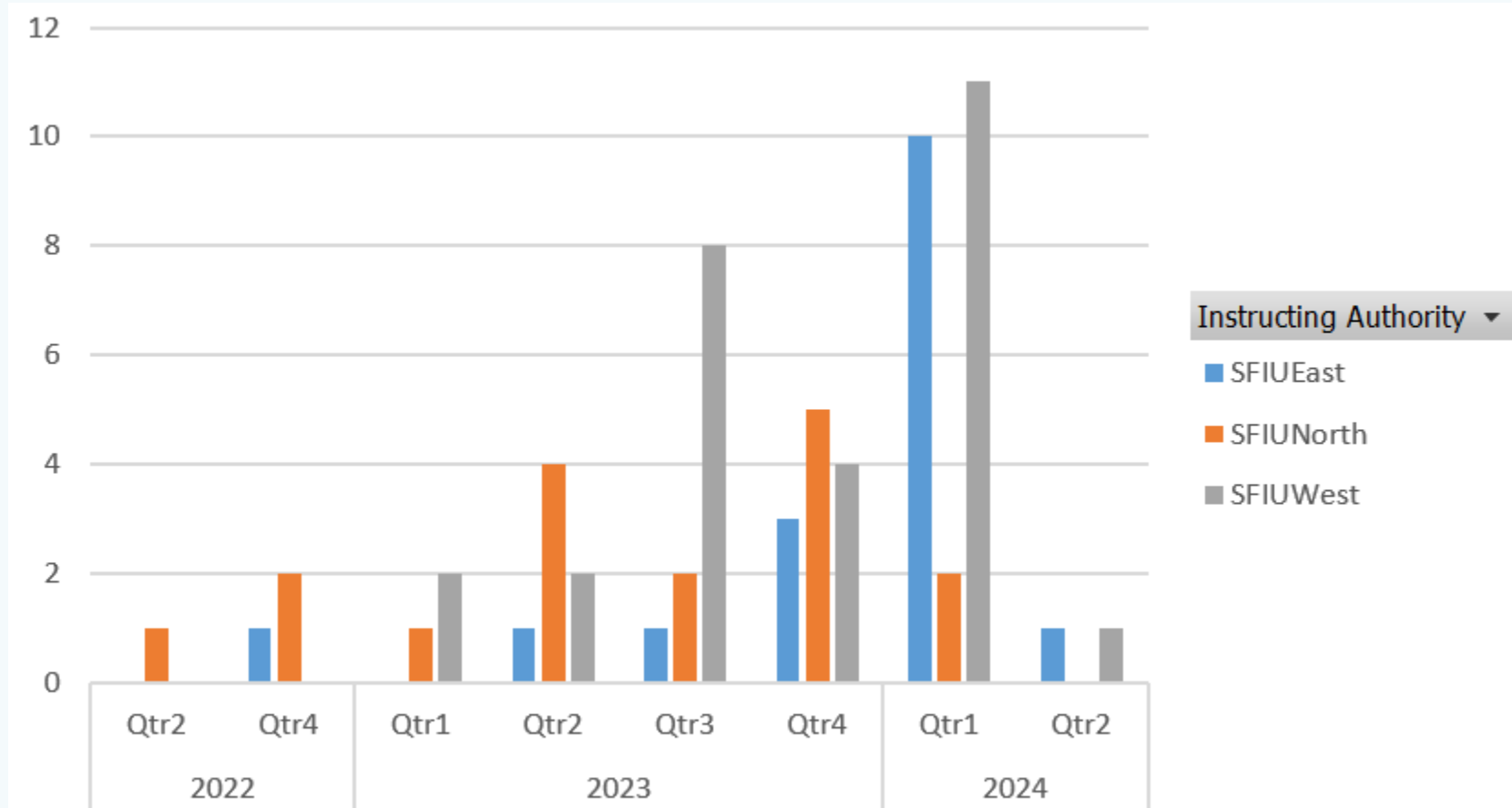


Evidence of increasing prevalence of **delayed deaths** due to **poly drug use**?

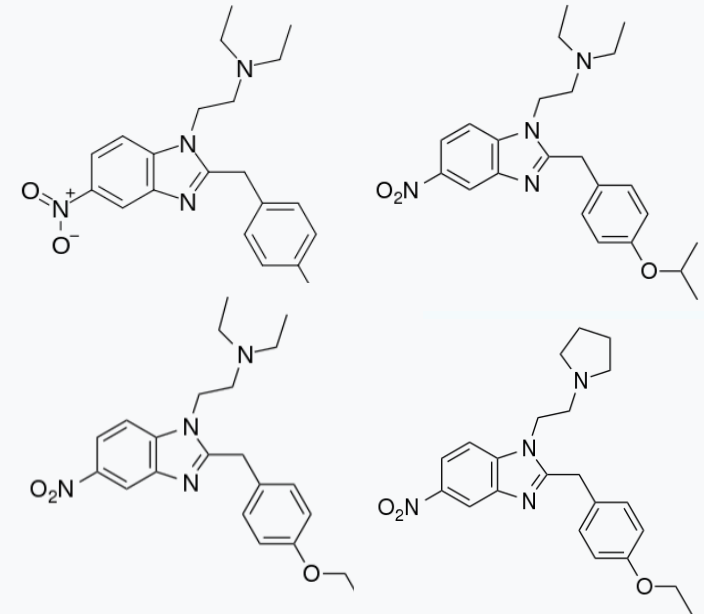
Service Data 2014-2023: “Valium”



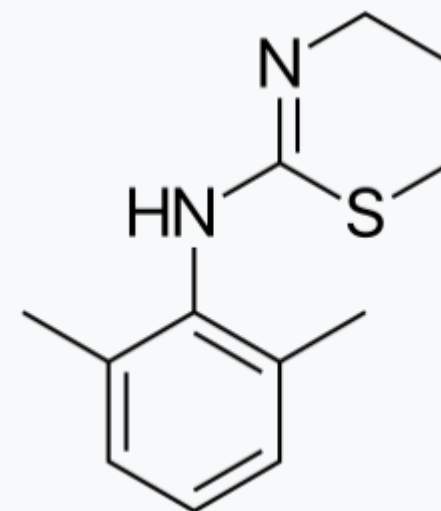
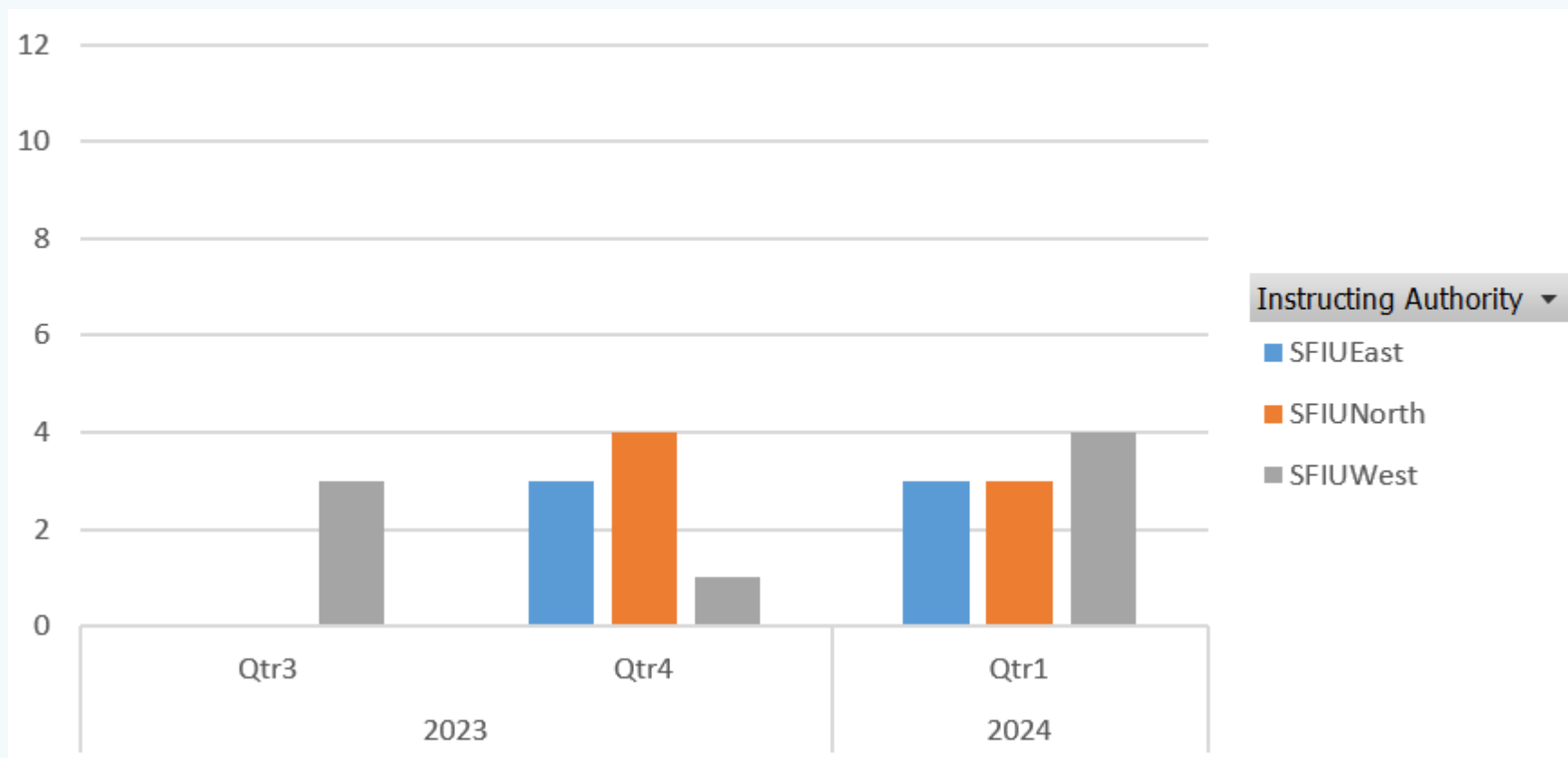
Scotland Wide Data: Nitazenes



Metonitazene
 Protonitazene
 Isotonitazene
 Etonitazepyne

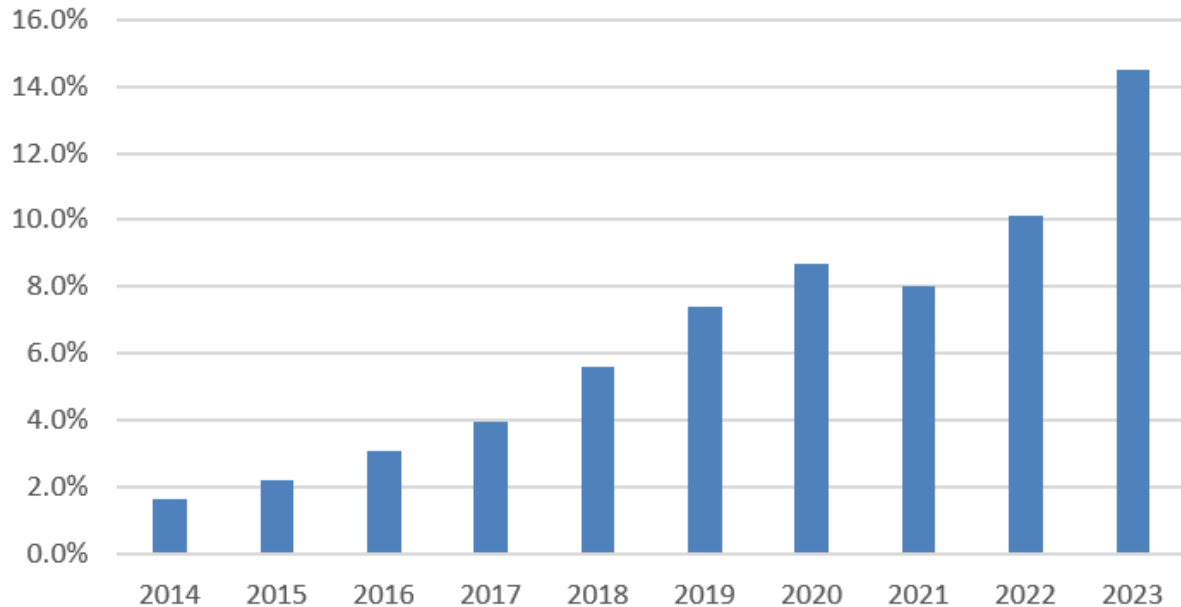


Scotland Wide Data: Xylazine

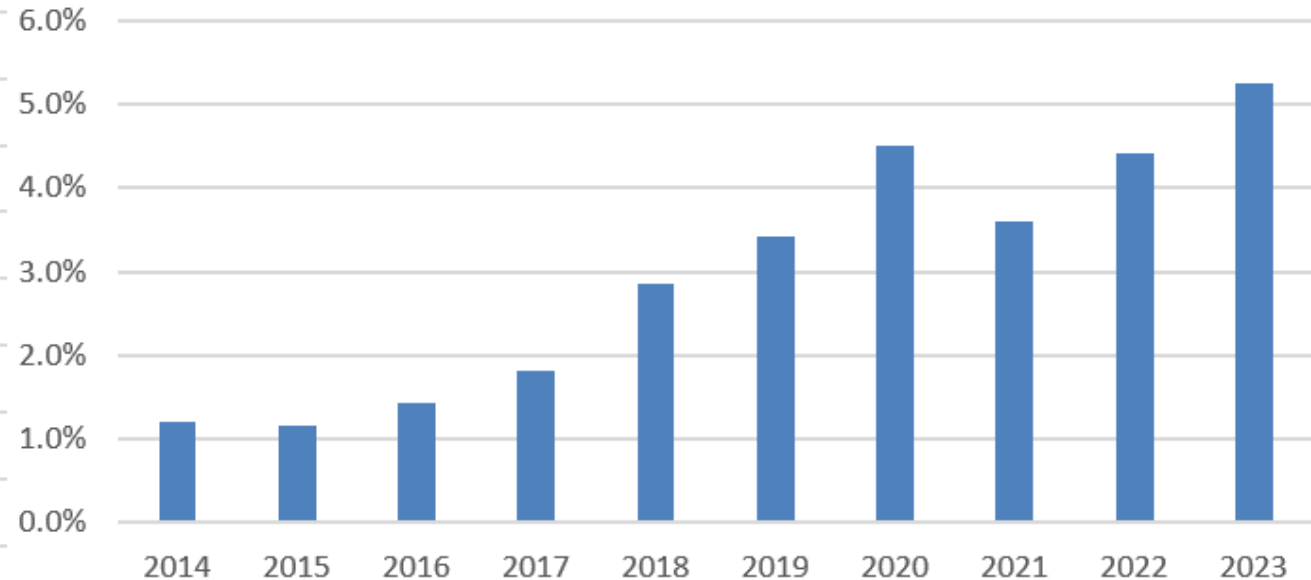


Service Data 2014-2023: Cocaine

Cocaine % Prevalence in Casework

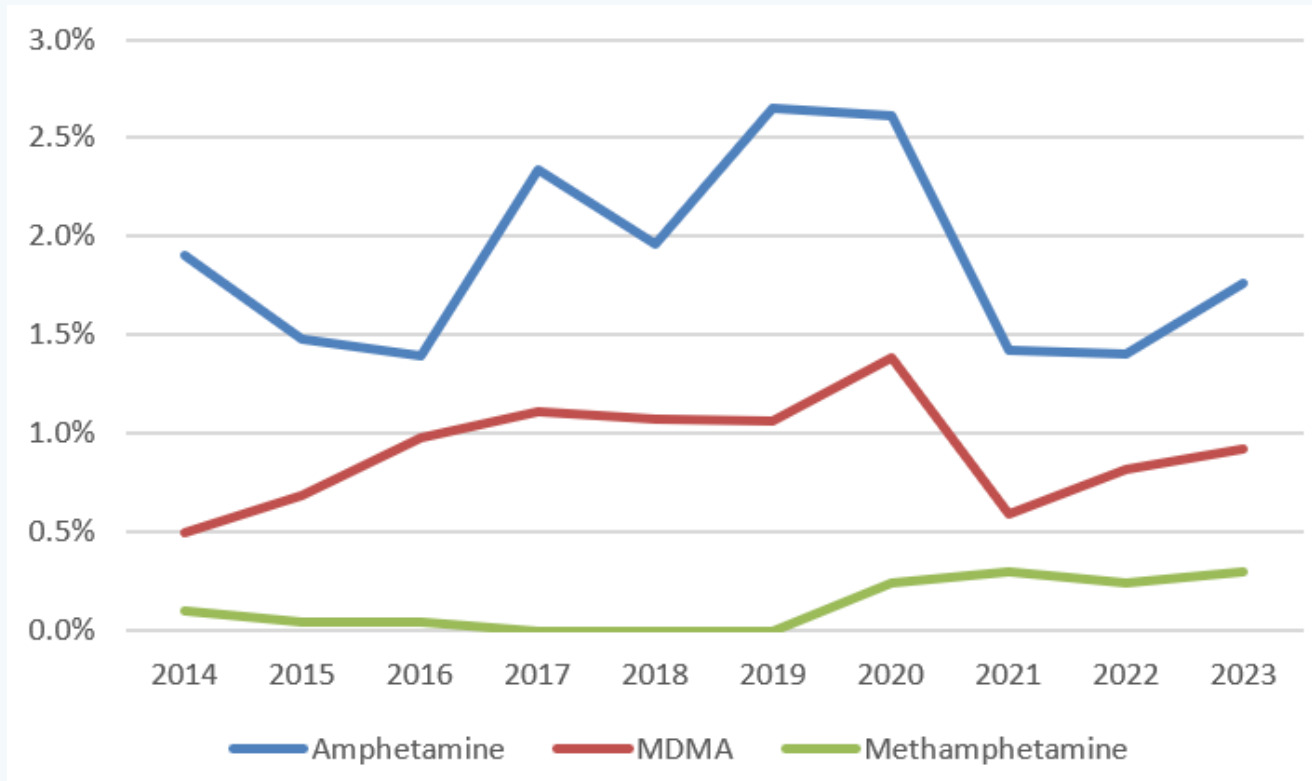


Cocaethylene % Prevalence in Casework



Evidence of increasing Cocaine purity/route of ingestion/cocaine+alcohol?

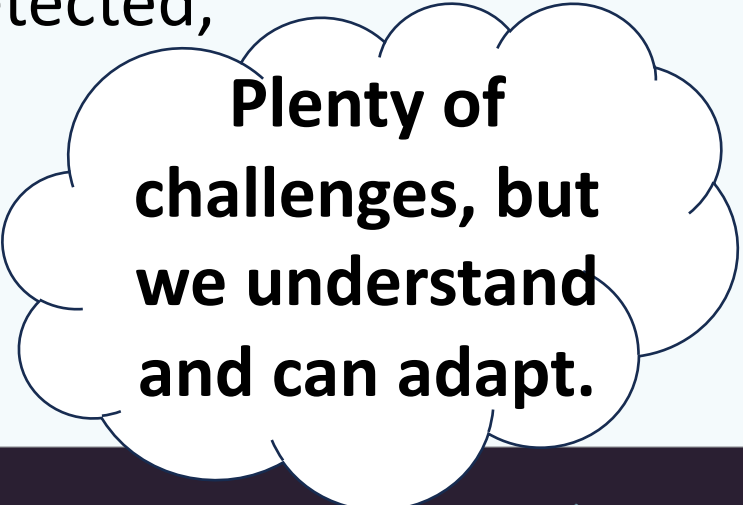
Service Data 2014-2023: Amphetamines



Trend of increasing
Methamphetamine use?

Conclusions – Trends in Drugs and Use

- Dip in 2021, in line with national drug related death statistics then **rebounding/increasing in 2022 and 2023.**
- Reduction of 6MAM prevalence indicative of increased poly-drug use and **more delayed deaths?**
- 4 different nitazenes detected in Scotland, **passed the peak?**
- No nitazene only deaths, very low concentrations detected, **significant to COD?**
- Xylazine is being detected **sporadically.**
- Initial signs of **increasing methamphetamine** use?
- Will **Bromazolam** replace **Etizolam** completely?



Plenty of challenges, but we understand and can adapt.

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Thank You

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