

Annual Report
Adroddiad Blynyddol

April 2022 - March 2023



Bromazolam
Cocaine
MDMB-4en-PINACA

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Foreword

In September 2013, the **WEDINOS** programme received our first sample: an unknown white powder from Newport submitted via Kaleidoscope. Our analysis identified the substance as para-chloroamphetamine, amphetamine, benzocaine and N-Ethyl-norketamine. Thus began a drug checking programme unlike any other in the United Kingdom.

Over the past ten years, with the support of Welsh Government, **WEDINOS** has processed almost 30,000 samples submitted from community members, drug services, health care providers, criminal justice settings, night time economy venues and other sources across Wales and the wider UK. **WEDINOS** is the widest ranging drug checking programme in the UK and forms an integral part of the harm reduction strategy here in Wales.

Over the past decade, we have seen increasing demands for our services. As detailed in this report, in the past year **WEDINOS** processed nearly 6,700 samples, three times the number processed five years ago. Almost 5,000 of these came from community sources, illustrating the important role the programme plays in monitoring drug trends in Wales and the UK. It enables **WEDINOS** to flag the entry of new and potentially dangerous substances, such as nitazines and xylazine, into the drug market, allowing us to issue community alerts and create new harm reduction messaging.

This report shows benzodiazepines remain the most commonly identified group of psychoactive substances submitted, with a total of 18 identified. **WEDINOS** analysis again highlights concerns of substance substitution within the UK drug market. Over the past year, Bromazolam was the most commonly identified benzodiazepine, and most often purchased with the belief that it was Diazepam. Because Bromazolam is more potent than Diazepam, this creates enhanced risk of harm and overdose as individual consumers are not aware of dose, time of onset of effects, duration of effects or contraindications with other substances.

WEDINOS continues to provide a high quality, accessible and important service that is critical to the harm reduction response in Wales. A big thanks to the **WEDINOS** team, our collaborating partners, and all those submitting samples to ensure this valuable work continues

Professor Rick Lines,
Head of Substance Misuse, Public Health Wales and
WEDINOS Programme Lead

Headline Figures 2022/23

Total to date:

33,917 samples received
 29,954 analysed

- 641 substances identified either in isolation or combination.
- Over 300 organisations and services - Including: Emergency Departments, Local Health Teams, Substance Misuse Services, Housing and Homelessness, Education Centres, Training Providers, Night Time Economy Venues, Festivals, Criminal Justice Services and Welsh Prisons.

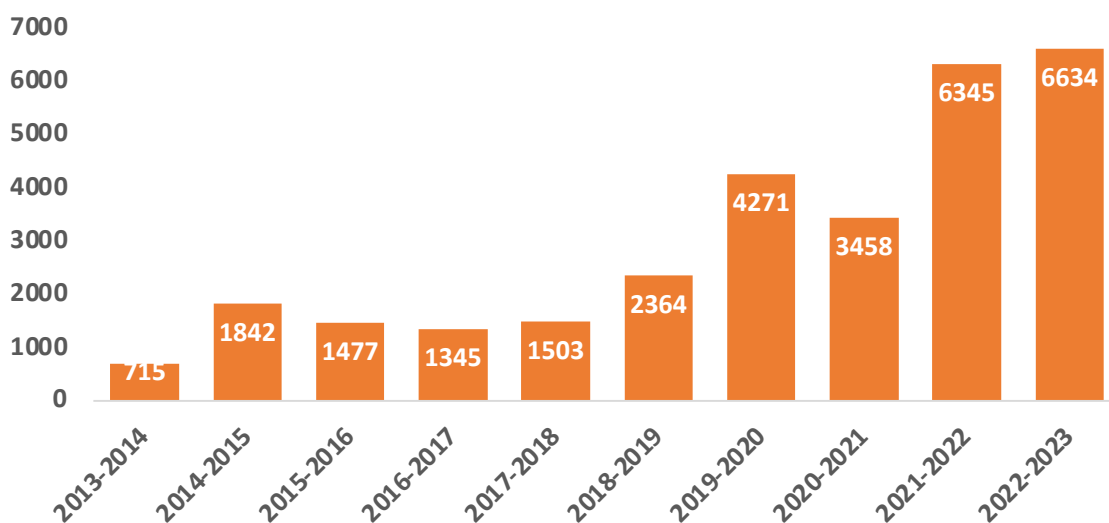
Samples are also provided by individuals not engaged with / accessing services.

This Year 2022/23:

- 7,744 samples received representing an increase ▲ from 7,457 in 2021/22.
- 6,656 analysed ▲ from 6,345.
- Community samples increased ▲ to 4,979 from 4,684.
- 185 substances identified ▲ from 181.
- 75 different organisations, services and Night Time Economy (NTE) venues.
- Median age of sample providers 33 years (range 12 to 80 years).
- As in the previous five years benzodiazepines were the most commonly identified class of psychoactive substance with 18 identified.
- Cocaine was the most commonly identified substance.
- Most commonly identified in the community was bromazolam, followed by MDMA.
- Cocaine was the most commonly identified substance in the NTE.
- Criminal justice settings – the Synthetic Cannabinoid Receptor Agonist (SCRA) MDMB-4en-PINACA was the most commonly identified substance, however more samples were profiled as “no active compound”.

benzodiazepines
 bromazolam
 cocaine
 MDMB-4en-PINACA

Fig. 1: Number of samples submitted to WEDINOS by year



A Wider Perspective . . .

Global, European, England & Wales, and Welsh estimates:

10th
Anniversary

October 2023 marks the 10th anniversary of the launch of the WEDINOS programme, along with receipt, analysis and the publications of results of the first sample. This was an unknown white powder, submitted via one of the community based drug services. Following analysis this sample that had caused the unexpected effects of nosebleeds, depression and suicidal ideation, it was profiled as containing para-chloroamphetamine, amphetamine, N-ethylnormetamine and benzocaine.

Since then WEDINOS has monitored drug trends across Wales and the UK, whilst sharing information with, and receiving information from, regional national and international partners to ensure the continued provision of timely and pragmatic harm reduction information for people who use drugs and those working or concerned with the care of people who use drugs.

Globally, the United Nations Office for Drugs and Crime (UNODC) estimates that in 2020 around 284 million people use drugs, equating to 5.6 per cent of the global population aged 15 to 64 years. This figure represents a 26 per cent increase from 2010. This includes an estimated 11.2 million people who inject drugs, there was no measurable difference from the previous year (2020 compared to 2019).

38.6 million people are estimated to be drug dependent and/or require treatment services. The majority of these individuals are people who use cannabis or opioids.¹

Global Burden of Disease Study, which estimated that there were 494,000 drug-related deaths in 2019. This indicates a 17.5 per cent increase in deaths attributed to drugs between 2009 and 2019.

Of those deaths 366,000 were deaths indirectly related to drug use, e.g. liver disease due to hepatitis, HIV and AIDS, self-harm associated with drug use.

Deaths attributed to drug use disorders (128,000) accounted for 26 per cent, of which opioid use disorders contributed to 69 per cent, or 88,000 deaths.²

For the European Union, the European Monitoring Council for Drugs and Drug Addiction (EMCDDA), reported that around 83.4 million people, or 29 per cent of the population aged 15 to 64, had tried illicit drugs at least once in their lifetime. With over 22 million reporting use in the last year.^{3,*}

In the United Kingdom, the Crime Survey for England and Wales (CSEW), drug misuse in England and Wales: year ending June 2022 reported that approximately 3 million people, or 9.2 per cent of adults aged 16 to 59 had taken a drug in the last year. Around 1 in 5 of 16 to 24 year olds, 18.6 per cent, reported taking a drug in the last year.

Cannabis remains the most commonly used substance in the UK, having been reported as such since records began in 1995. There was no change in the prevalence of cocaine use, year ending June 2022, compared to the year ending June 2020.⁴

366,000
people died as a result of drug use

1. UNODC - World Drug Report 2022 (United Nations publication, Sales No. E.21.XI.8), https://www.unodc.org/res/wdr2022/MS/WDR22_Booklet_2.pdf [accessed 2nd May 2023]

2. UNODC - World Drug Report 2021 (United Nations publication, Sales No. E.21.XI.8), https://www.unodc.org/res/wdr2021/field/WDR21_Booklet_2.pdf [accessed 2nd May 2023]

3. European Monitoring Centre for Drugs and Drug Addiction (2022), European Drug Report 2022: Trends and Developments, Publications Office of the European Union, Luxembourg; https://www.emcdda.europa.eu/publications/edr/trends-developments/2022_en [accessed 2nd May 2023]

4. Crime Survey for England and Wales 2021/22; Drug misuse in England and Wales: year ending June 2022. <https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/drugmisuseinenglandandwales/yearendingjune2022> [accessed 2nd May 2023]

* This should be regarded as a minimum estimate due to reporting biases.

A Picture from Wales

Provisional headline figures for problem drug use estimates in Wales,** including populations not in contact with any services, suggest that the total number of problem drug users in 2020-21 was 51,110 (95 per cent confidence interval (CI) 38,100 – 68,340).

There were 17,396 assessments (15,215 unique individuals) within substance misuse services in Wales in 2021-22, representing an increase of 0.8 per cent compared to the previous year (17,259 assessments).

Of the individuals assessed:

- 7,423 (48.8 per cent) were primary problematic alcohol clients
- 6,730 (44.2 per cent) were primary problematic drug clients
- 1,062 (7.0 per cent) did not have a substance recorded

Amongst assessments for problematic drug use, opioids, principally heroin, were cited as the most prevalent primary substance with 2,808 assessments (37.0 per cent). Cannabis was the next most frequently reported substance with 1,663 assessments (21.9 per cent). The number of assessments with cocaine as the primary substance has increased from 928 in 2016-17 to 970 in 2021-22. This is an increase of 4.5 per cent and represents 12.8 per cent of all referrals to substance misuse services in 2021-22.

In Wales, overall, the number of hospital admissions for poisonings with named illicit drugs has decreased by 12.8 per cent in the last year, from 5,561 in 2020-21 to 4,849 in 2021-22. Opioids accounted for the highest number of individuals admitted to hospital for illicit drugs, followed by cannabinoids.***

In 2021, 322 deaths due to drug poisoning were registered in Wales, an increase of 43.8 per cent from the previous calendar year. Of all drug-poisoning deaths, 210 (65.2 per cent) were identified as a drug misuse death, an increase of 40.9 per cent from 149 deaths in 2020. Deaths involving opioids remain by far the most common substance group in relation to drug misuse deaths, predominantly deaths involving heroin/morphine.⁵

** In this context problem drug use (PDU) is defined by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) as "injecting drug use or long duration or regular use of opioids, cocaine and/or amphetamines (including amphetamine type substances)".

*** It is important to note that no distinction is possible in hospital admission data for differentiation between cannabinoid products: cannabis resin, stronger strains of herbal cannabis 'skunk;' or newer forms of synthetic cannabinoid receptor agonists (SCRAs), sometimes referred to as 'Spice'

5. Data mining Wales: The annual profile for substance misuse 2020-21; Public Health Wales; Cardiff; 2022; <https://phw.nhs.wales/publications/publications1/data-mining-wales-the-annual-profile-for-substance-misuse-2021-22/> [accessed 2nd May 2023]

WEDINOS.....Samples

In total, WEDINOS received and analysed 6,656 samples from 74 services and settings across the UK, as well as from individuals. These samples can be separated into three broad categories:

- Community
- Night Time Economy (NTE)
- Criminal Justice Settings

Samples submitted from the NTE and Criminal Justice Settings are submitted from amnesty bins or are non-attributable finds and therefore are not accompanied by any information relating to purchase intent, effects or demographics.

Key Findings What?

Within the 6,656 samples analysed by WEDINOS, 185 substances were profiled either in isolation or combination.

benzodiazepines

The most commonly identified chemical group of psychoactive substances for the fifth year were benzodiazepines, with 18 benzodiazepines identified (20 were identified in 2021/22). However, six were identified on ten or less occasions.

bromazolam

Bromazolam, a substance that is 99 per cent of the time profiled as a substitute within the illicit benzodiazepine market, was the most commonly identified benzodiazepine (n=678). Diazepam was the second most commonly identified substance, with 593 identifications, despite it being reported on 1,208 occasions as the purchase intent.

Bromazolam is more potent than diazepam. This is a potential risk for individuals using benzodiazepines as dosage and potency varies greatly.

cocaine

As in 2021/22 and pre-COVID-19 restriction trends, cocaine was the most commonly identified psychoactive substance identified by WEDINOS.

The most recently published CSEW 2021/22 report, stated that there was no change in last year's use of cocaine among adults aged 16 to 59 from the previous year. However, Public Health Wales has reported an increase in the number of assessments completed by substance misuse services where the primary drug of choice is cocaine.

Consistent with previous years, caffeine was the most popular bulking/cutting agent identified, as well as being found in combination with other substances, several samples of powders and tablets were found to contain caffeine in isolation, in particular amongst samples submitted as MDMA.

Table 1: Most commonly identified mind altering/psychoactive substance WEDINOS samples

	2022/23	2021/22
1	Cocaine	Cocaine
2	MDMA	MDMA
3	Bromazolam	Diazepam
4	Diazepam	Ketamine
5	Ketamine	Caffeine
6	Caffeine	No Active Component Identified
7	Tetrahydrocannabinol	Etizolam
8	Alprazolam	Tetrahydrocannabinol
9	Paracetamol	Cannabidiol
10	Nicotine	Flubromazolam

As previously mentioned, WEDINOS receives samples from a wide variety of community settings. WEDINOS works closely with the six Welsh prisons, reporting separately on finds that have no evidentiary value. In the next section of this report we focus on samples from community settings.

Community Settings . . .

4,979 samples were submitted from community settings including education, health (incl. Emergency Departments), mental health, housing and homelessness, substance misuse services and individuals.

Of these 4,979 samples, demographic information was available for 97 per cent (n=4,812).

79 **21**

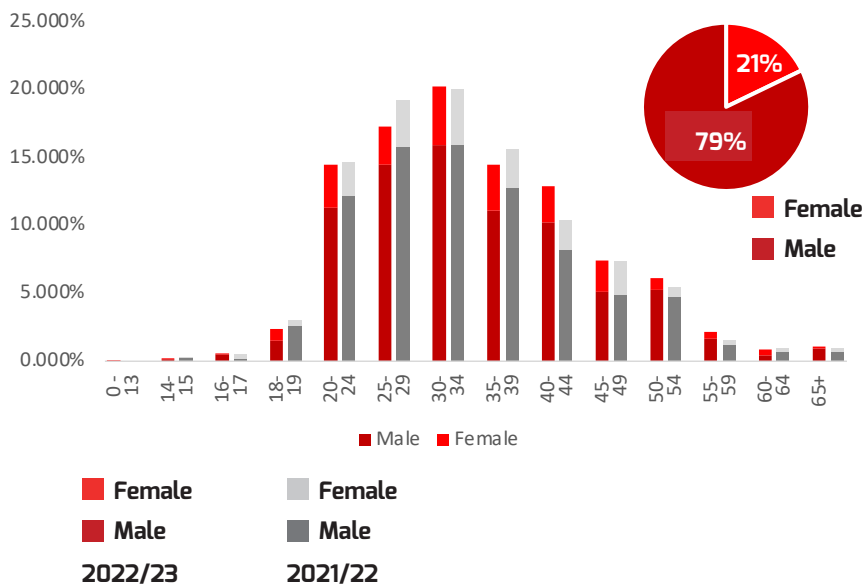
 Per cent

Where demographic data was available 79 per cent of the samples were submitted by males and 21 per cent by females. This is the same male/female split amongst sample providers as the previous year.

The median age for all mind altering / psychoactive sample providers (Wales and wider UK) was 33 years, range 12 to 80 years, in comparison to 33 years and 14 to 80 years in 2021-2022.

- Females - median age was 34 years (33 years in 2021-2022) (range: 12-74 years)
- Males - median age was 33 years (32 years in 2021-2022) (range: 14-80 years)

Chart 1: Profile of Psychoactive Sample Providers



Community Samples: What?

Since the launch of **WEDINOS** in 2013, the project has consistently evidenced the substitution of substances within the UK's illicit drug market.

In the 4,684 samples submitted via community based sample providers, 170 substances were profiled either in isolation or combination.

Table 2 shows the changes in the "top ten most common" substances at the submission stage (purchase intent) and the post analysis stage.

Samples may be categorised as unknown for several reasons, this includes: where the purchase intent lists a sample as unknown, or found; such as those submitted from a health care setting, such as an emergency department or mental health ward

Table 2: Most common substances pre (perceived) and post (actual) analysis

	Community purchase intent	Community post analysis
1	Diazepam	Bromazolam
2	MDMA	MDMA
3	Alprazolam	Diazepam
4	Cocaine	Cocaine
5	Unknown	Caffeine
6	Cannabis/THC/CBD product	Ketamine
7	Ketamine	Alprazolam
8	Amphetamine	No Active Component Identified
9	Zopiclone	Tetrahydrocannabinol
10	2C-B	Amphetamine

Table 2 demonstrates changes between the substance most commonly reported pre analysis; and the most commonly identified contents post analysis.

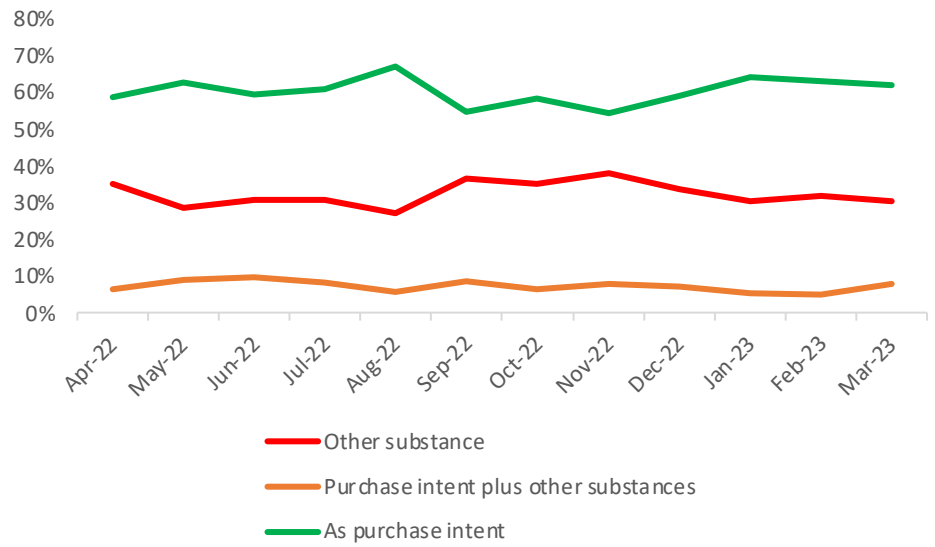
Bromazolam was the most commonly identified substance identified overall, with another benzodiazepine, etizolam, the eleventh most common. Following analysis these substances were identified a combined total of 819 times. However, these substances were only named 44 times as the substance intended for purchase (8 bromazolam and 36 etizolam).

It may be argued that the high pre analysis presence of "unknown" substances would be the biggest influencer of this change. However, even following removing these samples we find that over the past year 39 per cent of samples submitted to **WEDINOS** with a substance listed in the purchase intent did not contain what was expected, this is up from 35 per cent 2021-22.

Some samples were found to contain the purchase intent and other substances, such as sample purchased as MDMA, that were found to contain MDMA and 3-methylmethcathinone upon analysis. Other samples were found to contain a different substance or substances. For example, a sample purchased as diazepam, which was found to contain bromazolam.

The levels of additional substances and substitution are shown in graph 1.

Graph 1: Sample contents - post analysis

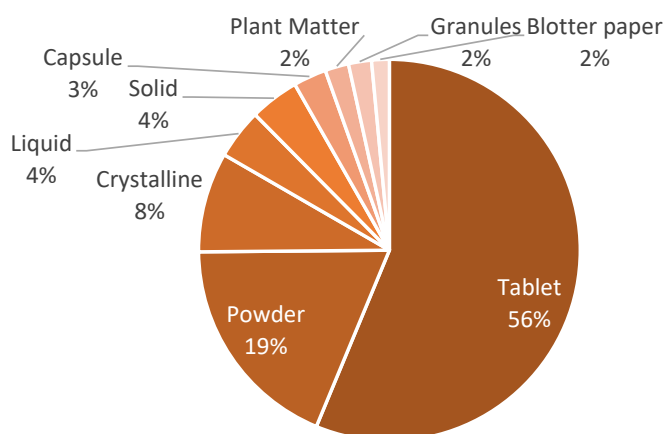


Community: How?

Form of sample

WEDINOS requests the 'form of sample' for each submission to monitor and report the various forms substances appear on the market and potential differences in method of consumption.

Chart 2: Form of Psychoactive Samples



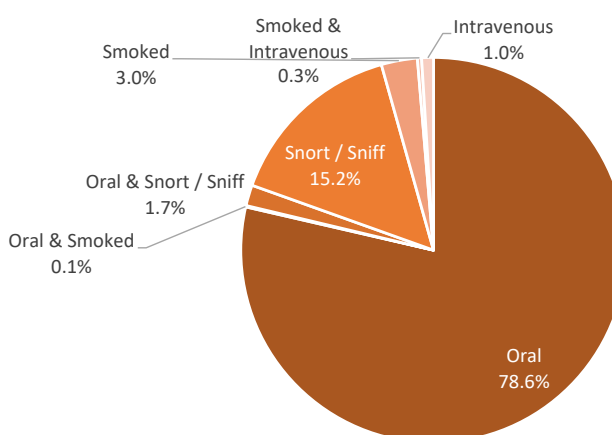
As in the previous two years, we see a high proportion of tablets submitted overall, this is mirrored by the high numbers of samples submitted believed to be diazepam and alprazolam.

Method of Consumption and Harm Reduction Advice

Assuming that all plant matter samples and vape liquids are smoked/vaped, the remaining samples (pills, liquids, tabs, granules etc.) were ingested through a variety of methods. The most common of these was oral ingestion (swallowing, 'bombing') reported in 78.6 per cent of samples. This high prevalence of oral consumption is likely linked to the high number of submissions purchased as benzodiazepines, particularly diazepam and alprazolam, alongside a prevalence of MDMA tablets

Oral consumption is followed by snorting/sniffing at 15.2 per cent, as shown in Chart 3.

Chart 3: Method of Consumption



1.3 per cent of sample providers reported intravenous injecting of substances.

Samples injected were purchased as, and found to contain, heroin, amphetamine, methamphetamine, mephedrone and ketamine.

Injecting drug use carries with it inherent risks of bacterial and viral infection over and above the potential risks/toxicity of the substance being injected.

Regardless of substance, injecting drug use carries potential risk of infection (especially if sharing or reusing injecting equipment) and overdose. Individuals who currently inject drugs, or have previously injected, should get tested for blood borne viruses.

Injecting

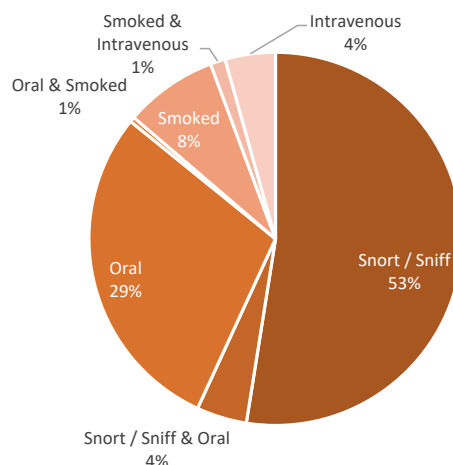


Do not share any injecting equipment; this includes water, spoons and filters as well as needles and syringes. It is best practice to use a filter for drawing up.
 Ensure you have enough needles for repeat injecting.
 Rotate sites.
 Ensure any wounds are treated as soon as possible
 If you experience heat or redness at an injecting site - seek medical attention
 Ensure that your equipment is correct for its intended use
 Injecting intensifies everything about the drug experience
 Most New Psychoactive Substances are water soluble and do not require the addition of an acid (usually citric acid or ascorbic acid (Vit C)).

Powders and Crystalline Materials

The most common method of consumption of powders, granules and crystalline materials was snorting / sniffing, with 53 per cent reporting this method (as shown in Chart 4). This figure is comparable to 2021-22 when including it with mixed methods of consumption, including oral consumption.

Chart 4 : Method of Consumption: Powders



Snorting/sniffing potentially caustic or toxic substances carries additional risks related to damage to the nasal passages, as well as potential transmission of blood borne viral infection when sharing snorting paraphernalia in the presence of nasal passage damage and blood.

Insufflation (Sniffing/Snorting)



- Always use clean devices (snorter).
- User your own device.
- Do not share devices as there may be traces of blood on your equipment.
- Snort high up the nostril to avoid the most sensitive soft tissue.
- Clean out nasal passages after use with damp tissue or an ear bud.
- Alternate nostrils to lesson damage to one side.
- If your nose is bleeding - give it a rest.

Benzodiazepine toxicity

The primary toxicity of benzodiazepines is on the central nervous system. These effects can be potentially more severe when depressant drugs such as alcohol and opioids are consumed at the same time, or during the period in which benzodiazepines are still present and active in the body.

The duration of effects of benzodiazepines can vary greatly depending on whether it is a short, medium or long acting benzodiazepine. For example the duration of action for bromazolam is 5 to 8 hours.⁹ However the half-life* of these substances can be much longer. For example, the half-life of diazepam can be between 20 and 100 hours.¹⁰

Benzodiazepine deaths

The Office for National Statistics reported a 13 per cent increase in deaths involving benzodiazepines in England and Wales in 2021, rising from 476 to 538 deaths. They also reported a significant increase in deaths involving psychoactive substances, commenting that this rise was driven by the number of deaths involving new benzodiazepines, primarily flubromazolam and etizolam. Deaths involving new benzodiazepines rose from 62 in 2020 to 171 in 2021.¹¹

Benzodiazepines are being commonly mentioned within drug related death reports in some European countries, however, most commonly they are mentioned in combination with other substances.¹²

In the United States of America there was an increase from 0.46 drug deaths involving benzodiazepines per 100,000 individuals to 2.96 per 100,000 individuals in 2019. During that period 118,208 drug related deaths mentioned benzodiazepines. Nine per cent (n=10,677) did not involve opioids, cocaine, other psychostimulants, barbiturates, or alcohol. Among these deaths, 4709 involved no other specified substance.¹³

McAuley et al., when describing drug related deaths in Scotland, found there had been a 19-fold increase in deaths involving the benzodiazepine etizolam in the five years between 2015 (43 in 706 deaths) and 2020 (806 in 1,339 deaths). However, out of the 806 deaths where etizolam was mentioned, it was only mentioned one per cent of the time (n=8) in isolation.¹⁴

However, the increased risk of adverse effects does not just lie with poly-drug use. As WEDINOS has evidenced over the past several years there is a high rate of substitution within the illicit benzodiazepine market, with the European Monitoring Council for Drugs and Drug Addiction (EMCDDA) citing concerns over the growing crossover between the illicit drugs and the novel psychoactive substance markets. In this section we will describe this crossover in relation to samples submitted to WEDINOS as diazepam (Valium) that, following analysis are found to contain other substances, primarily new / designer benzodiazepines. In 2021, the EMCDDA reported monitoring 30 of these new benzodiazepines.¹⁵

9. World Health Organisation, Critical review report: Bromazolam, Expert Committee on Drug Dependence, Forty-fifth Meeting, Geneva, 10–14 October 2022: https://cdn.who.int/media/docs/default-source/controlled-substances/45th-ecdd/bromazolam_draft.pdf?sfvrsn=f1bc761e_1#:text=Informational%20websites%20for%20users%20list%20a%20dosage%20range,and%20the%20duration%20of%20action%20is%205%E2%80%938%20h [accessed 4th May 2023]

* Half-life is the time taken for blood concentration of a substance to fall to half its peak value after a single dose.

10. Benzodiazepine equivalence table: <https://www.benzo.org.uk/bzequiv.htm> [accessed 4th May 2023]

11. Drug misuse in England and Wales: year ending March 2021; Office for National Statistics, 3rd August 2022: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2021registrations> [accessed 4th May 2023]

12. European Monitoring Centre for Drugs and Drug Addiction (2022), European Drug Report 2022: Trends and Developments, Publications Office of the European Union, Luxembourg. https://www.emcdda.europa.eu/publications/edr/trends-developments/2022_en [accessed 4th May 2023]

13. Kleinman, R.A., Weiss, R.D. Benzodiazepine-Involved Overdose Deaths in the USA: 2000–2019. *J GEN INTERN MED* 37, 2103–2109 (2022). <https://doi.org/10.1007/s11606-021-07035-6> [accessed 4th May 2023]

14. A McAuley, C Matheson, JR Robertson, From the clinic to the street: the changing role of benzodiazepines in the Scottish overdose epidemic, *International Journal of Drug Policy*, Volume 100, 2022, 103512, ISSN 0955-3959, <https://doi.org/10.1016/j.drugpo.2021.103512> [accessed 4th May 2023]

15. European Monitoring Centre for Drugs and Drug Addiction (2021), New benzodiazepines in Europe – a review, Publications Office of the European Union, Luxembourg. https://www.emcdda.europa.eu/publications/rapid-communications/new-benzodiazepines-europe-review_en [accessed 4th May 2023]

These substances can often be more potent than the ones they replace, have a different time of onset and duration of effects, and therefore pose an increased risk of adverse effects.

Benzodiazepines - A Welsh Perspective

In 2021-22 there were 507 benzodiazepine related hospital admissions in Wales, involving 459 individuals. The European Age Standardised Rate was 27.1 admissions per 100,000 population. Compared to the last year (2020-2021) there has been a 37.9 per cent decrease in the number of admissions related to benzodiazepines.

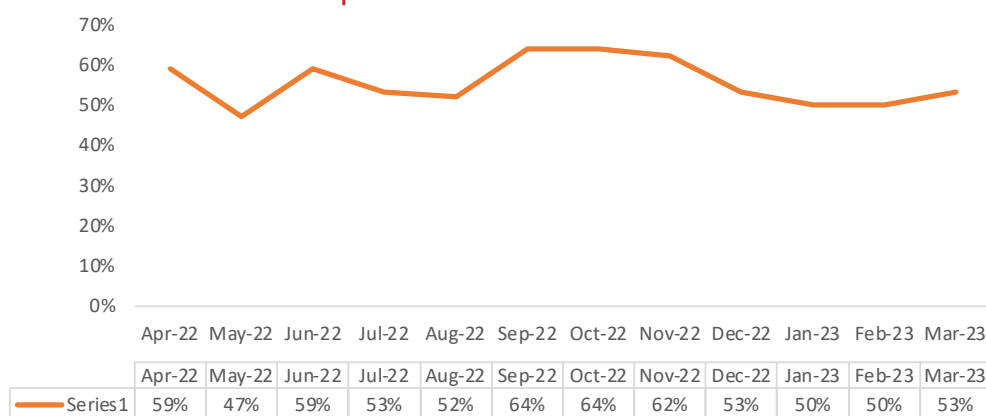
In 2021, 61 drug misuse deaths in Wales involved benzodiazepines, up from 35 in 2020.

Substitutions

In the reporting period 2022-23, WEDINOS received 1,208 samples submitted in the belief they were diazepam. Within these samples 38 substances were identified, either in isolation or combination. 28 samples were profiled as containing no active compounds.

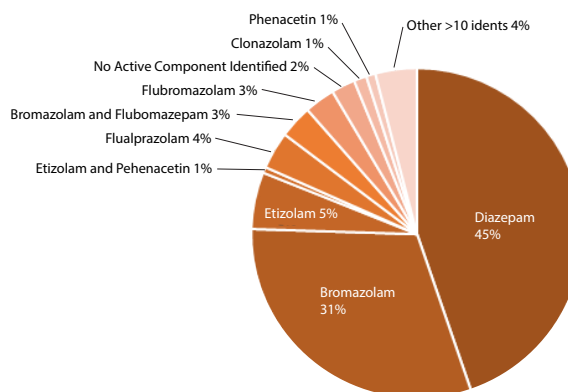
Despite being the purchase intent, diazepam (in isolation) was profiled as being the sample content following analysis in 45 per cent (n=539) of submissions, meaning a substitution rate of 55 per cent. This is a slight decrease in the level of substitution compared with 2021-22 (57 per cent). Throughout the year, the range of substitutions amongst samples submitted as diazepam was between to 47 per cent (May 2022) to 64 per cent (September and October 2022).

Graph 2: Percentage of substitution amongst samples submitted as diazepam



The most commonly identified substitute was the triazolobenzodiazepine, bromazolam. Bromazolam was identified in 34 per cent (n=411) of samples submitted as diazepam. Of those 411 samples, 91 per cent (n=372) contained etizolam in isolation, 9 per cent contained etizolam and phenacetin.

Chart 5: Diazepam Samples - Contents Post Analysis



Bromazolam is a triazolobenzodiazepine, structurally related to alprazolam. Originally developed as a candidate medicine, it was never approved for use. There is currently little scientific literature available relating to bromazolam.

A “common” oral dose of bromazolam, as described by users of the substance, is 1 to 3mg.¹⁶ The onset of effects is between 15 and 45 minutes, with a duration of action of 5 to 8 hours.

Self-reported effects of bromazolam consumption include: hypnotic, sedative, muscle relaxing, pain relieving, euphoria, increased confidence, empathy and amnesia.¹⁷

In the United Kingdom, bromazolam is controlled under the Psychoactive Substances Act 2016.

No data are available on the dependence and abuse potential of bromazolam. However, it can be assumed that the abuse liability and the potential to produce dependence are similar those of other chemically related benzodiazepines, such as alprazolam.

Direct access submission of samples to WEDINOS allows capture of evidence based local and national drug market trend data, enabling drug services to provide pragmatic information on relevant drug substitutions and harms. Combining this with other data sources such as hospitalisations, toxicology and drug related death data, further enables services to provide targeted information relating to specific substances and contraindications, in this instance addressing poly-drug use involving street purchased “diazepam”.

In March 2020 the Medicines and Healthcare products Regulatory Agency (MHRA), published a reminder to healthcare professionals in relation to benzodiazepines and opioids, a reminder of risk of potentially fatal respiratory depression. This highlighted the increased risk of sedation, respiratory depression, coma, and death whilst the substances are prescribed together.¹⁸

This message is also delivered by drug services to individuals who use illicit substances, including benzodiazepines (such as diazepam), opioids (heroin/morphine/tramadol) and alcohol.

W032012

Date Received: 23 Mar 2023

Postcode: KY39 -

Purchase Intent: Diazepam

Package Label: Not Stated

Sample Colour: Blue

Sample Form: Tablet

Consumption Method: Oral

Self-Reported Effects: Relaxed, Memory Loss, Loss of consciousness, Depression, Suicidal Ideation

Sample Upon Analysis (Major): Bromazolam

Sample Upon Analysis (Minor):



Click to Enlarge

16. European Monitoring Centre for Drugs and Drug Addiction (2021). New benzodiazepines in Europe – a review, Publications Office of the European Union, Luxembourg.

17. World Health Organization, Critical review report: Bromazolam, Expert Committee on Drug Dependence, Forty-fifth Meeting, Geneva, 10–14 October 2022; [https://cdn.who.int/media/docs/default-source/controlled-substances/45th-ecdd/bromazolam_draft.pdf?sfvrsn=f1bc761e_1#:text=informational%20websites%20for%20users%20list%20a%20dosage%20range.and%20the%20duration%20of%20action%20is%205%E2%80%938%20h](https://cdn.who.int/media/docs/default-source/controlled-substances/45th-ecdd/bromazolam_draft.pdf?sfvrsn=f1bc761e_1#:text=informational%20websites%20for%20users%20list%20a%20dosage%20range.and%20the%20duration%20of%20action%20is%205%E2%80%938%20h.). [accessed 4th May 2023]

18. Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression; Medicines and Healthcare products Regulatory Agency; 18th March 2020; <https://www.gov.uk/drug-safety-update/benzodiazepines-and-opioids-reminder-of-risk-of-potentially-fatal-respiratory-depression> [accessed 25th May 2022]

Nitazines

What are nitazenes?

2-Benzyl benzimidazole (nitazene) opioids were originally developed in the 1950s as analgesics. Several were shown to have potent opioid effects, but none were subsequently marketed anywhere as human or veterinary medicines. This group of opioids are structurally unrelated to other opioid drug groups, including morphine and fentanyl.

They are generally highly active, with potencies and efficacies of several analogues exceeding that of fentanyl. However there is very little information on their effects in humans.

Animal studies have shown a wide range in potency for this group of substances, which may also vary depending on the route of administration. When administered to mice subcutaneously, potency ranged from 1 (equal to morphine) for flunitazene to 1000 for etonitazene.¹⁹

The rank order of potency of a series of nitazenes was reported to be etonitazene >= isotonitazene > protonitazene >= metonitazene > butonitazene >= etodesnitazene >> 5-aminoisotonitazene = flunitazene > metodesnitazene.¹⁹

Preliminary unpublished data suggested that etonitazepyne is among the most potent of the nitazene opioids, being more potent than fentanyl and with MOR activation similar to that of etonitazene.¹⁹

United Kingdom Legal Status

In the UK, etonitazene and clonitazene are controlled under the Misuse of Drugs Act 1971 as Class A. All other 2-benzyl benzimidazole opioids are not currently controlled under the Misuse of Drugs Act 1971, although they are controlled under the Psychoactive Substances Act 2016.

Nitazenes and fatal drug related overdoses (United Kingdom)

Nitazene opioids have also been detected in the UK, where there were at least 24 fatalities involving isotonitazene and 3 involving etonitazepyne during 2021. In the majority of these cases nitazenes were mentioned alongside other substances.²⁰

Naloxone, responding to a nitazene overdose

There is a lack of evidence relating to the use of naloxone for specifically treating nitazene overdoses. However, there is evidence of its use reversing life-threatening respiratory depression and coma caused by subcutaneous metonitazene.²¹

19. ACMD report – A review of the evidence on the use and harms of 2-benzyl benzimidazole ('nitazene') and piperidine benzimidazolone ('bromphine-like') opioids; July 2022;

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1091152/ACMD_advice_on_2-benzyl_benzimidazole_and_piperidine_benzimidazolone_opioids.pdf [accessed 5th May 2023]

20. Vandeputte MM, Van Uytvanghe K, Layle NK, St Germaine DM, Iula DM, Stove CP. Synthesis, Chemical Characterization, and μ -Opioid Receptor Activity Assessment of the Emerging Group of "Nitazene" 2-Benzylbenzimidazole Synthetic Opioids. *ACS Chem Neurosci*. 2021 Apr 7;12(7):1241-1251. doi: 10.1021/acscchemneuro.1c00064. Epub 2021 Mar 24. PMID: 33759494.

21. Bromig, G. 'Über neue starkwirkende Analgetika und ihre klinische Erprobung', *Klinische Wochenschrift*, 36(20), pages 960-963. 1958 doi: 10.1007/BF01486702

In the article “What are Nitrazines?”, Prof. Ryan Marino (Emergency Medicine and Psychiatry at Case Western School of Medicine, Cleveland) states naloxone should be effective in treating people suffering from a nitrazine overdose, though higher doses may be needed, although more research is required into its effectiveness. In the same article Dr Krotulski added there is no evidence to suggest that the new synthetic opioids are naloxone-resistant. The question is around the dose required and re-dosing.²²

TOXBASE and the UK National Poisons Information Service suggest the use of naloxone if a patient has been exposed to any opioid drug and develops respiratory depression, airway obstruction or vomiting with impaired consciousness.

22. Castaneda, R. What are Nitrazines?
<https://health.usnews.com/drugs/articles/nitazenes>

WEDINOS and Nitazenes

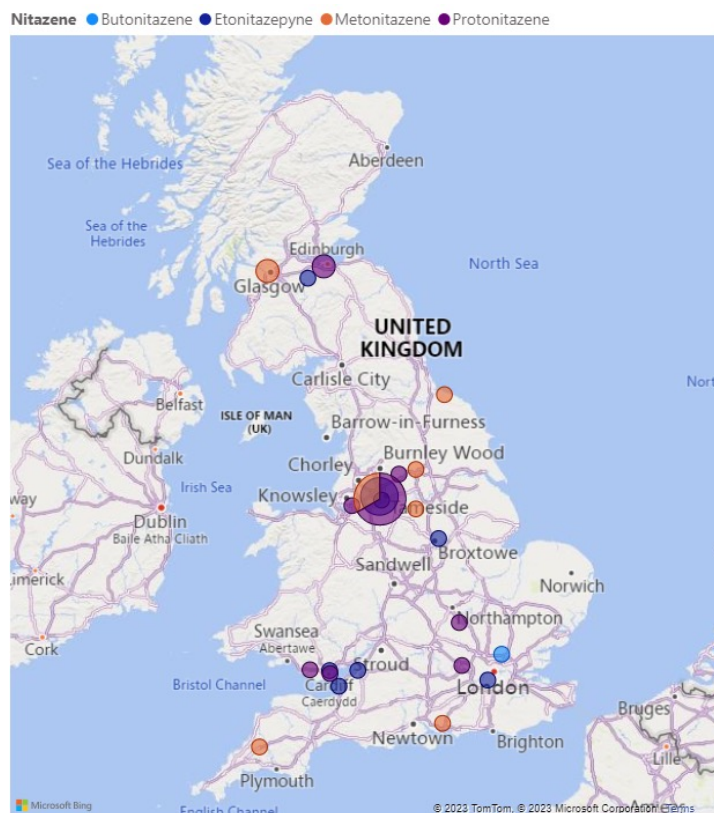
WEDINOS received the first sample profiled by the programme containing a nitazene on 14th April 2021. This sample (WEDINOS reference: W018254), was submitted as a found white powder, from the WF1 postcode, Wakefield. This sample contained metonitazene.

Since then the programme has received and analysed 45 samples that were also profiled as containing a nitazene. To date, WEDINOS has identified five nitazenes in samples submitted to the programme: butinitazene, etonitazepyne (N-pyrrolidino etonitazene), isotonitazene, metonitazene and protonitazene.

During the period April 2022 to March 2023, 36 samples were submitted that were profiled as containing a nitazene post analysis. None of these samples were submitted with a nitazene listed as the purchase intent. 64 per cent (n=23) of these samples were submitted in the belief that they were oxycodone.

22 per cent (n=8) were submitted in the belief that they were the benzodiazepines alprazolam (n=7) and diazepam (n=1). These samples were submitted in yellow powder form.

Samples containing nitazenes were submitted from throughout the UK mainland.



Xylazine

What is xylazine?

Xylazine is a partial alpha-2 adrenergic agonist, non-opioid, sedative analgesic medication used as a veterinary tranquilliser for non-human mammals.

Initially discovered in 1962 as an antihypertensive medication, but early clinical trials found xylazine to have excessive central nervous system depressant effects.²³ As a result of these hazardous side effects xylazine is not approved for human use .

Xylazine has been identified as a substance of misuse, primarily as an adulterant in the heroin and cocaine market in Puerto Rico and the United States of America.²⁴

The most common features include drowsiness, coma, bradycardia and hypotension. Other features may include hypertension, hypothermia, respiratory depression, apnoea, agitation, hallucinations, headache, dry mouth, hyperglycaemia, cardiac arrhythmias (including AV block), pulmonary oedema and convulsions.²⁵

In their study, Reyes et al (2012) identified skin ulcerations as a primary health concern for individuals who had used xylazine, they discussed the potential for this being as a result of the skins oxygenation response and lower oxygenation. Lower skin oxygenation is associated with less wound healing and higher incidence of wound infections.²⁴

United Kingdom Legal Status

In the UK, xylazine is not controlled under the Misuse of Drugs Act 1971.

Xylazine and fatal drug related overdoses

On April 12th 2023, the White House designated fentanyl combined with xylazine as an emerging threat to the United States.²⁶

According to data from the Centers for Disease Control and Prevention, the estimated number of drug-poisoning deaths in the United States involving xylazine rose from 260 in 2018 to 3480 in 2021, an increase of 1238 per cent.²⁷

Naloxone, responding to a xylazine overdose

In the event of a suspected xylazine overdose, experts recommend giving the opioid overdose reversal medication naloxone because xylazine has been evidenced to be frequently combined with opioids (US data above). However, because xylazine is not an opioid, naloxone does not address the impact of xylazine on breathing.²⁸

As a result, additional care may be necessary in the treatment of a xylazine overdose. This may include maintaining a patent airway, administering supplemental oxygen, performing rescue breathing and treating hypotension as needed.²⁷

TOXBASE and the UK National Poisons Information Service highlight xylazine as a Highly Toxic Substance, and all patients should be referred to an Emergency Department after exposure to any amount by any route.

23. Greene, S.A. and Thurmon, J.C. (1988), Xylazine – a review of its pharmacology and use in veterinary medicine. *Journal of Veterinary Pharmacology and Therapeutics*, 11: 295-313. <https://doi.org/10.1111/j.1365-2885.1988.tb00189.x> [accessed 8th May 2023]
24. Reyes JC, Negrón JL, Colón HM, Padilla AM, Millán MY, Matos TD, Robles RR. The emerging of xylazine as a new drug of abuse and its health consequences among drug users in Puerto Rico. *J Urban Health*. 2012 Jun;89(3):519-26. doi: 10.1007/s11524-011-9662-6. PMID: 22391983; PMCID: PMC3368046.
25. [Toxbase.org, poisons-index-a-z, xylazine](https://toxbase.org/poisons-index-a-z/xylazine) [accessed 8th May 2023]
26. Biden- Harris Administration Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States, The White House, 12th April 2023; <https://www.whitehouse.gov/ondcp/briefing-room/2023/04/12/biden-harris-administration-designates-fentanyl-combined-with-xylazine-as-an-emerging-threat-to-the-united-states/> [accessed 8th May 2023]
27. Gupta, R. Holtgrave, D.R. Ashburn, M.A., Xylazine – Medical and Public Health Imperatives, April 26, 2023 DOI: 10.1056/NEJMp2303120; <https://www.nejm.org/doi/full/10.1056/NEJMp2303120#:~:text=According%20to%20data%20from%20the%20Centers%20for%20Disease,reported%20in%20Pennsylvania%2C%20Maryland%2C%20New%20York%2C%20and%20Connecticut.> [accessed 8th May 2023]
28. Xylazine, National Institute of Health, National Institute on Drug Abuse; <https://nida.nih.gov/research-topics/xylazine#:~:text=In%20the%20event%20of%20a%20suspected%20xylazine%20overdose%2C,should%20always%20be%20alerted%20to%20a%20suspected%20overdose.> [accessed 8th May 2023]

WEDINOS and Xylazine

WEDINOS received the first sample profiled by the programme containing xylazine on 8th January 2020. This sample (WEDINOS reference: W012473), was submitted as a ketamine from the KA4 postcode, Galston, East Ayrshire, Scotland.

Since then the programme has received and analysed 10 samples that were also profiled as containing xylazine. The vast majority were received during this reporting period.

During the period April 2022 to March 2023, nine samples were submitted that were profiled as containing a xylazine post analysis. None of these samples were submitted with xylazine listed as the purchase intent.

Six of these samples were submitted in the belief that they were benzodiazepines. Five were in tablet form and one a powder. Three of these samples were submitted in the belief that they were diazepam. One each were submitted as alprazolam, bromazolam and temazepam. Two were submitted as THC vape liquid and one as a combination of heroin and fentanyl.

Self reported effects are limited and vary from sample provider. Where available the following effects were reported:

Sample provider one: Relaxed, Panic Attack, Insomnia, Depression

Sample provider two: Relaxed, Panic Attack, Insomnia, Depression

Sample provider three: No effect

Sample provider four: Euphoria, Memory Loss, Increased Energy, Increased Confidence, Enhanced Senses, Increased Libido, Relaxed

Sample provider five: Euphoria, Increased Confidence, Empathy, Relaxed

Samples containing xylazines were submitted from England, Scotland and Wales.





Night Time Economy Venues and Music Festivals

Through partnership working with the Welsh police forces, WEDINOS receives samples from some Night Time Economy Venues and Music Festivals in Wales which have been surrendered in amnesty bins.

These samples have no forensic or evidentiary value, and as they are anonymously surrendered they are not accompanied by any demographic, purchase intent, dosage or effects data. However, they do provide important insight into the drugs in circulation in this specific market.

Between April 2021 and March 2022, WEDINOS analysed 1,112 samples from 22 night time economy venues and 2 festivals across the Aneurin Bevan, Cardiff and Vale, Cwm Taf Morgannwg and Swansea Bay University Health Board areas.

Within these samples, the most commonly identified primary substance (excluding bulking and cutting agents and metabolites) was cocaine (n=682), followed by ketamine (n=206) and MDMA (n=113). This is the same top three most commonly identified substances amongst samples submitted via the Night Time Economy as in 2021-2022.

Within samples of cocaine the main bulking and cutting agents profiled were levamisole (n=96/682) and benzocaine (n=60/682).

Although we cannot discuss substitutions in relation to samples submitted via Night Time Economy venues and Music Festivals as we do not have any information relating to purchase intent, we can comment on the most commonly identified substances based on data from community submissions.

Cocaine

Cocaine is a powerful central nervous system stimulant extracted from the coca plant which grows in regions of South America. Cocaine is available as powder cocaine (primarily snorted) and crack cocaine (primarily smoked).

Global cocaine manufacture increased by 11 per cent from 2019 to 2020, to an estimated 1,982 tons (expressed at 100 per cent purity). This is the highest level ever recorded. At that time there was an estimated 21 million global cocaine users.²⁹

On a European level, availability and use of cocaine remains high. Cocaine is the second most commonly consumed drug in Europe, with an estimated 2.2 million 15 to 34 year olds (2.2 per cent of this age group) having used cocaine in the last year (EMCDDA 2022).³⁰

The most recent Crime Survey for England and Wales reported that 2 per cent of adults aged 16 to 54 years had used cocaine in the last year (to year ending June 2022).

The Office for National Statistics reported that cocaine deaths in England and Wales rose for the tenth consecutive year (deaths registered in 2021). Of the 4,859 deaths related to drug poisoning registered in 2020, 840 deaths involved cocaine, an increase from 777 in 2020.³¹

29. UNODC, World Drug Report 2022 (United Nations publication, 2022). https://www.unodc.org/res/wdr2022/MS/WDR22_Booklet_4.pdf [accessed 9th May 2023]

30. European Monitoring Centre for Drugs and Drug Addiction (2022), European Drug Report 2022: Trends and Developments, Publications Office of the European Union, Luxembourg; https://www.emcdda.europa.eu/publications/edr/trends-developments/2022_en [accessed 9th May 2023]

31. Deaths related to drug poisoning in England and Wales: 2021 registrations; Office for National Statistics, 3rd August 2022; <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/latest#drug-poisonings-from-selected-substances> [accessed 9th May 2023]

W031816

Date Received: 15 Mar 2023

Postcode: B26 -

Purchase Intent: MDMA

Package Label: Not Stated

Sample Colour: White, Colourless

Sample Form: Crystalline

Consumption Method: Not Stated

Self-Reported Effects: Not Stated

Sample Upon Analysis (Major): Dipentylone

Sample Upon Analysis (Minor): Ketamine, Cocaine, MDMA



Click to Enlarge

In Wales in 2021-22 there were 408 cocaine related hospital admissions involving 365 individuals. This represents a decrease on the number of admissions compared with the previous year.³²

Between April 2022 and the end of March 2023, 419 samples were submitted in the belief that they were cocaine. 6 per cent of these samples (n=26) were profiled as containing other substances. The most commonly identified substitutes were samples that contained no active substances (n=6) paracetamol (n=5) and ketamine (n=3).

17 per cent of these samples (n=73) contained cocaine and other substances.

The large majority of these samples contained cocaine and levamisole. Levamisole is an anthelmintic medication (used for expelling parasitic worms), there is some evidence of levamisole enhancing cocaine's effects in vivo, highlighting a potential synergistic relationship between the two.³³

Ketamine

Ketamine, 2-(2-chlorophenyl)-2-(methylamino)-cyclohexan-1-one, is a dissociative sedative with analgesic and anaesthetic properties.

The most recent Crime Survey for England and Wales reported that around 0.9 per cent of adults aged 16 to 54 years had used ketamine in the last year (to year ending June 2022). This is an increase from 0.8 per cent for April 2019 to March 2020.

During 2021-2022, 204 samples were submitted as purchased as ketamine. Within these samples 6 per cent (n=12), were profiled as containing no ketamine. The most commonly identified substitute substance was cocaine (n=4).

Eleven samples (5 per cent), contained other substances including lidocaine (n=2) and benzocaine (n=2).

MDMA

MDMA (3,4-Methylenedioxymethamphetamine) is a stimulant, it is structurally similar to amphetamine.

MDMA is primarily manufactured in Europe, most notably Central and Western Europe.

The European Drug Report 2022 suggests that 1.9 million young adults (15-34) used MDMA in the last year (1.9 per cent of this age group). Estimates for those aged 15-24 years are higher, with 2.2 per cent (1.0 million) estimated to have used MDMA in the last year (EMCDDA 2022).

32. Data Mining Wales: The annual profile for substance misuse 2020-21; Public Health Wales; Cardiff: 2022;

<https://phw.nhs.wales/publications/publications1/data-mining-wales-the-annual-profile-for-substance-misuse-2021-22/> [accessed 9th May 2023]

33. Tallarida, C. S., Egan, E., Alejo, G. D., Raffa, R., Tallarida, R. J., & Rawls, S. M. (2014). Levamisole and cocaine synergism: a prevalent adulterant enhances cocaine's action in vivo. *Neuropharmacology*, 79, 590-595. <https://doi.org/10.1016/j.neuropharm.2014.01.002> [accessed 11th May 2023]

For year ending March 2020, the Office for National Statistics Crime Survey for England and Wales, estimated that 0.7 per cent of adults aged 16 to 54 had used MDMA in the past year.

Of the 4,859 deaths related to drug poisoning registered in 2021, 67 deaths involved MDMA.³⁴

During this WEDINOS reporting period, 668 samples were submitted with MDMA listed in the purchase intent. Of these samples 15 per cent (n=102) contained no MDMA.

The most commonly identified substitutes were caffeine (n=45) and cathinones (n=35).

CATHINONE	NUMBER OF IDENTIFICATIONS
4-CHLOROMETHCATHINONE	19
EUTYLONE	8
DIBUTYLONE	6
3-METHYLMETHCATHINONE	1
MEPHEDRONE	1

34. Deaths related to drug poisoning in England and Wales: 2021 registrations; Office for National Statistics, 3rd August 2022; <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/latest#drug-poisonings-from-selected-substances> (accessed 9th May 2023)



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