Environment International 178 (2023) 108075

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Full length article

Festivals following the easing of COVID-19 restrictions: Prevalence of new psychoactive substances and illicit drugs

Nikolaos Rousis [a,b,1,*], Richard Bade [a,1,*], Iván Romero-Sánchez [c], Jochen F. Mueller [a], Nikolaos S. Thomaidis [b], Kevin V. Thomas [a], Emma Gracia-Lor [c,*]

[a] Queensland Alliance for Environmental Health Sciences (QAEHS), The University of Queensland, 20 Cornwall Street, Woolloongabba, Queensland 4102, Australia
[b] Laboratory of Analytical Chemistry, Department of Chemistry, National and Kapodistrian University of Athens, Panepistimiopolis Zografou, 15771 Athens, Greece
[c] Department of Analytical Chemistry, Faculty of Chemistry, Complutense University of Madrid, Avenida Complutense s/n, 28040 Madrid, Spain

ARTICLE INFO

Handling Editor: Adrian Covaci

Keywords:
Wastewater-based epidemiology
Synthetic cathinones
3-chloromethcathinone (3-CMC)
N,N-dimethylpentylone
2F-deschloroketamine (2F-DCK)
Substance abuse

ABSTRACT

The market for illicit drugs and new psychoactive substances (NPS) has grown significantly and people attending festivals have been identified as being at high risk (high extent and frequency of substance use). Traditional public health surveillance data sources have limitations (high costs, long implementation times, and ethical issues) and wastewater-based epidemiology (WBE) can cost-effectively support surveillance efforts. Influent wastewater samples were analyzed for NPS and illicit drug consumption collected during New Year period (from 29-Dec-2021 to 4-Jan-2022) and a summer Festival (from 29-June-2022 to 12-July-2022) in a large city in Spain. Samples were analyzed for phenethylamines, cathinones, opioids, benzodiazepines, plant-based NPS, dissociatives, and the illicit drugs methamphetamine, MDA, MDMA, ketamine, heroin, cocaine, and pseudoephedrine by liquid chromatography mass spectrometry. High consumption rates of specific NPS and established illicit drugs were identified at the peak of each event. Furthermore, a dynamic change in NPS use (presence and absence of substances) was detected over a period of six months. Eleven NPS, including synthetic cathinones, benzodiazepines, plant-based NPS and dissociatives, and seven illicit drugs were found across both the New Year and summer Festival. Statistically significant differences ($p < 0.05$) were seen for 3-MMC (New Year *vs* summer Festival), eutylone (New Year *vs* summer Festival), cocaine (summer Festival *vs* normal week and summer Festival *vs* New Year), MDMA (New Year *vs* normal week and summer Festival *vs* normal week), heroin (summer Festival *vs* New Year) and pseudoephedrine (summer Festival *vs* New Year). This WBE study assessed the prevalence of NPS and illicit drugs at festivals following the reduction of the COVID-19 pandemic restrictions highlighting the high use of specific substances at the peak of each event. This approach identified in a cost-effective and timely manner without any ethical issues the most used drugs and changes in use patterns and, thus, can complement public health information.

1. Introduction

Over recent decades, the market for established illicit drugs and new psychoactive substances (NPS) has grown significantly. The prevalence of synthetic drugs is increasing dynamically due to globalization, their availability from online marketplaces and the evolution of clandestine laboratories around the world (Baumann and Volkow, 2016; Das and Horton, 2019; EMCDDA, 2022a; Peacock et al., 2019; Van Buskirk et al., 2017). Likewise, many traditional plant-based illicit drugs continue to show increasing trends in their use, remaining at the highest consumption levels worldwide (Baumann and Volkow, 2016; Das and Horton, 2019; EMCDDA, 2022b, 2022a; Peacock et al., 2019; Van Buskirk et al., 2017). These drugs are used by various population groups exhibiting different socio-economic characteristics and motivations, both recreational and therapeutic. One of the population groups identified as being at high risk is people attending festivals and other special events, as the extent and frequency of illicit drug use might be particularly high (Bade et al., 2023b, 2020b; Feltmann et al., 2022; Fernández-

* Corresponding authors at: Queensland Alliance for Environmental Health Sciences (QAEHS), The University of Queensland, 20 Cornwall Street, Woolloongabba, Queensland 4102, Australia (N.R.).
E-mail addresses: nrousis@chem.uoa.gr (N. Rousis), r.bade@uq.edu.au (R. Bade), emgracia@ucm.es (E. Gracia-Lor).
[1] Co-first authors.

https://doi.org/10.1016/j.envint.2023.108075
Received 15 March 2023; Received in revised form 15 May 2023; Accepted 29 June 2023
Available online 29 June 2023

Calderón et al., 2018; Peacock et al., 2019).

Drug use is considered one of the major contributors to the global burden of disease and its risks are related to the frequency and amount of use. Indeed, people who have used illicit drugs once or occasionally do not usually experience the same harm to their health compared to systematic users or those who consume more than one type of drug. In general, the health consequences of illicit drug use could be classified as acute toxic effects (including fatal overdose), acute effects of intoxication, dependence, and adverse health effects of chronic use. In addition, other problems that arise for users are their discrimination and stigmatization. Therefore, the issue of illicit drug use is complex and may require different intervention approaches for different population groups (Blanco et al., 2020; Degenhardt and Hall, 2012; Farrell et al., 2019; Han et al., 2021; O'Connor et al., 2020; Whitley et al., 2022).

Data on the incidence of illicit drug use and the effect on human health is difficult to ascertain. Regarding NPS, the United Nations Office of Drugs and Crime (UNODC) has reported more than 1100 NPS and acts as an early warning system for all countries. Research on drug problems in Europe is mainly conducted by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) which uses multiple data sources and provides information on traditional illicit drugs, such as cocaine, heroin, and amphetamines, among others (EMCDDA, 2022b). In addition, EMCDDA has monitored hundreds of NPS the last twenty-five years delivering useful data at national and international level (EMCDDA, 2022a). However, information on the population groups that use illicit drugs is not always available and, thus, any intervention is limited and may not be effective.

The aim of this study was to investigate the prevalence of NPS and established illicit drugs in festivals after the reduction of most restrictions resulting from the COVID-19 pandemic. The sampling campaigns were performed during the New Year (2021–2022) and a Festival held in July 2022 in a large city in Spain. A wastewater-based epidemiology approach was used to evaluate the drug use pattern using two analytical methodologies based on liquid chromatography mass spectrometry.

2. Materials and methods

2.1. Sampling

Influent wastewater samples were collected as 24-hour composite samples (flow-proportional mode) from one treatment plant in a large city in Spain over two sampling periods: 29 December 2021 – 4 January 2022 and 29 June 2022 – 12 July 2022. These two periods incorporated the New Year period and a large Festival during the summer (July), where no restrictions were imposed due to COVID-19 pandemic. Both festivals took place across the city, with many special events throughout. In addition, data from samples collected during a normal week (June 2021) at the same treatment plant was compared to the events for some compounds.

2.2. Sample treatment and analysis

Wastewater samples were collected and stored at −20 °C prior to sample treatment. Then, samples were solid phase extracted and analysed by different validated analytical protocols (ACIC, 2022; Bade et al., 2023, 2020a, 2020c). Briefly, samples were filtered, pH adjusted to approximately 5 and extracted. The dried cartridges were shipped to The University of Queensland, where they eluted and analysed within 48 h. The elution was done in dichloromethane:isopropanol:aqueous ammonia (80:16:4 v/v/v, 6 mL) and the dry residue was reconstituted in 100 μL of 0.1 % formic acid in methanol (20 μL) and 0.1 % formic acid in ultrapure water (80 μL). The concentration factor was 1000 times.

A liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) method was used for the determination of NPS (phenethylamines, synthetic cathinones, opioids, benzodiazepines, plant-based NPS and dissociatives) and established illicit drugs (Table S1). A liquid chromatography coupled to quadrupole-time-of-flight mass spectrometry (LC-QTOF-MS) method was used to screen against the HighResNPS database (Mardal et al., 2019), which has entries for more than 2000 NPS, illicit drugs, opioids, and other drugs of toxicological concern. The targeted analysis of NPS and established illicit drugs as well as the screening against the HighResNPS database were performed in both the New Year period and summer Festival. In addition, benzoylecgonine, MDMA, and methamphetamine were also investigated during a normal week. Details on analytical protocols (Section S1) and quality criteria (Section S2) can be found in the Supplementary Material.

2.3. Calculations

For quantification using the LC-MS/MS approach, two transitions needed to be present, while the ion ratio (within 20 %) as well as retention time (within 2 %) had to compare with the standard. Concentrations were calculated based on the peak area ratios between native and internal standards compared to an external calibration curve. All data were acquired and processed using SCIEX OS software. Normalised mass loads were estimated using concentrations, wastewater flow rates and number of inhabitants. Back-calculation of the consumption to the parent substance was performed for the compounds where a correction factor (CF) has been established and is widely used; cocaine consumption was calculated from benzoylecgonine (CF = 3.59), MDMA consumption from MDMA (CF = 4.4), heroin from 6-monoacetylmorphine (6-MAM, CF = 86.9) and methamphetamine consumption from methamphetamine (CF = 2.44) (see Section S3). Consumption of ketamine, pseudoephedrine and MDA was not back-calculated. For the latter, information is available on the proportion of MDA excreted following MDMA consumption, which was considered when calculating the excreted mass load.

For identification using the LC-QTOF-MS suspect screening approach, at least two fragment ions needed to be present, mass error lower than 5 ppm and the retention time had to be within 1 min. compared to that predicted; a validated retention time prediction model based on the HighResNPS database was used (Pasin et al., 2021). All data were acquired and processed using SCIEX OS software. As no concentrations were available, the "pseudo-mass loads" were calculated to further elaborate this data using the approach previously proposed (Rousis et al., 2022). This approach is based on the response (area) of each compound and internal standards, the flow rate, and the population size. In a WBE context normalized mass loads are considered necessary to elaborate data and the pseudo-mass loads are good alternatives when no quantitative or semi-quantitative HRMS data is available (Rousis et al., 2022). MDMA-D5 was used as the internal standard.

2.4. Statistical analysis

An F-test was performed to determine whether the variances of the two sampling campaigns were equal or unequal. A *t*-test assuming equal or unequal variances was carried out on every compound that was found in both time periods. All calculations were made on Microsoft Excel.

3. Results

A total of eleven NPS (Fig. 1) were detected across both the New Year and summer Festival sampling periods (3-methylmethcathinone (3-MMC), etizolam, eutylone, N-ethylhexedrone, 2F-deschloroketamine (2F-DCK), mitragynine, pentylone, methcathinone, N,N-dimethylpentylone, mephedrone and methylone). All but etizolam, N, N-dimethylpentylone and pentylone were found in both campaigns, with these three specific to the summer Festival period. In addition, seven drugs of abuse (Figs. 2 and 3) were also quantified in these periods (methamphetamine, MDA, MDMA, ketamine (as metabolite norketamine), heroin (as metabolite 6-MAM), cocaine (as metabolite

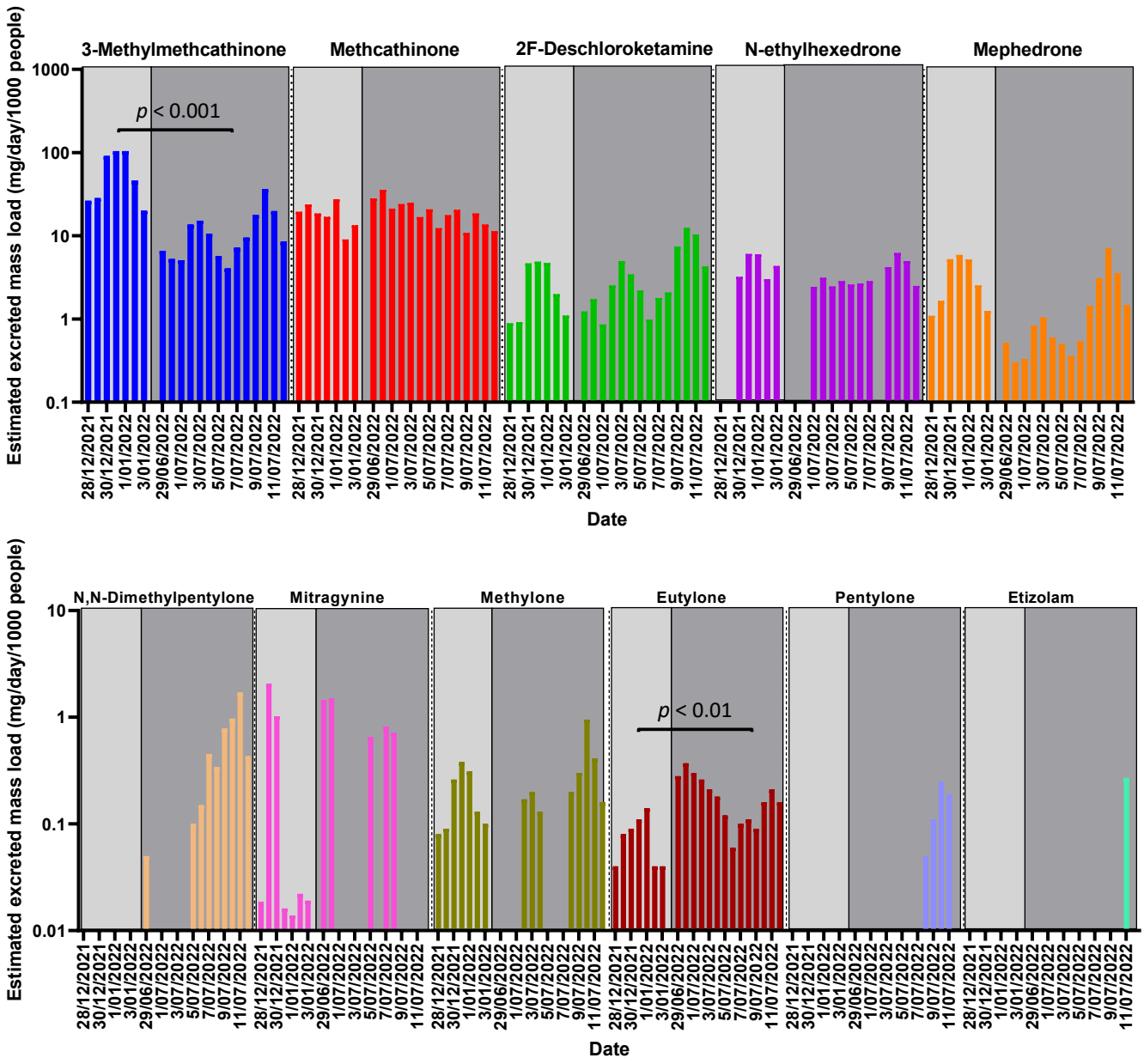

Fig. 1. Estimated excreted mass loads for NPS. Both the New Year (light grey) and Summer Festival (dark grey) sampling periods are shown. Note that the y-axis is on a log scale, to better show the NPS present at lowest levels.

benzoylecgonine) and pseudoephedrine). Twelve compounds were identified from the HighResNPS database, 3-chloromethcathinone (3-CMC), amantadine, O-desmethylvenlafaxine, gabapentin, hydroxybupropion, levamisole, levorphanol, memantine, nordazepam, tapentadol, tramadol, and venlafaxine. All compounds except 3-CMC showed a stable trend across days, indicating no misuse due to special events (New Year and summer Festival). The synthetic cathinone 3-CMC presented high consumption during the peak of each event, 31-Dec-2021 until 02-Jan-2022 and from 07-Jul to 11-Jul (Fig. S1). No statistically significant difference ($p = 0.32$) was observed for 3-CMC between the two periods, although pseudo-mass loads at the summer Festival peak (10-Jul) doubled compared to the New Year peak (31-Dec).

The NPS normalised mass loads ranged from below the limit of detection to more than 100 mg/day/1000 people. The highest levels were seen for 3-MMC across both periods. Despite this, there was a significant decrease in mass loads observed between the New Year and the summer Festival ($p < 0.05$). In addition, a significant increase was found on the consumption of eutylone during the summer Festival ($p < 0.05$). Most NPS (3-MMC, 2F-DCK, mephedrone, methylone, N,N-dimethylpentylone and pentylone) showed highest consumption rates during the peaks of the events (Fig. 1).

All the drugs of abuse investigated in this study were found at quantifiable levels (Table S2). Cocaine had the highest consumed mass loads of up to 3150 mg/day/1000 people, while MDMA was up to 1040 mg/day/1000 people and methamphetamine up to 158 mg/day/1000 people. These three drugs have previously been analysed during a normal week, when no special events took place (Fig. 3). Comparing these three separate sampling campaigns, the summer Festival had the highest mass loads of all. However, a statistically significant difference ($p < 0.05$) was seen for cocaine (summer Festival *vs* normal week and summer Festival *vs* New Year) and MDMA (New Year *vs* normal week and summer Festival *vs* normal week). In addition, the consumed mass loads of heroin reached 43 mg/day/1000 people, with significantly higher levels during summer ($p < 0.05$).

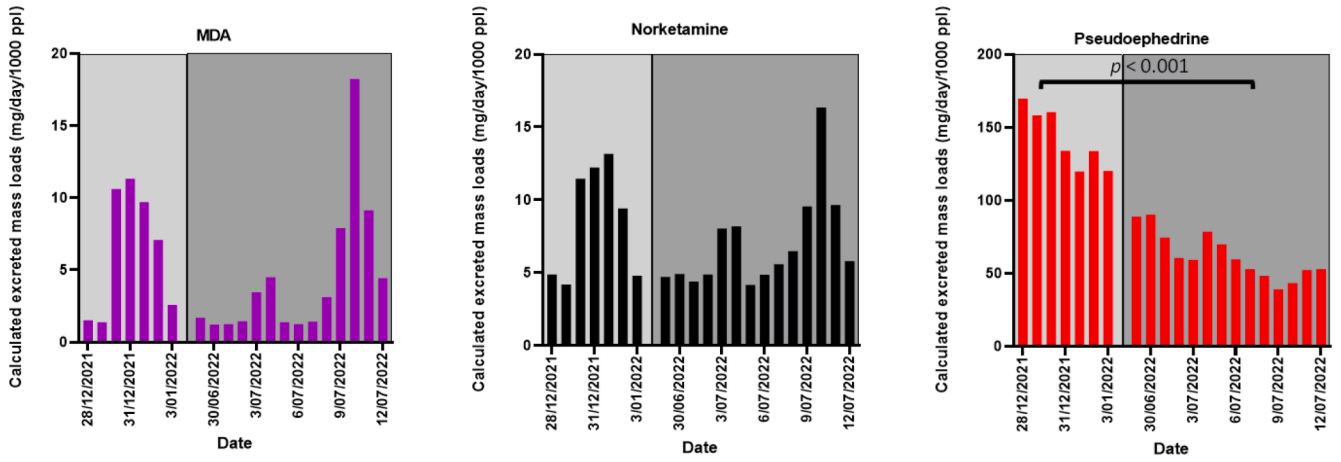

Fig. 2. Estimated excreted mass loads for MDA, norketamine, and pseudoephedrine. Both the New Year (light grey) and Summer Festival (dark grey) sampling periods are shown.

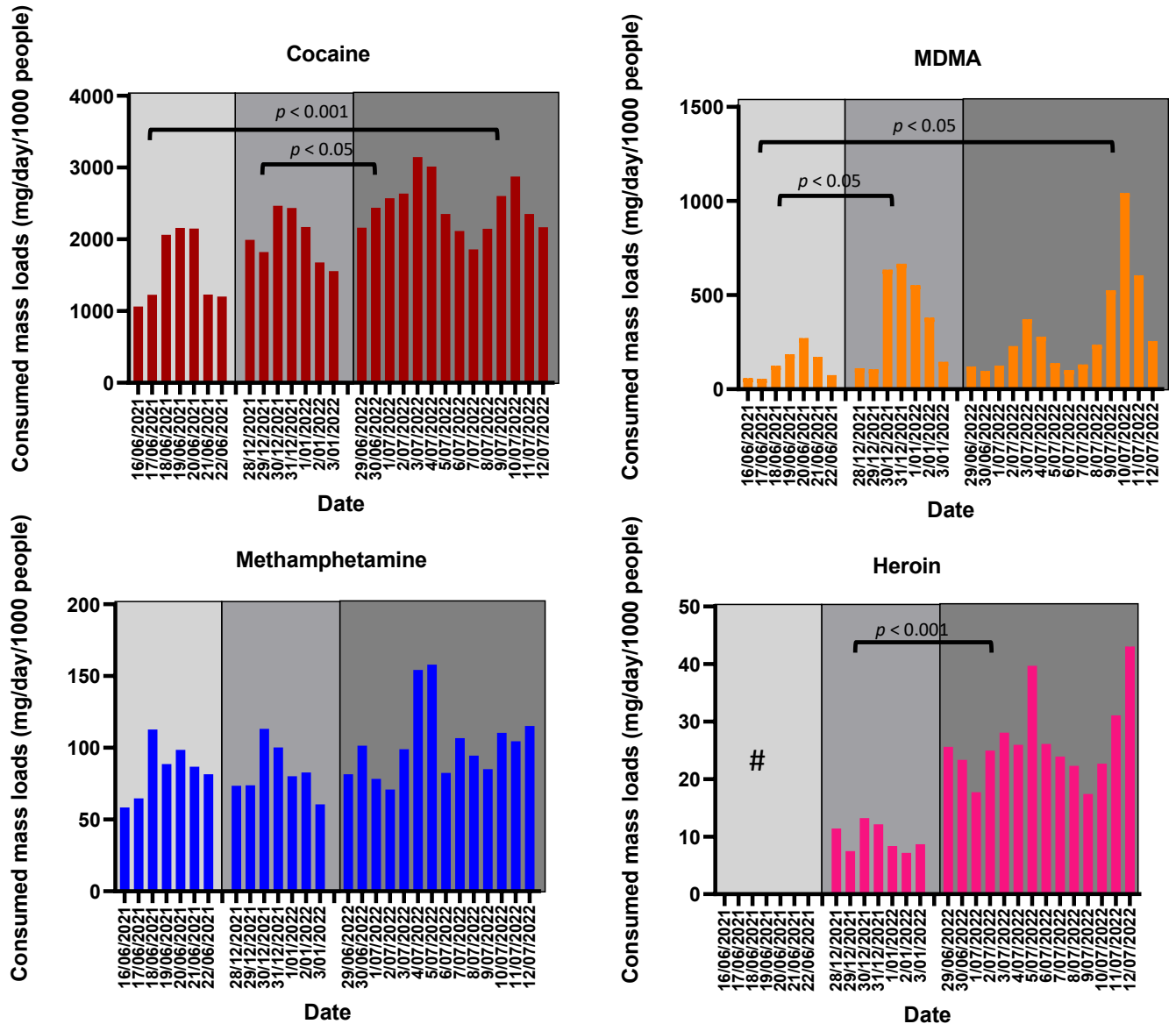

Fig. 3. Consumed mass loads for cocaine, MDMA, methamphetamine and heroin during three sampling periods: normal week (left; light grey), New Year (centre; grey) and summer Festival (right; dark grey). #: not analysed.

For the rest, pseudoephedrine had the highest excreted mass loads (up to 170 mg/day/1000 people), followed by norketamine (up to 16.4 mg/day/1000 people), and MDA (up to 3.9 mg/day/1000 people) (Fig. 2 and Table S2). Despite the contribution from MDMA metabolism included in the calculation of the mass load of MDA, there were clear peaks, similar to MDMA. Only pseudoephedrine showed a significant difference between the two periods ($p < 0.05$) with lower levels during summer.

4. Discussion

The present WBE work investigated the prevalence of NPS and illicit drugs at festivals following the reduction of restrictions associated with the COVID-19 pandemic, highlighting the high use of specific substances at the peak of each event and the dynamic change in NPS use (presence and absence of substance within six months). NPS consumption increased at the peak of both events (30-Dec-2021 until 02-Jan-2022, New Year and from 09 to 11-July-2022, summer Festival) and showed another peak, although lower, from 02 to 04-July-2022 which corresponded to the first weekend of the summer Festival. The main contributor was 3-MMC, although levels during the summer Festival were much lower, followed by 2F-DCK. In addition, the second peak during the summer Festival was the most "active" period including a parade, music and other events and, thus, higher consumption was expected. Similar peaks were found for the established illicit drugs, such as cocaine, MDA, MDMA and ketamine (Figs. 2 and 3). However, it should be noted that cocaine had the same levels during the two peaks of the summer Festival, in contrast to MDA, MDMA and ketamine that presented higher consumed mass loads at the main, second peak. This work indicated that illicit drug consumption increases at festivals, and this could be due to systematic users who consume higher amounts and/or to occasional users. Differences in the total amount of drugs and their type among the peaks of each event could be due to the population group attending the event, the period (winter *vs* summer) and any control actions taken by authorities.

The WBE approach identified the dynamic change in NPS use in a period of six months, among the two events, as etizolam, N,N-dimethylpentylone and pentylone were only detected in the summer Festival. Etizolam is a benzodiazepine used for anxiety disorders, insomnia and illicitly as NPS and was detected on the last day of the sampling campaign, after the summer Festival. The day of detection could coincide with relaxation/sleeping difficulties experienced by the participants resulting to consumption of other stimulants. N,N-dimethylpentylone is a synthetic cathinone with similar effects to MDMA and is often mis-sold as MDMA (Walton et al., 2022). This is the first time that N,N-dimethylpentylone is reported in a WBE study, although it has been found in the USA (CFSRE, 2022; Walton et al., 2022) and New Zealand (High Alert, 2021) since late 2021, according to on-site pill testing, analysis of seized materials and forensic toxicology analyses. Pentylone, the metabolite of N,N-dimethylpentylone, was mainly found in the second peak of the summer Festival, showing traces (non-quantifiable data) for the remaining days. Pentylone has never been detected in wastewater from Europe, but it has been found in the USA during New Year period (2019/2020 and 2020/2021) (Bade et al., 2022, 2021). It should be mentioned that this city was not monitored in the previous international New Year NPS monitoring campaigns (Bade et al., 2022, 2021) and future research (e.g., sampling in New Year 2022/2023, special events and/or music festivals) could show the life cycle of these compounds. The prevalence life cycle of NPS stimulants frequently lasts one year or even less and the period of appearance and disappearance is usually a few years (Mohr et al., 2021). Hence, it is a challenging task to monitor and track the rapid changes in the NPS market and this WBE study proved to be suitable for this mission.

Most of the findings of this work, relating to NPS, are supported with data from the UNODC and EMCDDA. According the UNODC EWA on NPS (UNODC, 2023), the most reported stimulants in Europe are 3-MMC, 3-CMC and mephedrone, while N-ethylhexedrone is one of the most commonly seized cathinone in Europe (EMCDDA, 2022b). However, eutylone, methylone, pentylone and N,N-dimethylpentylone are not in the top 10 most frequently reported stimulants. Eutylone, methylone and mephedrone were previously detected in wastewater collected in Australia, New Zealand, the USA and Canada (Bade et al., 2022, 2021).

As reported by both the UNODC and EMCDDA, 3-MMC is one of the primary stimulant NPS in Europe. Previous international wastewater studies have also shown that 3-MMC had highest levels in sites in Europe (Bade et al., 2022, 2021; Salgueiro-González et al., 2022). In March 2022, the European Commission adopted measures to control 3-MMC and 3-CMC in the European Union. Interestingly, there was a significant decrease ($p < 0.05$) in the mass load of 3-MMC between New Year and the Festival in July – potentially associated with these control measures.

Methcathinone was one of the first NPS of the synthetic cathinone class (EMCDDA, 2023) but has only been seen rarely since then. It is therefore remarkable to find it at quite a consistent mass load across both sampling periods. Previous studies have looked into the identification of methcathinone in wastewater and its possible formation from pseudoephedrine and showed that it can be formed from pseudoephedrine (and ephedrine) (Huang et al., 2022; Simpson et al., 2022). Considering that pseudoephedrine is sold as a decongestant over-the-counter at pharmacies in Spain and was found at high levels in wastewater (Fig. 2), it is therefore assumed that the methcathinone in this work is more likely formed from in-sewer transformation of (pseudo) ephedrine rather than illicit consumption.

2F-DCK is a dissociative, closely related to ketamine. It has been one of the most prevalent NPS in Asia and is currently the second-most reported dissociative in Europe, behind ketamine, according to the UNODC (UNODC, 2023). 2F-DCK showed increases over both festival periods, particularly over the two peaks of the summer Festival and New Year's Eve. The pattern of use for this compound mirrors that of norketamine, potentially indicating either co-consumption or 2F-DCK being mis-sold as ketamine.

Mitragynine was found infrequently during these events, at low levels. Despite mitragynine being one of the most reported plant-based NPS (UNODC, 2023), it is typically used as opioid-like pain relief, and less frequently for its stimulant-type effects. It is a legal drug in many countries and has become particularly popular in many states in the USA, where it is not federally regulated. There is generally less uptake of this compound in Europe, so the low levels seen in this work were expected.

In this study, seven established drugs or their metabolites were quantified in both campaigns (Table S2). Cocaine, ketamine, MDMA, and MDA were extensively consumed at the peak of both events. Cocaine had the highest consumed mass loads followed by MDMA, and MDA. The consumed methamphetamine mass loads did not show a similar trend as the other substances except on New Year where a small increase was estimated on 30-Dec and 31-Dec. No specific profile was observed during the summer Festival and, thus, its consumption was not affected by this event. Similarly, heroin and pseudoephedrine consumption were not attributed to the events participants as no characteristic peak was found. The higher levels of pseudoephedrine on New Year could be attributed to the winter season as it is used as nasal decongestant and is associated with colds and allergies. Likewise, a study conducted in Benicassim (Spanish Mediterranean coast) in July 2008 during a music festival showed that levels of benzoylecgonine, MDMA, and MDA increased during the event while levels of methamphetamine were not affected (Bijlsma et al., 2014). Although the location, date, and type of festivals were different, common trends in drug consumption were observed.

Studies carried out in Spain before the COVID-19 pandemic estimated the consumption of several illicit drugs, such as cocaine (range: 1100–2800 mg/day/1000 people), MDMA (range: 0.2–206 mg/day/

1000 people), methamphetamine (range: 0.7–117 mg/day/1000 people) and amphetamine (range: 2–766 mg/day/1000 people) (Andrés-Costa et al., 2014; Baz-Lomba et al., 2016; Bijlsma et al., 2021; Castrignanò et al., 2018; Estévez-Danta et al., 2021). The consumption of cocaine, MDMA, and methamphetamine in the present study was from the highest found in Spain, especially at the peaks of the events, indicating the impact of festivals in human habits. However, it must be noted that these studies were conducted when no special events were occurring. Data on ketamine and MDA are limited and more research is needed. No exact comparison can be made between the present and previous studies, as illicit drug consumption has shown spatial and temporal variations. In addition, other aspects that should be considered to further evaluate the data are the lifestyle of the residents of each city and the socio-economic characteristics of the population.

Several WBE studies have been conducted around the world to assess illicit drug use during specific periods. In the USA elevated levels of amphetamine, methamphetamine, cocaine, morphine, and methadone were found on Independence Day and during the observation of the solar eclipse. However, levels of many drugs of abuse remained stable in the first week of semester (Foppe et al., 2018). In addition, spiked levels of stimulants, opioids, hallucinogens, pharmaceuticals and NPS in wastewater were detected during sport events in Kentucky, the USA (Montgomery et al., 2021). Illegal drug use was also seen during a youth festival (Spring Scream, pop music festival) in Taiwan, where pseudoephedrine, ketamine, and MDMA were extensively consumed. MDMA levels were ten times higher during the festival compared to normal days. In contrast, amphetamine, methamphetamine, and flunitrazepam levels showed no discernible difference between event and normal days (Jiang et al., 2015). Another study investigated methamphetamine use between different holidays in China and showed variations for the different events; for instance, increased levels were observed on Spring Festival and lower levels on New Year's Day compared to working days (Song et al., 2020). Drug consumption at a school-leaver festival in Australia showed that MDMA and MDA were the drugs of choice for this event (mass loads increased 40-fold). Cocaine and alcohol doses were slightly increased and methamphetamine use decreased during this festival (Bade et al., 2020b). At a summer festival (including music, multicultural performances, visual arts, craft workshops and guest speakers) in Australia, the use of MDMA increased considerably during the festival, but methamphetamine and cocaine use decreased slightly (Lai et al., 2013). Many studies have also been carried out in Europe. For instance, the consumption of MDMA, amphetamine and methamphetamine was higher during a music festival in Switzerland, but cocaine use remained at the same levels compared to normal days (Benaglia et al., 2020). Furthermore, the World Music Day in France had no observable effect on the consumption of cocaine, MDMA and cannabis (Devault et al., 2020). Finally, a study in the Czech Republic and the Slovak Republic during seven music festivals observed that consumption of specific drugs was associated with different genres of music (e.g., high use of MDMA and cocaine in pop/rock and dance music) (Mackuľak et al., 2019). The emergence of established drugs at festivals is a global concern that needs to be further explored by considering different aspects. Indeed, the state of the illicit drug market at festivals depends on various factors, such as the quality of drug in each location, the availability of drugs in each country, the type of festival, the population habits in each country, the time of year and the location of the event (e.g., indoor, or outdoor event).

From a public health perspective, it is more useful to report data as doses consumed rather than average consumed mass loads; law enforcement authorities and policy makers need this data to identify the most important drug issue and, consequently, to address and minimize the harms caused by these substances. However, this is not always possible as drug doses and CF are not always available. For instance, cocaine had the highest consumed mass loads and showed an increase of 40 % among the baseline (average values of no characteristic peak days) and the peak of each event (high consumption loads attributed to the specific event). Norketamine consumption increased 185 % (New Year) and 220 % (summer Festival). Considering that the drug dose of ketamine is less than that of cocaine and, furthermore, a user can consume up to 10 doses of cocaine per day, instead of one (or two) for ketamine, the number of doses consumed, and users was probably higher for ketamine than cocaine. Nevertheless, the most important drug issue during these events was probably ketamine, due to its high growth (Fig. 2).

The WBE approach can provide a wealth of data on the prevalence of NPS and illicit drugs in festivals and everyday life. It complements important public health information that can be used to aid health authorities, policy makers and (inter)national organizations to face and suppress illicit drug trade (Camilleri et al., 2021). However, to improve WBE for future surveillance, particularly regarding NPS, alternate sources of information are necessary. For example, monitoring of social media and the dark web for new drugs can help target specific WBE methods (Barenholtz et al., 2021; EMCDDA, 2020). Moreover, pill testing, forensic toxicology analyses and emergency departments can give information regarding current drugs of greatest harm. Hence, a better and comprehensive understanding of the drug problem requires the collection of data from various sources and continued collaboration and data triangulation between stakeholders is necessary.

5. Conclusions

This wastewater-based epidemiology study found that the use of NPS (synthetic cathinones, benzodiazepines, plant-based NPS, and dissociatives) and illicit drugs (cocaine, ketamine, MDMA, and MDA) was increased during the New Year and the summer Festival showing high consumption rates at the peak of each event. In addition, rapid changes in NPS use were identified, underscoring the imperative for continued monitoring of NPS in the population and inclusion of new substances in databases. This study suggested wastewater surveillance is an important tool that can deliver public health information in a cost-effective and timely manner without presenting ethical issues. WBE can provide longitudinal and spatial data notifying authorities about changes in the drug market, use patterns and levels of drug consumption.

CRediT authorship contribution statement

Nikolaos Rousis: Conceptualization, Validation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Project administration, Funding acquisition. **Richard Bade:** Conceptualization, Validation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Project administration, Funding acquisition. **Iván Romero-Sánchez:** Investigation, Writing – review & editing. **Jochen F. Mueller:** Resources, Writing – review & editing, Funding acquisition. **Nikolaos S. Thomaidis:** Resources, Writing – review & editing. **Kevin V. Thomas:** Resources, Writing – review & editing, Funding acquisition. **Emma Gracia-Lor:** Conceptualization, Formal analysis, Resources, Writing – review & editing, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

All data are published in this paper.

Acknowledgments

The authors sincerely thank the wastewater treatment plant operators for their help in collecting samples. The authors also thank SCIEX

for the use of their instruments. Nikolaos Rousis: This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska–Curie Grant Agreement No. 896141. Richard Bade: The Queensland Alliance for Environmental Health Sciences, The University of Queensland, gratefully acknowledges the financial support of the Queensland Department of Health. R. B. is the recipient of an Australian Research Council Discovery Early Career Award (project number DE220100381), and J. M. is the recipient of an Australian Research Council Australian Laureate Fellowship (project number FL200100028) funded by the Australian Government. Emma Gracia-Lor: This work was supported by the Madrid Government (Comunidad de Madrid-Spain) under the Multiannual Agreement with Complutense University in the line Program to Stimulate Research for Young Doctors in the context of the V PRICIT (Regional Programme of Research and Technological Innovation, project number PR65/19-22432). Iván Romero-Sánchez acknowledges the Complutense University of Madrid for his predoctoral grant [CT63/19-CT64/19]. The views expressed in this article are those of the author(s) and not necessarily those of the funding agencies.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.108075.

References

ACIC (Australian Criminal Intelligence Commission), 2022. National Wastewater Drug Monitoring Program, Report 17.

Andrés-Costa, M.J., Rubio-López, N., Morales Suárez-Varela, M., Pico, Y., 2014. Occurrence and removal of drugs of abuse in Wastewater Treatment Plants of Valencia (Spain). Environ. Pollut. 194, 152–162. https://doi.org/10.1016/j.envpol.2014.07.019.

Bade, R., Abdelaziz, A., Nguyen, L., Pandopulos, A.J., White, J.M., Gerber, C., 2020a. Determination of 21 synthetic cathinones, phenethylamines, amphetamines and opioids in influent wastewater using liquid chromatography coupled to tandem mass spectrometry. Talanta 208, 120479. https://doi.org/10.1016/j.talanta.2019.120479.

Bade, R., White, J.M., Nguyen, L., Pandopulos, A.J., Gerber, C., 2020b. What is the drug of choice of young festivalgoers? Drug Alcohol Depend. 216, 108315 https://doi.org/10.1016/j.drugalcdep.2020.108315.

Bade, R., White, J.M., Nguyen, L., Tscharke, B.J., Mueller, J.F., O'Brien, J.W., Thomas, K.V., Gerber, C., 2020c. Determining changes in new psychoactive substance use in Australia by wastewater analysis. Sci. Total Environ. 731, 139209 https://doi.org/10.1016/j.scitotenv.2020.139209.

Bade, R., White, J.M., Chen, J., Baz-Lomba, J.A., Been, F., Bijlsma, L., Burgard, D.A., Castiglioni, S., Salgueiro-Gonzalez, N., Celma, A., Chappell, A., Emke, E., Steenbeek, R., Wang, D., Zuccato, E., Gerber, C., 2021. International snapshot of new psychoactive substance use: case study of eight countries over the 2019/2020 new year period. Water Res. 193, 116891 https://doi.org/10.1016/j.watres.2021.116891.

Bade, R., White, J.M., Ghetia, M., Adiraju, S., Adhikari, S., Bijlsma, L., Boogaerts, T., Burgard, D.A., Castiglioni, S., Celma, A., Chappell, A., Covaci, A., Driver, E.M., Halden, R.U., Hernandez, F., Lee, H.-J., van Nuijs, A.L.N., Oh, J.-E., Pineda Castro, M.A., Salgueiro-Gonzalez, N., Subedi, B., Shao, X.-T., Yargeau, V., Zuccato, E., Gerber, C., 2022. A taste for new psychoactive substances: wastewater analysis study of 10 countries. Environ. Sci. Technol. Lett. 9, 57–63. https://doi.org/10.1021/acs.estlett.1c00807.

Bade, R., Eaglesham, G., Shimko, K.M., Mueller, J., 2023a. Quantification of new psychoactive substances in Australian wastewater utilising direct injection liquid chromatography coupled to tandem mass spectrometry. Talanta 251, 123767. https://doi.org/10.1016/j.talanta.2022.123767.

Bade, R., Rousis, N., Adhikari, S., Baduel, C., Bijlsma, L., Bizani, E., Boogaerts, T., Burgard, D.A., Castiglioni, S., Chappell, A., Covaci, A., Driver, E.M., Sodre, F.F., Fatta-Kassinos, D., Galani, A., Gerber, C., Gracia-Lor, E., Gracia-Marín, E., Halden, R.U., Heath, E., Hernandez, F., Jaunay, E., Lai, F.Y., Lee, H., Laimou-Geraniou, M., Oh, J., Olafsdottir, K., Phung, K., Castro, M.P., Psichoudaki, M., Shao, X., Salgueiro-Gonzalez, N., Feitosa, R.S., Gomes, C.S., Subedi, B., Löve, A.S.C., Thomaidis, N., Tran, D., van Nuijs, A., Verovšek, T., Wang, D., White, J.M., Yargeau, V., Zuccato, E., Mueller, J.F., 2023b. Three years of wastewater surveillance for new psychoactive substances from 16 countries. Water Res. X 19, 100179. https://doi.org/10.1016/j.wroa.2023.100179.

Barenholtz, E., Krotulski, A.J., Morris, P., Fitzgerald, N.D., Le, A., Papsun, D.M., Logan, B.K., Hahn, W.E., Goldberger, B.A., Cottler, L.B., Palamar, J.J., 2021. Online surveillance of novel psychoactive substances (NPS): Monitoring Reddit discussions as a predictor of increased NPS-related exposures. Int. J. Drug Policy 98, 103393. https://doi.org/10.1016/j.drugpo.2021.103393.

Baumann, M.H., Volkow, N.D., 2016. Abuse of new psychoactive substances: threats and solutions. Neuropsychopharmacology 41, 663–665. https://doi.org/10.1038/npp.2015.260.

Baz-Lomba, J.A., Salvatore, S., Gracia-Lor, E., Bade, R., Castiglioni, S., Castrignanò, E., Causanilles, A., Hernandez, F., Kasprzyk-Hordern, B., Kinyua, J., McCall, A.-K., van Nuijs, A., Ort, C., Plósz, B.G., Ramin, P., Reid, M., Rousis, N.I., Ryu, Y., de Voogt, P., Bramness, J., Thomas, K., 2016. Comparison of pharmaceutical, illicit drug, alcohol, nicotine and caffeine levels in wastewater with sale, seizure and consumption data for 8 European cities. BMC Public Health 16, 1035. https://doi.org/10.1186/s12889-016-3686-5.

Benaglia, L., Udrisard, R., Bannwarth, A., Gibson, A., Béen, F., Lai, F.Y., Esseiva, P., Delémont, O., 2020. Testing wastewater from a music festival in Switzerland to assess illicit drug use. Forensic Sci. Int. 309, 110148 https://doi.org/10.1016/j.forsciint.2020.110148.

Bijlsma, L., Serrano, R., Ferrer, C., Tormos, I., Hernández, F., 2014. Occurrence and behavior of illicit drugs and metabolites in sewage water from the Spanish Mediterranean coast (Valencia region). Sci. Total Environ. 487, 703–709. https://doi.org/10.1016/j.scitotenv.2013.11.131.

Bijlsma, L., Picó, Y., Andreu, V., Celma, A., Estévez-Danta, A., González-Mariño, I., Hernández, F., López de Alda, M., López-García, E., Marcé, R.M., Miró, M., Montes, R., de San, P., Román-Landa, U., Pitarch, E., Pocurull, E., Postigo, C., Prieto, A., Rico, A., Rodil, R., Valcárcel, Y., Ventura, M., Quintana, J.B., 2021. The embodiment of wastewater data for the estimation of illicit drug consumption in Spain. Sci. Total Environ. 772, 144794 https://doi.org/10.1016/j.scitotenv.2020.144794.

Blanco, C., Wiley, T.R.A., Lloyd, J.J., Lopez, M.F., Volkow, N.D., 2020. America's opioid crisis: the need for an integrated public health approach. Transl. Psychiatry 10, 167. https://doi.org/10.1038/s41398-020-0847-1.

Camilleri, A., Alfred, S., Gerber, C., Lymb, S., Painter, B., Rathjen, A., Stockham, P., 2021. Delivering harm reduction to the community and frontline medical practitioners through the South Australian Drug Early Warning System (SADEWS). Forensic Sci. Med. Pathol. 17, 388–394. https://doi.org/10.1007/s12024-021-00381-1.

Castrignanò, E., Yang, Z., Bade, R., Baz-Lomba, J.A., Castiglioni, S., Causanilles, A., Covaci, A., Gracia-Lor, E., Hernandez, F., Kinyua, J., McCall, A.-K., van Nuijs, A.L.N., Ort, C., Plósz, B.G., Ramin, P., Rousis, N.I., Ryu, Y., Thomas, K.V., de Voogt, P., Zuccato, E., Kasprzyk-Hordern, B., 2018. Enantiomeric profiling of chiral illicit drugs in a pan-European study. Water Res. 130 https://doi.org/10.1016/j.watres.2017.11.051.

CFSRE (The center for forensic science research and education), 2022. NPS stimulants and hallucinogens in the United States. https://www.cfsre.org/images/trendreports/2022-Q4-NPS-Stimulants-and-Hallucinogens-Trend-Report.pdf (accessed March 2023).

Das, P., Horton, R., 2019. The global drug problem: change but not progression. Lancet 394, 1488–1490. https://doi.org/10.1016/S0140-6736(19)32275-5.

Degenhardt, L., Hall, W., 2012. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. Lancet 379, 55–70. https://doi.org/10.1016/S0140-6736(11)61138-0.

Devault, D.A., Peyré, A., Jaupitre, O., Daveluy, A., Karolak, S., 2020. The effect of the Music Day event on community drug use. Forensic Sci. Int. 309, 110226 https://doi.org/10.1016/j.forsciint.2020.110226.

EMCDDA (European Monitoring Centre for Drugs and Drug Addiction), 2020. COVID-19 and drugs: Drug supply via darknet markets.

EMCDDA (European Monitoring Centre for Drugs and Drug Addiction), 2022a. New psychoactive substances: 25 years of early warning and response in Europe. An update from the EU Early Warning System (June 2022). doi: 10.2810/882318.

EMCDDA (European Monitoring Centre for Drugs and Drug Addiction), 2022b. European Drug Report 2022: Trends and Developments. Publications Office of the European Union, Luxembourg. doi: 10.2810/75644.

EMCDDA (European Monitoring Centre for Drugs and Drug Addiction), 2023. Synthetic cathinones drug profile. https://www.emcdda.europa.eu/publications/drug-profiles/synthetic-cathinones_en# (accessed March 2023).

Estévez-Danta, A., Montes, R., Bijlsma, L., Cela, R., Celma, A., González-Mariño, I., Miró, M., Gutmann, V., de San Román-Landa, U.P., Prieto, A., Ventura, M., Rodil, R., Quintana, J.B., 2021. Source identification of amphetamine-like stimulants in Spanish wastewater through enantiomeric profiling. Water Res. 206, 117719 https://doi.org/10.1016/j.watres.2021.117719.

Farrell, M., Martin, N.K., Stockings, E., Bórquez, A., Cepeda, J.A., Degenhardt, L., Ali, R., Tran, L.T., Rehm, J., Torrens, M., Shoptaw, S., McKetin, R., 2019. Responding to global stimulant use: challenges and opportunities. Lancet 394, 1652–1667. https://doi.org/10.1016/S0140-6736(19)32230-5.

Feltmann, K., Elgán, T.H., Böttcher, M., Lierheimer, S., Hermansson, S., Beck, O., Gripenberg, J., 2022. Feasibility of using breath sampling of non-volatiles to estimate the prevalence of illicit drug use among nightlife attendees. Sci. Rep. 12, 20283. https://doi.org/10.1038/s41598-022-24741-1.

Fernández-Calderón, F., Cleland, C.M., Palamar, J.J., 2018. Polysubstance use profiles among electronic dance music party attendees in New York City and their relation to use of new psychoactive substances. Addict. Behav. 78, 85–93. https://doi.org/10.1016/j.addbeh.2017.11.004.

Foppe, K.S., Hammond-Weinberger, D.R., Subedi, B., 2018. Estimation of the consumption of illicit drugs during special events in two communities in Western Kentucky, USA using sewage epidemiology. Sci. Total Environ. 633, 249–256. https://doi.org/10.1016/j.scitotenv.2018.03.175.

Han, B., Compton, W.M., Jones, C.M., Einstein, E.B., Volkow, N.D., 2021. Methamphetamine use, methamphetamine use disorder, and associated overdose

deaths among US adults. JAMA Psychiat. 78, 1329. https://doi.org/10.1001/jamapsychiatry.2021.2588.
High Alert, 2021. New synthetic cathinone dimethylpentylone detected in NZ. https://www.highalert.org.nz/alerts-and-notifications/new-synthetic-cathinone-dimethylpentylone-detected-in-nz/ (accessed March 2023).
Huang, H., Bai, Y., Zhang, Y., Huang, J., Qin, J., Li, X., 2022. Occurrence and transformation of ephedrine/pseudoephedrine and methcathinone in wastewater in China. Environ. Sci. Tech. 56, 10249–10257. https://doi.org/10.1021/acs.est.2c02639.
Jiang, J.-J., Lee, C.-L., Fang, M.-D., Tu, B.-W., Liang, Y.-J., 2015. Impacts of emerging contaminants on surrounding aquatic environment from a youth festival. Environ. Sci. Tech. 49, 792–799. https://doi.org/10.1021/es503944e.
Lai, F.Y., Thai, P.K., O'Brien, J., Gartner, C., Bruno, R., Kele, B., Ort, C., Prichard, J., Kirkbride, P., Hall, W., Carter, S., Mueller, J.F., 2013. Using quantitative wastewater analysis to measure daily usage of conventional and emerging illicit drugs at an annual music festival. Drug Alcohol Rev. 32, 594–602. https://doi.org/10.1111/dar.12061.
Mackuľak, T., Brandeburová, P., Grenčíková, A., Bodík, I., Staňová, A.V., Golovko, O., Koba, O., Mackuľaková, M., Špalková, V., Gál, M., Grabic, R., 2019. Music festivals and drugs: wastewater analysis. Sci. Total Environ. 659, 326–334. https://doi.org/10.1016/j.scitotenv.2018.12.275.
Mardal, M., Andreasen, M.F., Mollerup, C.B., Stockham, P., Telving, R., Thomaidis, N.S., Diamanti, K.S., Linnet, K., Dalsgaard, P.W., 2019. HighResNPS.com: an online crowd-sourced HR-MS database for suspect and non-targeted screening of new psychoactive substances. J. Anal. Toxicol. 43, 520–527. https://doi.org/10.1093/jat/bkz030.
Mohr, A.L.A., Fogarty, M.F., Krotulski, A.J., Logan, B.K., 2021. Evaluating trends in novel psychoactive substances using a sentinel population of electronic dance music festival attendees. J. Anal. Toxicol. 45, 490–497. https://doi.org/10.1093/jat/bkaa104.
Montgomery, A.B., O'Rourke, C.E., Subedi, B., 2021. Basketball and drugs: wastewater-based epidemiological estimation of discharged drugs during basketball games in Kentucky. Sci. Total Environ. 752, 141712 https://doi.org/10.1016/j.scitotenv.2020.141712.
O'Connor, E., Thomas, R., Senger, C.A., Perdue, L., Robalino, S., Patnode, C., 2020. Interventions to prevent illicit and nonmedical drug use in children, adolescents, and young adults. J. Am. Med. Assoc. 323, 2067. https://doi.org/10.1001/jama.2020.1432.
Pasin, D., Mollerup, C.B., Rasmussen, B.S., Linnet, K., Dalsgaard, P.W., 2021. Development of a single retention time prediction model integrating multiple liquid chromatography systems: application to new psychoactive substances. Anal. Chim. Acta 1184, 339035. https://doi.org/10.1016/j.aca.2021.339035.
Peacock, A., Bruno, R., Gisev, N., Degenhardt, L., Hall, W., Sedefov, R., White, J., Thomas, K.V., Farrell, M., Griffiths, P., 2019. New psychoactive substances: challenges for drug surveillance, control, and public health responses. Lancet 394, 1668–1684. https://doi.org/10.1016/S0140-6736(19)32231-7.
Rousis, N.I., Li, Z., Bade, R., McLachlan, M.S., Mueller, J.F., O'Brien, J.W., Samanipour, S., Tscharke, B.J., Thomaidis, N.S., Thomas, K.V., 2022. Socioeconomic status and public health in Australia: a wastewater-based study. Environ. Int. 167, 107436 https://doi.org/10.1016/j.envint.2022.107436.
Salgueiro-González, N., Zuccato, E., Castiglioni, S., 2022. Nationwide investigation on the use of new psychoactive substances in Italy through urban wastewater analysis. Sci. Total Environ. 843, 156982 https://doi.org/10.1016/j.scitotenv.2022.156982.
Simpson, B.S., Jaunay, E.L., Ghetia, M., Nguyen, L., Bade, R., White, J.M., Gerber, C., 2022. Methcathinone in wastewater: drug of choice, or artefact? Sci. Total Environ. 836, 155696 https://doi.org/10.1016/j.scitotenv.2022.155696.
Song, X.-B., Shao, X.-T., Liu, S.-Y., Tan, D.-Q., Wang, Z., Wang, D.-G., 2020. Assessment of metformin, nicotine, caffeine, and methamphetamine use during Chinese public holidays. Chemosphere 258, 127354. https://doi.org/10.1016/j.chemosphere.2020.127354.
UNODC (United Nations Office on Drugs and crime), 2023. Data from the UNODC early warning advisory on new psychoactive substances. https://www.unodc.org/unodc/en/scientists/ewa/data.html (accessed March 2023).
Van Buskirk, J., Griffiths, P., Farrell, M., Degenhardt, L., 2017. Trends in new psychoactive substances from surface and "dark" net monitoring. Lancet Psychiatry 4, 16–18. https://doi.org/10.1016/S2215-0366(16)30405-9.
Walton, S., Fogarty, M., Papsun, D., Lamb, M., Logan, B., Krotulski, A., 2022. N, N-Dimethylpentylone–an emerging NPS stimulant of concern in the United States. Toxicol. Anal. Clin. 34, S67–S68. https://doi.org/10.1016/j.toxac.2022.06.091.
Whitley, P., LaRue, L., Fernandez, S.A., Passik, S.D., Dawson, E., Jackson, R.D., 2022. Analysis of urine drug test results from substance use disorder treatment practices and overdose mortality rates, 2013–2020. JAMA Netw. Open 5, e2215425. https://doi.org/10.1001/jamanetworkopen.2022.15425.