European Monitoring Centre
for Drugs and Drug Addiction

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PERSPECTIVES ON DRUGS

Wastewater analysis and drugs: a European multi-city study

The findings of the largest European project to date in the emerging science of wastewater analysis are taken up in this 'Perspective on drugs'. The project analysed wastewater in around 80 European cities and towns (hereinafter referred to as 'cities') to explore the drug-taking habits of those who live in them. The results provide a valuable snapshot of the drug flow through the cities involved, revealing marked geographical variations.

Wastewater analysis is a rapidly developing scientific discipline with the potential for monitoring real-time data on geographical and temporal trends in illicit drug use. Originally used in the 1990s to monitor the environmental impact of liquid household waste, the method has since been used to estimate illicit drug consumption in different cities (Daughton, 2001; van Nuijs et al., 2011; Zuccato et al., 2008). It involves sampling a source of wastewater, such as a sewage influent to a wastewater treatment plant. This allows scientists to estimate the quantity of drugs consumed by a community by measuring the levels of illicit drugs and their metabolites excreted in urine (Zuccato et al., 2008).

Wastewater testing in European cities

In 2010 a Europe-wide network (Sewage analysis CORe group — Europe (SCORE)) was established with the aim of standardising the approaches used for wastewater analysis and coordinating international studies through the establishment of a common protocol of action ([1]). The first activity of the SCORE group was a Europe-wide investigation, performed in 2011 in 19 European cities, which allowed the first ever wastewater study of regional differences in illicit drug use in Europe (Thomas et al., 2012). That study also included the first intercalibration exercise for the evaluation of the quality of the analytical data and allowed a comprehensive characterisation of the major uncertainties of the approach (Castiglioni et al., 2014). Following the success of this initial study, comparable studies were undertaken over the following years, covering 82 cities and 18 countries in the European Union in 2020. A standard protocol and a common quality control exercise were used in all locations, which made

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emcdda.europa.eu/topics/pods/waste-water-analysis

([1]) The protocol can be found on the EMCDDA website: www.emcdda.europa.eu/wastewater-analysis

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it possible to directly compare illicit drug loads in Europe over a one-week period during ten consecutive years (van Nuijs et al., 2018). Because of the impact of the COVID-19 pandemic, for the 2020 wastewater monitoring campaign, raw 24-hour composite samples were collected during a single week between March and May for most cities, rather than only during March, as is usually the case. These samples were analysed for the urinary biomarkers (i.e. measurable characteristics) of the parent drug (i.e. primary substance) for amphetamine, methamphetamine and MDMA. In addition, the samples were analysed for the main urinary metabolites (i.e. substances produced when the body breaks drugs down) of cocaine and cannabis, which are benzoylecgonine (BE) and THC-COOH (11-nor-9-carboxy-delta9-tetrahydrocannabinol).

The specific metabolite of heroin, 6-monoacetylmorphine, was found to be unstable in wastewater. Consequently, the only alternative is to use morphine, although it is not a specific biomarker and can also be excreted as a result of therapeutic use. This underlines the importance of collecting the most accurate figure for morphine use from prescription and/or sales reports.

Terms and definitions

Back-calculation is the process whereby researchers calculate/estimate the consumption of illicit drugs in the population based on the amounts of the target drug residue entering the wastewater treatment plant.

Liquid chromatography–tandem mass spectrometry (LC-MS/MS) is the analytical method most commonly used to quantify drug residues in wastewater. LC-MS/MS is an analytical chemistry technique that combines the separation techniques of liquid chromatography with the analysis capabilities of mass spectrometry. Considering the complexity and the low concentrations expected in wastewater, LC-MS/MS is one of the most powerful techniques for this analysis, because of its sensitivity and selectivity.

Metabolite Traces of drugs consumed will end up in the sewer network either unchanged or as a mixture of metabolites. Metabolites, the end products of metabolism, are the substances produced when the body breaks drugs down.

Residue Wastewater analysis is based on the fact that we excrete traces in our urine of almost everything we consume, including illicit drugs. The target drug residue is what remains in the wastewater after excretion and is used to quantify the consumption of illicit drugs in the population.

Urinary biomarkers Analytical chemists look for urinary biomarkers (measurable characteristics to calculate population drug use) in wastewater samples, which can be the parent drug (i.e. the primary substance) or its urinary metabolites.

Enantiomeric profiling Enantiomeric profiling is an analytical chemistry technique used to determine if studied drugs in wastewater originate from consumption or direct disposal (eq. production waste). It is based on the fact that chiral molecules (if only one chiral centre is present) exist as two enantiomers (opposite forms) which are non-superimposable mirror images of each other. As the enantiomeric ratio will change after human metabolism, the enantiomeric fraction can be used to determine whether the studied drugs in wastewater originate from consumption.

Patterns of illicit drug use: geographical and temporal variation

2020 key findings

The project revealed a picture of distinct geographical and temporal patterns of drug use across European cities (see Interactive: explore the data from the study).

The annual SCORE wastewater sampling presented here, from 82 cities, showed that, overall, the loads of the different stimulant drugs detected in wastewater in 2020 varied considerably across study locations.

The BE loads observed in wastewater indicate that cocaine use remains highest in western and southern European cities, in particular in cities in Belgium, the Netherlands and Spain. Very low levels were found in the majority of the eastern European cities, with the most recent data showing some signs of increase.

The loads of amphetamine detected in wastewater varied considerably across study locations, with the highest levels being reported in cities in the north and east of Europe, as in previous years. Amphetamine was found at much lower levels in cities in the south of Europe.

In contrast, methamphetamine use, generally low and historically concentrated in Czechia and Slovakia, was also present in Cyprus, the east of Germany, Spain and northern Europe. The observed methamphetamine loads in the other locations were very low to negligible.

The highest mass loads of MDMA were found in the wastewater in cities in Belgium, Germany, the Netherlands and Slovenia.

The highest mass loads of the cannabis metabolite (THC-COOH) were found in wastewater in cities in Croatia, France and the Netherlands.

Fourteen EU countries participating in the 2020 monitoring campaign included two or more study locations (Austria, Belgium, Cyprus, Czechia, Germany, Finland, Greece, Italy, Lithuania, Netherlands, Portugal, Spain, Slovenia, Sweden). The study highlighted differences between these cities within the same country, which may be explained in part by the different social and demographic characteristics of the cities (universities, nightlife areas and age distribution of the population). Some of these differences were related to the pandemic. In the large majority of countries with multiple study locations, BE, methamphetamine and MDMA loads were higher in large cities compared to smaller locations. No such differences could be detected for amphetamine and cannabis (THC-COOH).

In addition to geographical patterns, wastewater analysis can detect fluctuations in weekly patterns of illicit drug use. More than three-quarters of cities show higher loads of BE and MDMA in wastewater during the weekend (Friday to Monday) than during weekdays, although much of the night-time economy was closed in Europe in 2020. In contrast, amphetamine, cannabis (THC-COOH) and methamphetamine use was found to be distributed more evenly over the whole week.

Thirty-three cities have participated in at least five of the annual wastewater monitoring campaigns since 2011. This allows for time trend analysis of drug consumption based on wastewater testing. Any comparison with previous years and between cities should take into consideration the fact that wastewater samples in 2020 may have been collected when local lockdowns were in place, which might have impacted on both drug availability and drug-using habits.

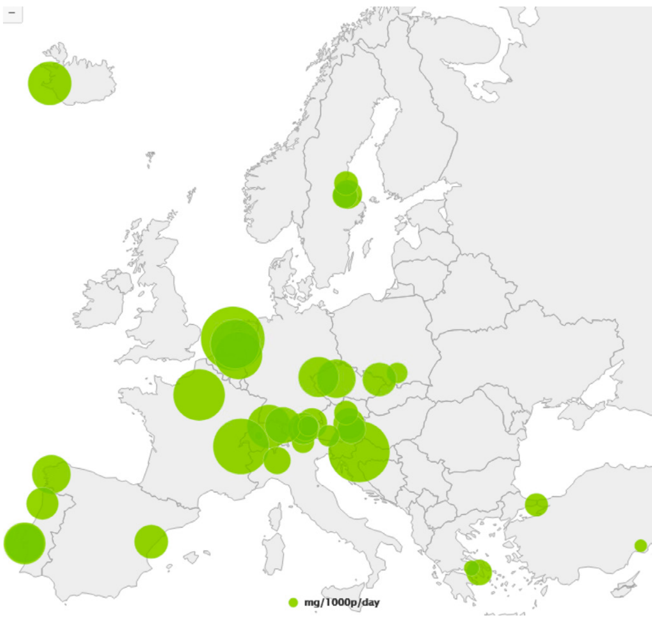
Cannabis

Cannabis is Europe's most commonly used illicit drug, with an estimated 22.2 million last year users. Cannabis use appeared to have been less affected during the pandemic lockdown periods, although differences between and within countries existed. Data from the European Web Survey on Drugs: COVID-19 (EWSD-COVID) also indicated that, among respondents, cannabis use patterns remained relatively stable during the first lockdown period, with more than two fifths (42 %) of the cannabis users who participated in the survey reporting no change in their use of the drug compared with the pre-confinement period (EMCDDA, 2020).

In wastewater, cannabis use is estimated by measuring its main metabolite, THC-COOH, which is the only suitable biomarker found so far. Although it is excreted in a low percentage and more research is still needed (Causanilles et al., 2017a), it is commonly used to report on cannabis use in the literature (Biljsma et al., 2020; Zucatto et al., 2016).

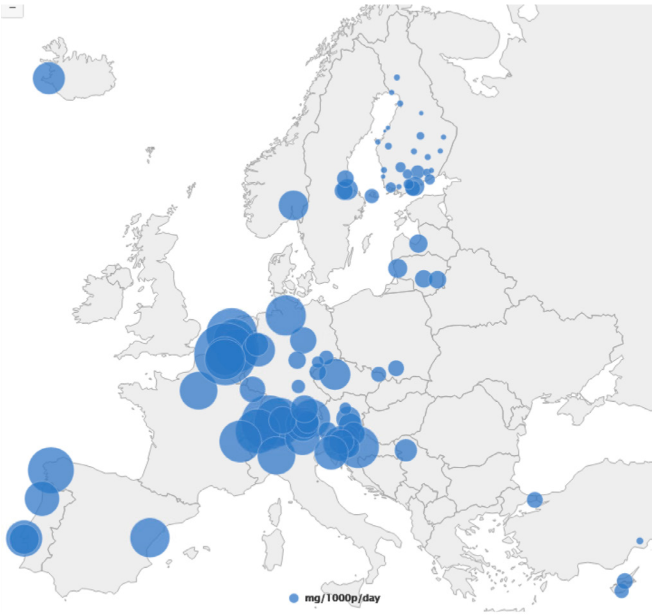
The THC-COOH loads observed in wastewater indicate that cannabis use was highest in western and southern European cities, in particular in cities in Croatia, France, Spain, the Netherlands and Portugal. Findings from wastewater analyses do not show large changes during 2020 when compared with 2019 data.

FIGURE 1
Relative geographical distribution of cannabis metabolite as detected in European cities, 2020 (daily mean)



To examine the data, use the data explorer in the online version:
www.emcdda.europa.eu/topics/pods/waste-water-analysis

FIGURE 2
Relative geographical distribution of cocaine metabolite as detected in European cities, 2020 (daily mean)



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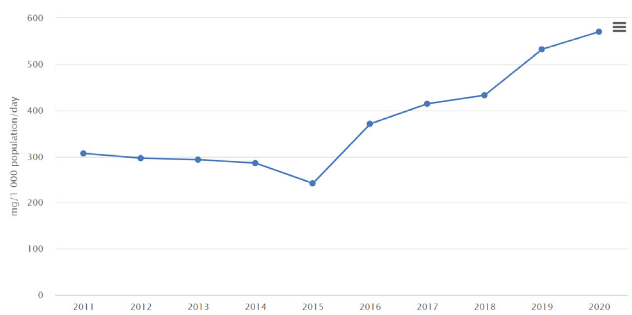
Cocaine

The BE loads observed in wastewater indicate that cocaine use remains highest in western and southern European cities, in particular in cities in Belgium, the Netherlands and Spain. Very low levels were found in the majority of the eastern European cities, but the most recent data show signs of increase.

A relatively stable picture of cocaine use was observed between 2011 and 2015 in most cities. In 2016, there were initial signs that this pattern was changing, with increases observed in the majority of cities each year since then. In 2020, trends diverged in the participating cities, with further increases in use in 19 of the 49 cities with data for 2020 and 2019, and 16 cities reporting a decrease. An overall increase is seen for all the 10 cities with data for both 2011 and 2020.

In the majority of countries with multiple study locations, BE (cocaine) loads were higher in large cities compared to smaller locations. In addition to geographical patterns, wastewater analysis can detect fluctuations in weekly patterns of illicit drug use. More than three-quarters of cities show higher loads of BE in wastewater during the weekend (Friday to Monday) than during weekdays, which may reflect a pattern of more recreational use.

FIGURE 3
Aggregated trends in cocaine residues in 8 EU cities, 2011 to 2020



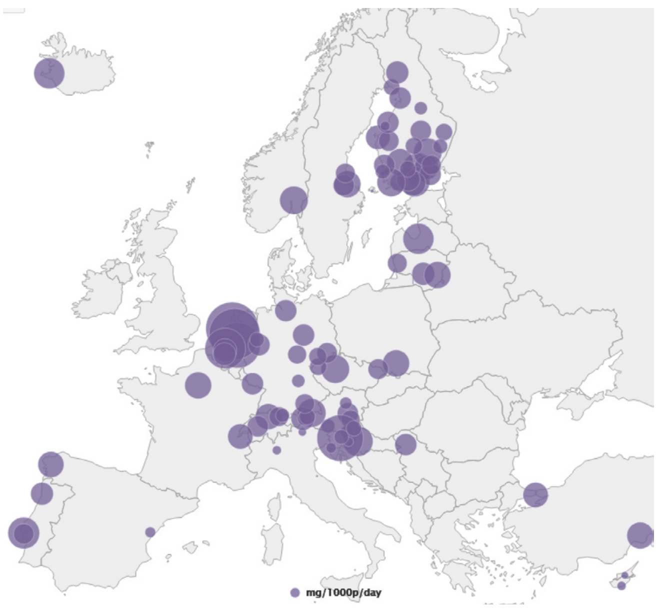
NB: : Trends in mean daily amounts of benzoylecgonine in milligrams per 1 000 head of population in Antwerp Zuid (Belgium) Zagreb (Croatia), Paris Seine Centre (France), Milan (Italy), Eindhoven and Utrecht (Netherlands), Castellon and Santiago (Spain). These 8 cities were selected owing to the availability of annual data from 2011 to2020.

MDMA

The highest mass loads of MDMA were found in the wastewater in cities in Belgium, Germany, the Netherlands and Slovenia.

Until recently, general population surveys in many countries showed that MDMA prevalence was declining from peak levels attained in the early to mid-2000s. In recent years, however, the picture has remained mixed with no clear trends. Where prevalence is high, this may reflect MDMA no longer being a niche or subcultural drug limited to dance clubs and parties, but now being used by a broader range of young people in mainstream nightlife settings, including bars and house parties.

FIGURE 4
Relative geographical distribution of MDMA metabolite as detected in European cities, 2020 (daily mean)



To examine the data, use the data explorer in the online version:
www.emcdda.europa.eu/topics/pods/waste-water-analysis

Looking at longer-term trends in wastewater analysis, in 7 out of the 9 cities with data for both 2011 and 2020 MDMA loads were higher in 2020 than in 2011. Sharp increases were observed in some cities, including Amsterdam, Eindhoven and Antwerp. In most cases the loads increased between 2011-16, and have fluctuated after this. In 2020, possibly due to the fact that in the majority of countries nightlife was largely closed for long periods, almost half of the cities (24 of 49) reported a decrease with 18 reporting an increase.

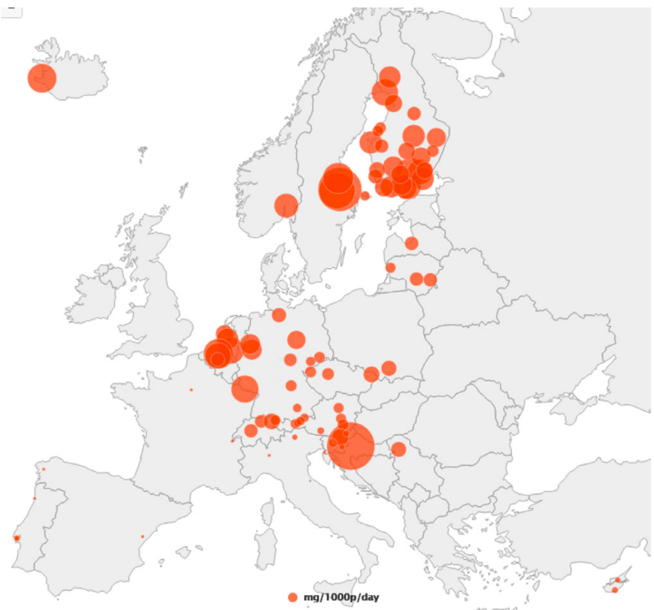
In the large majority of countries, MDMA loads were higher in large cities compared to smaller locations. Also, more than three-quarters of cities showed higher loads of MDMA in wastewater during the weekend (Friday to Monday) than during weekdays, reflecting the predominantly recreational use of ecstasy, although night-time economy was mostly closed.

Amphetamine and methamphetamine

Amphetamine and methamphetamine, two closely related stimulants, are both consumed in Europe, although amphetamine is much more commonly used. Methamphetamine consumption has historically been restricted to Czechia and, more recently, Slovakia, although recent years have seen increases in use in other countries.

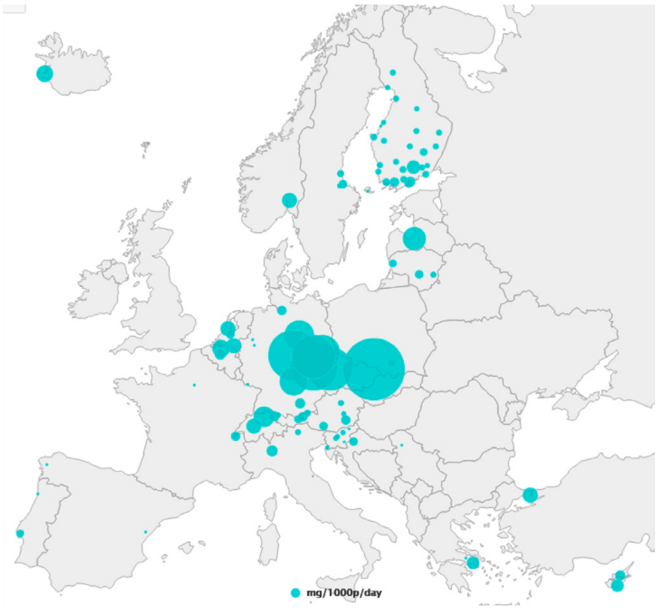
The loads of amphetamine detected in wastewater varied considerably across study locations, with the highest

FIGURE 5
Relative geographical distribution of amphetamine metabolite as detected in European cities, 2020 (daily mean)



To examine the data, use the data explorer in the online version: www.emcdda.europa.eu/topics/pods/waste-water-analysis

FIGURE 6
Relative geographical distribution of methamphetamine metabolite as detected in European cities, 2020 (daily mean)



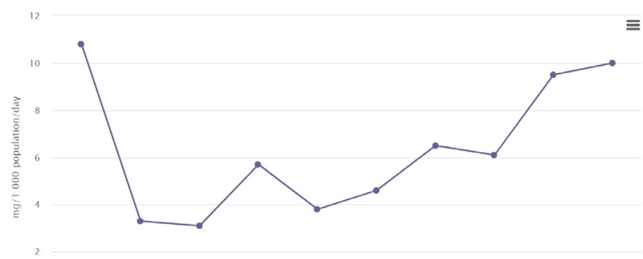
To examine the data, use the data explorer in the online version: www.emcdda.europa.eu/topics/pods/waste-water-analysis

levels reported in cities in the north and east of Europe. Amphetamine was found at much lower levels in cities in the south of Europe.

In contrast, methamphetamine use, generally low and historically concentrated in Czechia and Slovakia, now appears to be present also in Cyprus, the east of Germany, Spain and several northern European countries (Denmark, Finland, Lithuania, Norway). The observed methamphetamine loads in the other locations were very low to negligible.

Overall, the data related to amphetamine and methamphetamine from the ten monitoring campaigns showed no major changes in the general patterns of use

FIGURE 7
Aggregated trends in methamphetamine residues in 5 European cities, 2011 to 2020



NB: Trends in mean daily amounts of methamphetamine in milligrams per 1 000 head of population in Antwerp Zuid (Belgium), Paris Seine Centre (France), and Milan (Italy), Castellon and Santiago (Spain). These 5 cities were selected owing to the availability of annual data from 2011 to 2020.

observed. In 2020, the most recent data show that 20 of the 48 cities with data for 2019 and 2020 reported an increase for amphetamine and 19 cities a decrease. For methamphetamine use, the 2020 data show that 15 of the 50 cities with data for 2019 and 2020 reported an increase and 21 cities a decrease in the loads found.

In 2020, amphetamine and methamphetamine use were found to be distributed more evenly over the whole week than in previous years, possibly reflecting the use of these drugs being associated with more regular consumption by a cohort of high-risk users.

Comparison with findings from other monitoring tools

Because different types of information are provided by wastewater analysis (collective consumption of substances within a community) and by established monitoring tools, such as population surveys (prevalence in the last month or year), a direct comparison of the data is difficult. However, the patterns and trends being detected by wastewater analysis are largely, but not completely, in line with the analyses coming from other monitoring tools.

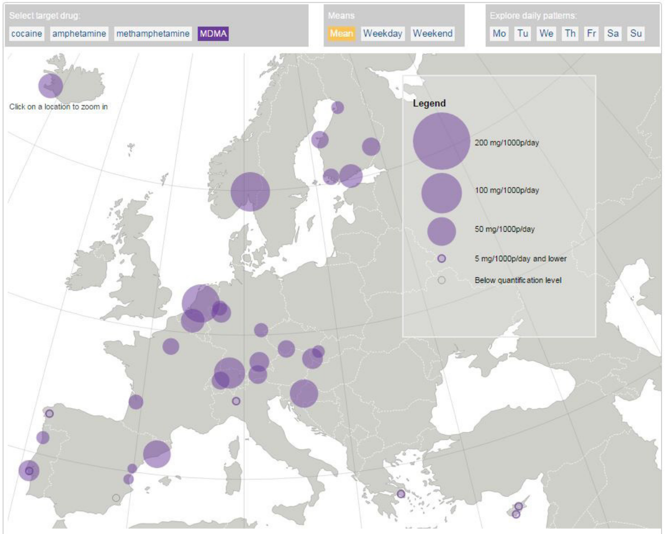
For example, both seizure and wastewater data present a picture of a geographically divergent stimulant market in Europe, where cocaine is more prevalent in the south and west, while amphetamines are more common in central and northern countries (EMCDDA, 2017). Similar results are also found in data coming from population surveys on drug use. While the general pattern detected in wastewater is in line with established monitoring tools, there are some exceptions.

Data from established indicators show that methamphetamine use have historically been restricted to Czechia, and more recently also Slovakia, although recent years have seen increased use in other countries (EMCDDA, 2016a). These findings have been confirmed by recent wastewater-based epidemiology, with the highest methamphetamine loads found in Czech, Slovak, German and Finnish cities.

Similarly, studies based on self-reported drug use and those using wastewater data both point towards the same weekly variations in use, with stimulants such as amphetamine and cocaine being primarily used at weekend music events and in celebratory contexts (Tossmann et al., 2001).

A limited but steadily increasing number of studies have been published comparing drug use estimates obtained through wastewater analysis and estimates provided by epidemiological surveys (EMCDDA, 2016b; van Wel et al., 2015). While in 2012 only one reported study tried to evaluate

Interactive element



Interactive: explore the data from the study, available on the EMCDDA website: emcdda.europa.eu/topics/pods/waste-water-analysis

sewage analysis alongside traditional epidemiological techniques (Reid et al., 2012), this number has now increased considerably in recent years.

A first study, performed in Oslo, Norway, and published in 2012, compared the results from three different datasets (a general population survey, a roadside survey and wastewater analysis) (Reid et al., 2012).

Other studies compare and correlate wastewater-based consumption estimates of illicit drugs with other data sources, including self-reported data (Been et al., 2015; Castiglioni et al., 2016; van Wel et al., 2016a), consumption offences (Been et al., 2016a), illicit drug seizures (Baz-Lomba et al., 2016; Kankaanpää et al., 2014, 2016), purity of drug seizures (Bruno et al., 2018), syringe distribution estimates (Been et al., 2015), toxicological data (Kankaanpää et al., 2014, 2016) and the number of drug users in treatment (Krizman et al., 2016).

The majority of comparative studies have been carried out within European countries, including Belgium (van Wel et al., 2016a), Croatia (Krizman et al., 2016), Germany (Been et al., 2016a), Finland (Kankaanpää et al., 2014, 2016), Italy (Castiglioni et al., 2016), Spain (Bijlsma et al., 2018), Switzerland (Been et al., 2015; Been et al., 2016b), Turkey (Daglioglu, 2019), and across European countries (Baz-Lomba et al., 2016; Castrignanò et al., 2018; Löve et al., 2018). Outside Europe, in recent years studies have been published comparing wastewater-based estimates with other data sources in China (Du et al., 2015), Australia (Tscharke et al., 2015) and in countries where data on drug use are limited due to financial constraints or lack of monitoring tools (Archer et al., 2018; Moslah et al., 2018; Nguyen et al., 2018).

These examples confirm the promising future of wastewater-based epidemiology as a complementary approach to obtain a more accurate and balanced picture of substance use within different communities. Wastewater analysis can predict results from population surveys and can be used as a 'first alert' tool in the identification of new trends in drug consumption. In order to check the quality and accuracy of data, further comparisons between wastewater analysis and data obtained through other indicators are needed.

Limitations of this method

Wastewater analysis offers an interesting complementary data source for monitoring the quantities of illicit drugs used at the population level, but it cannot provide information on prevalence and frequency of use, main classes of users and purity of the drugs. Additional challenges arise from uncertainties associated with the behaviour of the selected biomarkers in the sewer, different back-calculation methods and different approaches to estimate the size of the population being tested (Castiglioni et al., 2013, 2016; EMCDDA, 2016b; Lai et al., 2014). The caveats in selecting the analytical targets for heroin, for example, make monitoring this drug in wastewater more complicated compared to other substances (Been et al., 2015). Also, the purity of street products fluctuates unpredictably over time and in different locations. Furthermore, translating the total consumed amounts into the corresponding number of average doses is complicated, as drugs can be taken by different routes and in amounts that vary widely, and purity levels fluctuate (Zuccato et al., 2008).

Efforts are being made to enhance wastewater monitoring approaches. For example, work has been undertaken on overcoming a major source of uncertainty related to estimating the number of people present in a sewer catchment at the time of sample collection. This involved using data from mobile devices to better estimate the dynamic population size for wastewater-based epidemiology (Thomas et al., 2017).

New developments and the future

Wastewater-based epidemiology has established itself as an important tool for monitoring illicit drug use and future directions for wastewater research have been explored (EMCDDA, 2016b).

First, wastewater analysis has been proposed as a tool to address some of the challenges related to the dynamic new psychoactive substances (NPS) market. This includes the large number of individual NPS, the relatively low prevalence of use and the fact that many of the users are actually unaware of exactly which substances they are using. A technique has been established to identify NPS that involves the collection and analysis of pooled urine from stand-alone portable urinals from nightclubs, city centres and music festivals, thereby providing timely data on exactly which NPS are currently in use at a particular location (Archer et al., 2013a, 2013b, 2015; Causanilles et al., 2017b; Kinyua, et al., 2016; Mackulak et al., 2019; Mardal et al., 2017; Reid et al., 2014;). The European project 'NPS euronet' aimed to improve the capacity to identify and assess the NPS being used in Europe. The project applied innovative analytical chemical and epidemiological methods and a robust risk-assessment procedure to improve the identification of NPS, to assess risks, and to estimate the extent and patterns of use in specific groups (e.g. at music festivals) and among the general population (Bade et al., 2017; González-Mariño et al., 2016).

Second, in addition to estimating illicit drug use, wastewater-based epidemiology has been successfully applied in recent years to providing detailed information on the use and misuse of alcohol (Boogaerts et al., 2016; Mastroianni et al., 2017; Rodríguez-Álvarez et al., 2015), tobacco (Senta et al., 2015; van Wel et al., 2016b) and medicines in a specific population (Baz-Lomba et al., 2016, 2017; Been et al., 2015; Krizman-Matasic et al., 2018). Furthermore, wastewater analysis can potentially provide information on health and illness indicators within a community (Kasprzyk-Hordern et al., 2014; Thomaidis et al., 2016; Yang et al., 2015).

Third, the potential for wastewater-based epidemiology to be used as an outcome measurement tool, in particular in the evaluation of the effectiveness of interventions that target drug supply (e.g. law enforcement) or drug demand (e.g. public health campaigns) has not yet been fully explored. Close collaboration between the different stakeholders involved, including epidemiologists, wastewater experts and legal authorities, is highly recommended in order to start examining these potential wastewater-based epidemiology applications (EMCDDA, 2016b). The WATCH project included a 30-day synthetic drug production monitoring campaign in three cities in Belgium and the Netherlands. High levels of MDMA were recorded during the whole monitoring period in one city in the Netherlands, suggesting continuous discharges of unconsumed MDMA from sources within the wastewater catchment area, indicating drug production was taking place in this region.

Fourth, by back-calculating the daily sewer loads of target residues, wastewater analysis can provide total consumption estimates, and specific efforts are now being directed towards finding the best procedures for estimating annual averages. In 2016, the EMCDDA presented for the first time illicit drug retail market size estimates in terms of quantity and value for the main substances used (EMCDDA and Europol, 2016). It is envisaged that findings from wastewater analysis can help to further develop work in this area.

Finally, new methods such as enantiomeric profiling have been developed to determine if mass loads of drugs in wastewater originated from consumption or from the disposal of unused drugs or production waste. It is now important to assess the possible utility of wastewater analysis to report on drug supply dynamics, including synthetic drug production (Emke et al., 2014). For example, recent malfunctioning of a small wastewater treatment plant in the Netherlands was caused by direct discharges in the sewage system of chemical waste from a drug production site. Further analysis revealed the actual synthesis process used to manufacture the corresponding drugs. The study confirmed that the chemical waste from the illegal manufacturing of stimulants will result in a specific chemical fingerprint that can be tracked in wastewater and used for forensic purposes. Such profiles can be used to identify drug production or synthesis waste disposal in the wastewater catchment area (Emke et al., 2018).

Wastewater analysis has demonstrated its potential as a useful complement to established monitoring tools in the drugs area. It has some clear advantages over other approaches as it is not subject to response and non-response bias and can better identify the true spectrum of drugs being consumed, as users are often unaware of the actual mix of substances they take. This tool also has the potential to provide timely information in short timeframes on geographical and temporal trends. In order to check the quality and accuracy of data, further comparisons between wastewater analysis and data obtained through other indicators are needed.

As a method, wastewater analysis has moved from being an experimental technique to being a new method in the epidemiological toolkit. Its rapid ability to detect new trends can help target public health programmes and policy initiatives at specific groups of people and the different drugs they are using.

Understanding the wastewater method, and addressing ethical issues

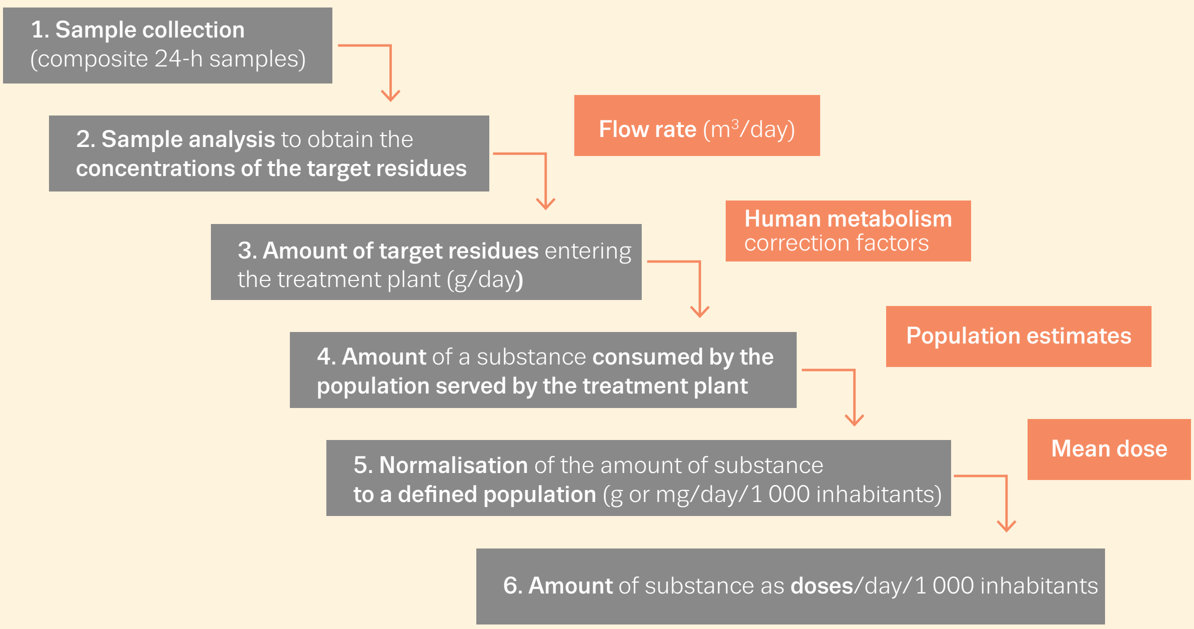
In order to estimate levels of drug use from wastewater, researchers attempt first to identify and quantify drug residues, and then to back-calculate the amount of the illicit drugs used by the population served by the sewage treatment plants (Castiglioni et al., 2014). This approach involves several steps (see figure). Initially, composite samples of untreated wastewater are collected from the sewers in a defined geographical area. The samples are then analysed to determine the concentrations of the target drug residues. Following this, the drug use is estimated through back-calculation by multiplying the concentration of each target drug residue (nanogram/litre) with the corresponding flow of sewage (litre/day). A correction factor for each drug is taken into account as part of the calculation. In a last step, the result is divided by the population served by the wastewater treatment plant, which shows the amount of a substance consumed per day per 1 000 inhabitants. Population estimates can be calculated using different biological parameters, census data, number of house connections, or the design capacity, but the overall variability of different estimates is generally very high.

Although primarily used to study trends in illicit drug consumption in the general population, wastewater analysis has also been applied to small communities, including workplaces, schools (Zuccato et al., 2017), music festivals, prisons (Nefau et al., 2017) and specific neighbourhoods (Hall et al., 2012).

Using this method in small communities can involve ethical risks (Prichard et al., 2014), such as possible identification of a particular group within the community.

In 2016 the SCORE group published ethical guidelines for wastewater-based epidemiology and related fields (Prichard et al., 2016). The objective of these guidelines is to outline the main potential ethical risks for wastewater research and to propose strategies to mitigate those risks. Mitigating risks means reducing the likelihood of negative events and/or minimising the consequences of negative events.

Wastewater analysis approach



Source: (Castiglioni et al., 2013a)

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