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 in question analysed wastewater in over 60 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.

Full edition of this article with interactive features available online at

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

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; Zuccato et al., 2008; van Nuijs et al., 2011). 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 four years, covering 53 cities and 20 countries in Europe in 2016. A standard protocol and a common quality control

([1]) The protocol can be found on the EMCDDA website: www.emcdda.europa.eu/wastewater-analysis exercise were used in all locations, which made it possible to directly compare illicit drug loads in Europe over a one-week period during six consecutive years. For the 2016 wastewater monitoring campaign, raw 24-hour composite samples were collected during a single week in March. 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).

This report is focused on illicit stimulants. No results for cannabis are reported, as the identification of THC-COOH loads in wastewater poses some sampling and analytical challenges.

Patterns of illicit drug use: geographical and temporal variation

2016 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 BE loads observed in wastewater indicate that cocaine use is highest in western and southern European cities, in particular in cities in Belgium, Spain and the United Kingdom. Wastewater analysis indicates that cocaine use is very low to negligible in the majority of eastern European cities.

The loads of amphetamine detected in wastewater varied considerably across study locations, with the highest levels reported in cities in the north 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 the Czech Republic and Slovakia, now appears to be present also in the east of Germany and northern Europe, particularly in cities in Finland. 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, the Netherlands and Norway.

Ten countries participating in the 2016 monitoring campaign included two or more study locations (Belgium, Cyprus, Germany, Spain, Finland, France, the Netherlands, Portugal, Slovakia and UK). 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). In the large majority of countries with multiple study locations, cocaine and MDMA loads were higher in large cities compared to smaller locations. No such differences could be detected for amphetamine and methamphetamine.

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. In contrast, amphetamine use was found to be distributed more evenly over the whole week.

Five-year trend data

A relatively stable picture of cocaine use can be observed over five years. The general patterns detected were similar in the six consecutive monitoring campaigns, with the highest and lowest BE loads found in the same cities and regions. Most cities show either a decreasing or a stable trend between 2011 and 2015, but there are signs that this pattern may have changed with 22 out of 33 cities that have data for 2015 and 2016 reporting an increase. In a few cases, including London and Zagreb, a longer-term increase in BE loads found in wastewater over the 2011–16 period has been notified.

Over the six years of monitoring the highest MDMA loads were consistently found in the wastewater of cities in Belgium and the Netherlands. Looking at longer term trends, in most cities with at least five data points wastewater MDMA loads were higher in 2016 than in 2011, with sharp increases observed in some cities, including Antwerp and Oslo.

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

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). While the general pattern detected in wastewater is in line with established monitoring tools, there are some exceptions: the amphetamine loads in wastewater in Paris have been below the level of quantification over the consecutive annual monitoring campaigns, contrary to indications from other monitoring tools.

Data from established indicators show that methamphetamine use has historically been restricted to the Czech Republic, 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.

Established indicators show that, until recently, MDMA prevalence was declining in many countries from peak levels in the early to mid 2000s. Data from wastewater and from established indicators show that this appears to be changing, with the large majority of cities reporting higher wastewater MDMA loads in 2016 than in 2011.

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 sewage analysis alongside traditional epidemiological techniques (Reid et al., 2012), this number has now increased to around 20 published research articles that are focused on comparing information provided by wastewater analysis and information provided by other indicators.

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.

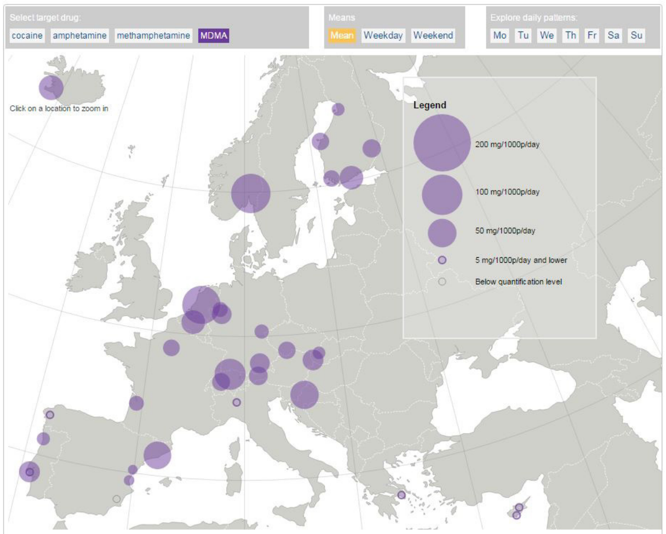
Urinary biomarkers Analytical chemists look for urinary biomarkers (measurable characteristics to calculate population drug use) in wastewater samples, which can be the parent drug (i.e. the primary substance) or its urinary metabolites.

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, more recent 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), 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 Europe, including in 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), Switzerland (Been et al., 2015; Been et al., 2016b)

Interactive element



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

and across European countries (Baz-Lomba et al., 2016). Outside Europe, in recent years studies have been published comparing wastewater-based estimates with other data sources in China (Du et al., 2015) and Australia (Tscharke et al., 2015).

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.

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; Lai et al., 2014; EMCDDA, 2016b). 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).

The necessary sampling intervals for wastewater samples to reduce random biases and produce reliable annual consumption estimates is an issue that will be further explored in the 2017 SCORE annual monitoring campaign (http://score-cost.eu/monitoring2017/).

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 new 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; Reid et al., 2014; Kinyua, 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; Rodríguez-Álvarez et al., 2015), tobacco (Senta et al., 2015; van Wel et al., 2016b) and medicines in a specific population (Been et al., 2015; Salvatore et al., 2016; Baz-Lomba, 2016). Furthermore, wastewater analysis can potentially provide information on health and illness indicators within a community (Yang et al., 2015; Kasprzyk-Hordern et al., 2014).

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).

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, 2016c). 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.

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

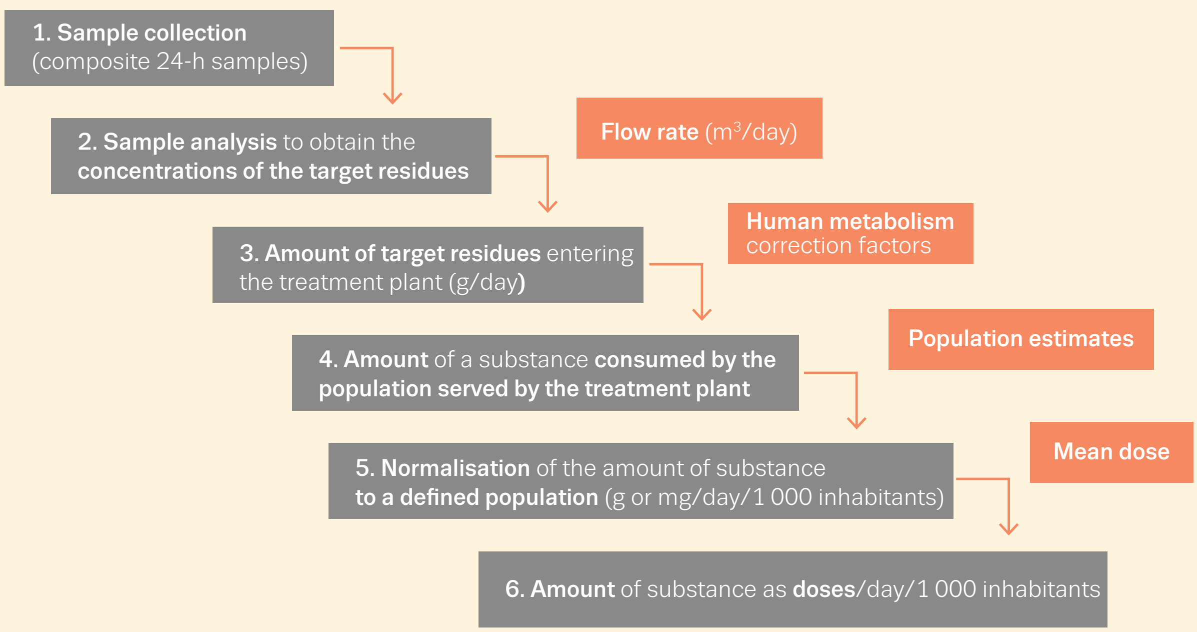
In order to estimate levels of drug use from wastewater, researchers attempt first to identify and quantify drug residues, and then to back-calculate the amount of the illicit drugs used by the population served by the sewage treatment plants (Castiglioni et al., 2014). This approach involves several 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 identify 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 (ng/L) with the corresponding flow of sewage (L/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, music festivals, prisons 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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