



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.

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. 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 up to 21 European countries in 2015. A standard protocol and a common quality control exercise were used in all locations, which made it possible to directly compare illicit drug loads in Europe over a one-week period

Full edition of this article with interactive features available online at

[emcdda.europa.eu/topics/
pods/waste-water-analysis](http://emcdda.europa.eu/topics/pods/waste-water-analysis)



during five consecutive years ⁽¹⁾. For the 2015 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).

Patterns of illicit drug use: geographical and temporal variation

2015 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 European cities, in particular in cities in Belgium, the Netherlands and the United Kingdom, and in some southern and northern European cities. 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 is concentrated in cities within Norway, the Czech Republic and Slovakia. High loads were also detected in Dresden, a German city near the border of the Czech Republic. The observed methamphetamine loads in the other locations were very low to negligible. Relatively low levels of the urinary biomarker loads related to MDMA were found in the majority of European countries, with the exceptions of high loads detected in wastewater from cities in Belgium and the Netherlands.

With regard to cannabis, the identification of THC-COOH loads in wastewater poses some sampling and analytical challenges, and as a result no findings from the 2015 monitoring campaign were available at the time of publication.

Ten countries that included two or more locations participated in the 2015 monitoring campaign. 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 distinct 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 and methamphetamine use were found to be distributed more evenly over the whole week.

Five-year trend data

Sixteen cities have participated in four or five of the annual wastewater monitoring campaigns since 2011, which allows for five-year time trend analysis of drug consumption based on wastewater testing.

A stable picture of cocaine use can be observed over five years. The general patterns detected were similar in the five 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 in a few cases, in particular Brussels and London, an increase in BE loads was observed in this period.

Over the five years of monitoring the highest MDMA loads were consistently found in the wastewater of Belgian and Dutch cities. Wastewater MDMA loads were higher in 2015 than in 2011 in most cities, with sharp increases observed in some cities, which may be related to the increased purity of MDMA or increased availability of the drug.

⁽¹⁾ In total, 27 countries and 67 cities worldwide participated in the 2015 SCORE wastewater monitoring campaign. For the purpose of this analysis data was analysed from 44 cities in 18 countries (EU and Norway). Additional data from other countries and cities can be found in the POD interactive element.

Overall, the data related to amphetamine and methamphetamine from the five 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 pure 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, prevalence data from surveys and wastewater analysis both 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, 2016a). While the general pattern detected in wastewater is in line with established monitoring tools, the amphetamine loads in wastewater in Paris and London were below the level of quantification, 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, Norwegian and German 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 majority of cities reporting higher wastewater MDMA loads in 2015 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).

To date, few case studies have been set up to compare the drug use estimates obtained through wastewater analysis and through epidemiological surveys (EMCDDA, 2016b; van Wel et al., 2016). One study, performed in Oslo, Norway, compared the results from three different datasets (a general population survey, a roadside survey

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.

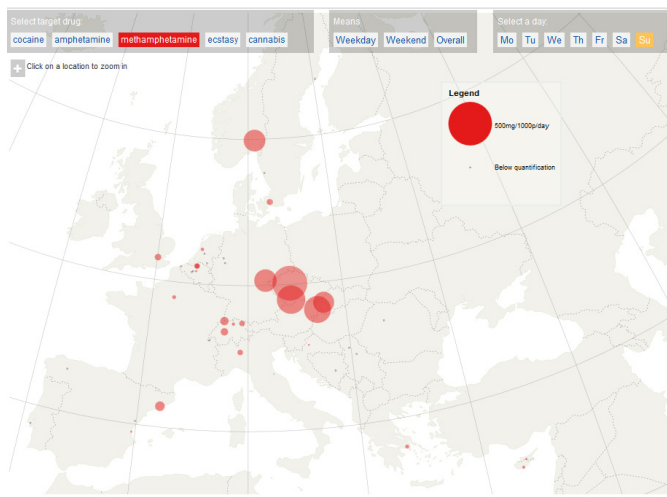
Urinary biomarkers Analytical chemists look for urinary biomarkers (measurable characteristics to calculate population drug use) in wastewater samples, which can be the parent drug (i.e. the primary substance) or its urinary metabolites.

and wastewater analysis) (Reid et al., 2012). A second study analysed the temporal and spatial trends of cocaine use in Italy through wastewater-based epidemiology and compared these with results from epidemiological surveys during the same period (Zuccato et al., 2016). A third study compared epidemiological, crime and wastewater data in 19 cities across Germany and Switzerland (Been et al., 2016). These case studies confirm that wastewater analysis can predict results from population surveys and suggest that wastewater-based epidemiology 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

Interactive element



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

uncertainties associated with the sampling of wastewater, the behaviour of the selected biomarkers in the sewer, the reliability of inter-laboratory analytical measurement, 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. 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).

New developments and the future

Wastewater-based epidemiology has established itself as an important tool for monitoring illicit drug use and it is now time to explore future directions for wastewater research (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; Reid et al., 2014).

Second, wastewater-based epidemiology can potentially provide information not only on illicit drugs, alcohol, tobacco and the misuse of medicines (Boogaerts et al., 2016; Rodríguez-Álvarez et al., 2015; Senta et al., 2015), but also about health and illness indicators within a community (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).

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 April 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. To date, there have been a few attempts to compare estimates produced from wastewater and more established techniques (Bramness et al., 2014; Reid et al., 2012; Thomas et al., 2012; Zuccato et al., 2016). Nonetheless, 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

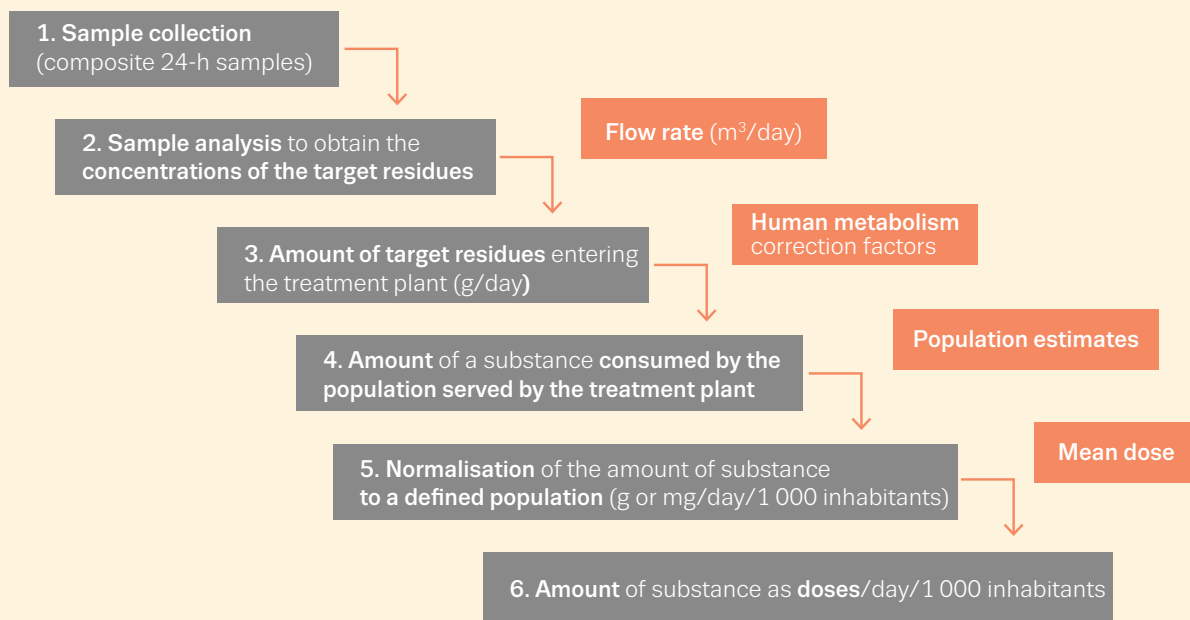
In order to estimate levels of drug use from wastewater, researchers attempt first to identify and quantify drug residues, and then to back-calculate the amount of the illicit drugs used by the population served by the sewage treatment plants (Castiglioni et al., 2013a). This approach involves several 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.

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. Consequently, there is a strong need for ethical guidelines for researchers using this technique (Hall et al., 2012). Ideally these guidelines should be interdisciplinary and international and should entail some consideration of how findings might be interpreted, how media outlets might misrepresent findings and how policymakers may respond (Prichard et al., 2014).

Wastewater analysis approach



Source: (Castiglioni et al., 2013a)

References

- Archer, J. R. H., Dargan, P. I., Hudson, S. and Wood, D. M. (2013a), 'Analysis of anonymous pooled urinals in central London confirms the significant use of novel psychoactive substances', *QJM*, 106(2), pp. 147–152.
- Archer, J. R. H., Hudson, S., Wood, D. M. and Dragan, P. I. (2013b), 'Analysis of urine from pooled urinals: a novel method for the detection of novel psychoactive substances', *Current Drug Abuse Reviews*, online publication, 5 December.
- Been, F., Bijlsma, L., Benaglia, L., et al. (2016), 'Assessing geographical differences in illicit drug consumption: A comparison of results from epidemiological and wastewater data in Germany and Switzerland', *Drug and Alcohol Dependence* 161, pp. 189–199.
- Bramness, J.G., Reid M.J., Solvik, K.F. and Vindenes, V. (2014), 'Recent trends in the availability and use of amphetamine and methamphetamine in Norway', *Forensic Science International*, 246, pp. 92–97.
- Boogaerts, T., Covaci, A., Kinyua, J., et al. (2016), 'Spatial and temporal trends in alcohol consumption in Belgian cities: A wastewater-based approach', *Drug and Alcohol Dependence* 160, pp. 170–176.
- Castiglioni, S., Borsotti, A., Riva, F. and Zuccato, E. (2016), 'Illicit drug consumption estimated by wastewater analysis in different districts of Milan: A case study', *Drug and Alcohol Review* 35, pp. 128–132.
- Castiglioni, S., Thomas, K. V., Kasprzyk-Hordern, B., Vandam, L. and Griffiths, P. (2014), 'Testing wastewater to detect illicit drugs: State of the art, potential and research needs', *Science of the Total Environment* 487, pp. 613–620.
- Castiglioni, S., Bijlsma, L., Covaci A., et al. (2013), 'Evaluation of uncertainties associated with the determination of community drug use through the measurement of sewage drug biomarkers', *Environmental Science and Technology*, 47(3), pp. 1452–1460.
- Daughton, C.G. (2001), 'Emerging pollutants, and communicating the science of environmental chemistry and mass spectrometry: pharmaceuticals in the environment', *American Society for Mass Spectrometry*, 12, pp. 1067–1076.
- EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) (2016a), *European Drug Report: Trends and Developments*, Publications Office of the European Union, Luxembourg.
- EMCDDA (2016b), *Assessing illicit drugs in wastewater: Advances in wastewater-based drug epidemiology*, Insights, Publications Office of the European Union, Luxembourg.
- EMCDDA and Europol (2016c), *EU Drug Markets Report*, Joint publications, Publications Office of the European Union, Luxembourg.
- Hall, W., Prichard, J., Kirkbride, P., et al. (2012), 'An analysis of ethical issues in using wastewater analysis to monitor illicit drug use', *Addiction*, 107(10), pp. 1767–1773.
- Lai, F.Y., Anuj, S., Bruno, R., et al. (2014), 'Systematic and day-to-day effects of chemical-derived population estimates on wastewater-based drug epidemiology', *Environmental Science and Technology* 49, pp. 999–1008.
- Ort, C., van Nuijs A.L.N., Berset J-D, et al. (2014), 'Spatial differences and temporal changes in illicit drug use in Europe quantified by wastewater analysis', *Addiction*, 109, doi: 10.1111/add.12570

- Prichard, J., Hall, W., de Voogt, P. and Zuccato, E. (2014), 'Sewage epidemiology and illicit drug research: the development of ethical research guidelines', *Science of the Total Environment*, 47(2), pp. 550–555.
- Reid, M. J., Langford, K. H., Grung, M., et al. (2012), 'Estimation of cocaine consumption in the community: a critical comparison of the results from three complimentary techniques', *BMJ Open*, 2(6).
- Reid, M. J., Baz-Lomba, J. A., Ryu, Y. and Thomas, K. V. (2014), 'Using biomarkers in wastewater to monitor community drug use: a conceptual approach for dealing with new psychoactive substances', *Science of The Total Environment* 487, pp. 651–658.
- Rodríguez-Álvarez, T., Racamonde, I., González-Mariño, I., et al. (2015), 'Alcohol and cocaine co-consumption in two European cities assessed by wastewater analysis', *Science of the Total Environment* 536, pp. 91–98.
- Senta, I., Gracia-Lor, M., Borsotti, A., et al. (2015), 'Wastewater analysis to monitor use of caffeine and nicotine and evaluation of their metabolites as biomarkers for population size assessment', *Water Research* 74, pp. 23–33.
- Thomas, K. V., Bijlsma, L., Castiglioni, S., et al. (2012), 'Comparing illicit drugs use in 19 European cities through sewage analysis', *Science of the Total Environment*, 432, pp. 432–439.
- Tossmann, P., Boldt, S. and Tensil, M.-D. (2001), 'The use of drugs within the techno party scene in European metropolitan cities', *European Addiction Research*, 7(1), pp. 2–23.
- Van Nuijs, A., Mougél, J.-F., Tarcomnicu, I., et al. (2011), 'Sewage epidemiology: a real-time approach to estimate the consumption of illicit drugs in Brussels, Belgium', *Environment International*, 27, pp. 612–621.
- Van Wel, J. H. P., Gracia-Lor, E., van Nuijs, A. L. N., et al. (2016), 'Investigation of agreement between wastewater-based epidemiology and survey data on alcohol and nicotine use in a community', *Drug and Alcohol Dependence* 162, pp. 170–175.
- Yang, Z., Anglès d'Auriac, M., Goggins, S., et al. (2015) 'A novel DNA biosensor using a ferrocenyl intercalator applied to the potential detection of human population biomarkers in wastewater', *Environmental Science and Technology* 49(9), pp. 5609–5617.
- Zuccato, E., Chiabrando, C., Castiglioni, S., Bagnati, R. and Fanelli, R. (2008), 'Estimating community drug abuse by wastewater analysis', *Environmental Health Perspectives*, 116(8), pp. 1027–1032.
- Zuccato, E., Castiglioni, S., Senta, I., et al. (2016), 'Population surveys compared with wastewater analysis for monitoring illicit drug consumption in Italy in 2010–2014', *Drug and Alcohol Dependence* 161, pp 178–188.