Spatial differences and temporal changes in illicit drug use in Europe quantified by wastewater analysis

Christoph Ort1,2*, Alexander L. N. van Nuij3,2*, Jean-Daniel Berset3, Lubertus Bijlsma4, Sara Castiglioni5, Adrian Covaci6, Pim de Voogt7,8, Erik Emke9, Despo Fatta-Kassinos9, Paul Griffiths10, Félix Hernández-Mariño10, Roman Grubic10, Barbara Kasprzyk-Hordern12, Nicola Mastroianni13, Axel Meierjohn14, Thomas Nefau15, Marcus Östman16, Yolanda Pico17, Ines Racamonde10, Malcolm Reid18, Jaroslav Slobodnik19, Senka Terzic20, Nikolaos Thomaidis21 & Kevin V. Thomas22

Swiss Federal Institute of Aquatic Science and Technology (Eawag), Dübendorf, Switzerland, 1 Toxicological Center, University of Antwerp, Antwerp, Belgium, 2 Water and Soil Protection Laboratory, Bern, Switzerland, 3 Research Institute for Pesticides and Water, University Jaume I, Castellón de la Plana, Spain, 4 Department of Environmental Health Sciences, IRCCS—Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy, 5 KWR Watertechnology Research Institute, Nieuwegein, the Netherlands, 6 Institute for Biodiversity and Ecosystem Dynamics, University of Amsterdam, Amsterdam, the Netherlands, 7 NIREAS—International Water Research Center, University of Cyprus, Nicosia, Cyprus, 8 European Monitoring Centre for Drugs and Drug Addiction, Lisbon, Portugal, 9 IAA—Institute of Food Analysis and Research, University of Santiago de Compostela, Santiago de Compostela, Spain, 10 University of South Bohemia in Ceske Budejovice, Faculty of Fisheries and Protection of Waters, South Bohemian Research Center of Aquaculture and Biodiversity of Hydrocenes, Vodnany, Czech Republic, 11 Department of Chemistry, University of Bath, Bath, UK, 12 Water and Soil Quality Research Group, Department of Environmental Chemistry, IDAEA-CSIC, Barcelona, Spain, 13 Laboratory of Organic Chemistry, Åbo Akademi University, Åbo, Finland, 14 Laboratoire Santé Publique Environnement, Université de Paris Sud, Châtenay-Malabry, France, 15 Department of Chemistry, Umeå University, Umeå, Sweden, 16 Food and Environmental Safety Research Group, University of Valencia, Valencia, Spain, 17 Norwegian Institute for Water Research (NIVA), Oslo, Norway, 18 Environmental Institute, Kos, Slovak Republic, 19 Division for Marine and Environmental Research, Rudjer Boskovic Institute Biokemika, Zagreb, Croatia and Laboratory of Analytical Chemistry, Department of Chemistry, University of Athens, Athens, Greece

*Co-first authors.

ABSTRACT

Aims To perform wastewater analyses to assess spatial differences and temporal changes of illicit drug use in a large European population. Design Analyses of raw wastewater over a 1-week period in 2012 and 2013. Setting and Participants Catchment areas of wastewater treatment plants (WWTPs) across Europe, as follows: 2012: 25 WWTPs in 11 countries (23 cities, total population 11.50 million); 2013: 47 WWTPs in 21 countries (42 cities, total population 24.74 million). Measurements Excretion products of five illicit drugs (cocaine, amphetamine, ecstasy, methamphetamine, cannabis) were quantified in wastewater samples using methods based on liquid chromatography coupled to mass spectrometry. Findings Spatial differences were assessed and confirmed to vary greatly across European metropolitan areas. In general, results were in agreement with traditional surveillance data, where available. While temporal changes were substantial in individual cities and years (P ranging from insignificant to <10<sup>−3</sup>), overall means were relatively stable. The overall mean of methamphetamine was an exception (apparent decline in 2012), as it was influenced mainly by four cities. Conclusions Wastewater analysis performed across Europe provides complementary evidence on illicit drug consumption and generally concurs with traditional surveillance data. Wastewater analysis can measure total illicit drug use more quickly and regularly than is the current norm for national surveys, and creates estimates where such data does not exist.

Keywords Amphetamine, cannabis, cocaine, drugs of abuse, ecstasy, methamphetamine, sewage.

INTRODUCTION

Illicit drug use is a covert and hidden activity that presents methodological challenges for drug surveillance systems. Questionnaire-based survey methods have traditionally been an important component of the approaches employed to monitor drug use, but it is recognized that these methods are not sufficient to monitor...
trends in drug use adequately and quickly, and require complementary data from other sources [1,2]. The analysis of the excretion products of illicit drugs in wastewater [wastewater analysis (WWA)] has been explored since 2008 as an additional approach for estimating illicit drug use within specified regions, i.e. the catchment areas of wastewater treatment plants (WWTP) [3,4]. While the approach cannot provide information on the behaviour of single users and on their demographics, there are a number of ways in which WWA can complement other survey methods and provide additional information to understand the illicit drug situation more clearly. Wastewater data can be obtained within short time-frames, are not prone to response biases and can help in identifying the spectrum of illicit drugs being used by a population. This is potentially important, given the emergence of new psychoactive substances [5]. Drug users are often unaware of the actual substance or mix of substances they are consuming, which makes self-report data unreliable. Wastewater analysis is therefore a potential approach to detect and estimate the use of new psychoactive substances; however, it should be noted that more information is necessary regarding their biotransformation pathways.

Wastewater analysis can provide information on daily, weekly, monthly and annual variations in illicit drug use. The weekly profile of cocaine and amphetamine-like stimulants use has already been assessed by collecting consecutive daily wastewater samples, which revealed higher use of these substances during weekends [6–12]. The monitoring of temporal trends in illicit drug consumption over a longer period of time (months) by WWA has been evaluated in three studies, and the major conclusions were that there was typically an increase of illicit drug use during holiday periods [11,13,14]. Wastewater analysis was further applied to detect yearly trends in illicit drug consumption in Italy and Australia [15,16]. In conclusion, this approach can provide important and timely information on short- and long-term trends in illicit drug use.

Wastewater studies in different countries have also detected regional variations in illicit drug use [17–22]. The influence of urbanization on the use of illicit drugs was evaluated in Oregon (USA) and South Australia and Queensland (Australia), concluding that the use of illicit drugs was higher in urban regions compared to more rural areas [9,14,23]. Wastewater analysis has also been applied to detect transnational differences in illicit drug use. The consumption of five substances was evaluated by analysing wastewater from 19 European cities for a 1-week period in 2011 [24]. Wastewater analysis can thus complement survey methods for a clearer understanding of actual spatial differences and temporal changes in illicit drug use.

However, until now no international study has been performed covering multiple countries over multiple years with a common protocol and adequate quality control measures. Therefore, the aims of this study were to:

1. collect wastewater samples from multiple European locations in 2012 and 2013;
2. calculate population-normalized mass loads of benzoylecgonine [BE; as indicator for cocaine (COC) use], amphetamine (AMP), methamphetamine (METH), ecstasy [3,4-methylenedioxy-methamphetamine (MDMA)] and 11-nor-carboxy-delta9-tetrahydrocannabinol [THC-COOH; as indicator for tetrahydrocannabinol (THC) use]; and
3. perform analytical quality control through inter-laboratory tests.

**METHODS**

**Sewer system characterization**

Relevant information for each WWTP catchment was gathered systematically by means of a standardized questionnaire. An extended version of the questionnaire developed for earlier studies [24,25] was used (Supporting information, Appendix S1). It comprises more than 50 questions classified according to importance. The number of the most important questions per category is indicated in brackets (year 2012/year 2013): General information (1/1), Catchment and population (2/5), Sewer system (2/2), WWTP influent (1/1), Sampling (5/5), Flow meter (3/3), Sample handling (9/9), Monitoring period (5/5).

**Sampling and analysis**

A 1-week period was targeted in 2012 (17–23 April) and 2013 (6–12 March). Daily 24-hour composite raw wastewater samples were collected over 7 consecutive days. Considering stability, metabolism and unambiguous indication of drugs actually having been consumed, the most suitable target residues were targeted: BE, AMP, METH, MDMA and THC-COOH [4]. It should be noted that the consumption of COC and THC was monitored through the analysis of their main metabolite because of higher concentrations and higher stability in wastewater.

Samples were spiked with isotope-labelled internal standards, either filtered and extracted immediately on solid-phase extraction cartridges or frozen at −20 °C until analysis. Each laboratory used fully validated analytical methods: target compounds present in the liquid phase of the wastewater were quantified in final extracts or with direct injection applying liquid chromatography coupled to tandem mass spectrometry or high-resolution mass spectrometry [25].

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For quality assurance, each laboratory participated in yearly inter-laboratory tests (de Voogt et al., unpublished). External quality control samples were evaluated (one standard in methanol and two fortified raw wastewater samples). A reliable estimation of the method limit of quantification (LOQ) was performed by evaluating the signal-to-noise ratio in these samples. In 2012, one of 14 laboratories did not meet the requirements for any compound in the inter-laboratory test and was excluded. In 2013, only METH results of one of 15 laboratories had to be excluded.

Calculations

Daily mass loads (g/day) of drug residues entering the WWTPs were calculated by multiplying measured concentrations (ng/L) in daily samples with the corresponding wastewater volumes (L/day). To compare cities of different sizes, mass loads are normalized by the population size of the catchment (mg/1000 people/day). The estimated consumption of COC (section Benzoylecgonine) was back-calculated from the population-normalized mass loads of BE using a correction factor of 3.59 that takes the urinary excretion rate of COC into account for BENZ.

Uncertainty assessment

Mainly four components of uncertainty may affect the estimation of population-normalized drug loads: sampling (US), chemical analysis (UC), flow rate measurement (UF) and population estimation (UP). Because the focus of this study is on mass loads in wastewater, uncertainties related to excretion rates and biodegradation in sewers are not considered. When estimating the overall uncertainty UT of a mean value over an n-day monitoring period, uncertainty components that are random and independent on every day will be reduced by \(\sqrt{n}\). This applies to US, as each sample is collected physically independent of the day before. All other components cannot be reduced by \(\sqrt{n}\) because of their systematic nature. As long as US, UC and UF \(\leq 30\%\) and UP \(\leq 10\%\) (relative standard deviation (RSD)), an estimation of UT is valid with an approximative formula (e.g. [26]). A Monte Carlo simulation was used to avoid underestimating UT systematically because a conservative estimate of UP in our study is 20% (see Supporting information, Appendix S2).

RESULTS

Table 1 lists participating cities: in 2012, 25 WWTPs in 11 countries were included (23 cities, total population 11.50 million); in 2013, there were 47 WWTPs in 21 countries (42 cities, total population 24.74 million). For comparison, 2011 data [24] were also used (21 WWTPs in 11 countries; 19 cities, total population 14.12 million). Figures 1–5 summarize all results. Countries are ordered based on average loads over all years. The numbers in brackets indicate cities’ overall ranks. While absolute variability within 1-week periods (grey range) is obviously higher for high loads, relative variability is not substantially different throughout the entire load range and may vary from year to year, even within a location. The colour of the lines between the means indicate whether the change from 1 week in 1 year to 1 week in another year is significant (Wilcoxon, \(\alpha = 0.05\)). Table 2 summarizes overall means, separately for cities that participated in all 3 years (cities in bold type in Figs 1–5) and for all cities per year (excluding cities that exhibited explainable anomalies, i.e. cities in italic type in Figs 1–5). Concentration values that were <LOQ were treated as follows: (1) if all values at a location for a certain compound were <LOQ, loads were set to zero; (2) if at least one value was >LOQ, values <LOQ were replaced with \(0.5 \times LOQ\). Dashed grey lines indicate a population-weighted overall mean for 2013 (all cities except cities in italics). When weekly patterns were evaluated in 2012, previous findings were confirmed, i.e. higher loads on weekends for BE, and MDMA and no substantial variation for AMP, METH and THC-COOH [24] (see Supporting information, Appendix S4).

Benzoylecgonine

The highest weekly mean BE loads in the period 2011–13 were observed in wastewater from Amsterdam, Antwerp, London and Zurich and were between 400–850 mg/1000 people/day (Fig. 1). Loads were also relatively high (between 200–550 mg/1000 people/day) in Barcelona, Basel, Geneva, Utrecht and Eindhoven. The lowest values (<100 mg/1000 people/day) were observed in locations from northern, eastern and southern Europe. These results suggest a clear geographical difference in COC consumption, with higher use in western Europe. This is further demonstrated when BE loads in locations from Germany are evaluated. Loads in Dresden (eastern Germany) are negligible, similar to the amounts seen in the Czech Republic, while loads in Dortmund (western Germany) are comparable to the loads observed in the Belgian, Dutch and Swiss cities.

The overall population-weighted mean loads of BE for the 16 locations included in all 3 years were almost identical (Table 2). This suggests a stable use of COC in the investigated locations in the period 2011–13. Location-specific results from 2011, 2012 and 2013 are generally in agreement (Fig. 1); however, in some cases, variations
Table 1 Summary of participating cities and wastewater treatment plants (WWTP). More detailed information can be found in Supporting information (Appendix S3), which includes raw data and answers from the questionnaire.

<table>
<thead>
<tr>
<th>Country</th>
<th>City</th>
<th>WWTP</th>
<th>Population of the city under investigation</th>
<th>Estimated population in WWTP catchment</th>
<th>Targeted 1-week monitoring period (√) (n = 7 days)</th>
<th>Loss of wastewater (%)</th>
<th>Com-maters (%)</th>
<th>Special events</th>
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**Table 1 Cont.**

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<tr>
<th>Estimated population in WWTP catchment</th>
<th>Targeted 1-week monitoring period (n = 7 Days)</th>
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<tbody>
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<td>(year)</td>
<td>(n = 6)</td>
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</table>

- Method for population estimation in WWTP catchment (year of estimate). a, Influent nutrient load over corresponding calendar year; b, influent nutrient load over actual sampling period; c, census; d, house connections/drinkling water subscribers; e, values adopted from previous estimation; f, WWTP different from 2011/13 but wastewater from same catchment (central collection with subsequent distribution to different WWTPs). *Population estimate indicated in [24] was erroneous and population-normalized consumption estimates are corrected with updated value.*
- Loss of wastewater (exfiltration, questionnaire 2013). *Population estimate indicated in [24] was erroneous and population-normalized consumption estimates are corrected with updated value.*
- Commuters (work days versus weekend, questionnaire 2013). *Population estimate indicated in [24] was erroneous and population-normalized consumption estimates are corrected with updated value.*
- Special events during/adjacent to monitoring period. Y, please see Supporting information, Appendix S3 for type of event (year provided in brackets); R, rain before/during monitoring period (higher flows but no substantial effect on drug loads expected).
Figure 1  Population-normalized benzoylecgonine (BE) loads of a single 1-week period per year. See Table 1 for more information. LOQ: concentrations in all daily samples were below limit of quantification (LOQ). Grey dashed line: 2013 overall mean of all participating cities. Dot colour: white: concentrations in all samples were above LOQ; grey shading: one or more concentrations were below LOQ and set to 0.5×LOQ (the darker the grey, the more concentrations were below LOQ). Numbers in brackets: cities’ rank (average over all available years). Cities in bold type participated in all 3 years and were used to calculate annual overall means (see Table 2). All P-values can be found in Supporting information, Appendix S3.
Figure 2. Population-normalized amphetamine (AMP) loads of a single 1-week period per year. See Table 1 for more information. LOQ: concentrations in all daily samples were below limit of quantification (LOQ). Grey dashed line: 2013 overall mean of all participating cities (except Eindhoven). Dot colour: white: concentrations in all samples were above LOQ; grey shading: one or more concentrations were below LOQ and set to 0.5*LOQ (the darker the grey, the more concentrations were below LOQ). Numbers in brackets: cities’ rank (average over all available years). Cities in bold type participated in all 3 years and were used to calculate annual overall means (see Table 2). Cities in italic type exhibited abnormal high values in at least 1 year (see text for more details). All P-values can be found in Supporting information, Appendix S3.
Figure 3  Population-normalized methamphetamine (METH) loads of a single 1-week period per year. See Table 1 for more information. <LOQ concentrations in all daily samples were below limit of quantification (LOQ). Grey dashed line: 2013 overall mean of all participating cities. Dot colour: white: concentrations in all samples were above LOQ; grey shading: one or more concentrations were below LOQ and set to 0.5*LOQ (the darker the grey, the more concentrations were below LOQ). Numbers in brackets: cities’ rank (average over all available years). Cities in bold type participated in all 3 years and were used to calculate annual overall means (see Table 2). All P-values can be found in Supporting information, Appendix S3.
Figure 4 Population-normalized 3,4-methylenedioxy-methamphetamine (MDMA) loads of a single 1-week period per year. See Table 1 for more information. LOQ: concentrations in all daily samples were below limit of quantification (LOQ). Grey dashed line: 2013 overall mean of all participating cities (except Utrecht and Eindhoven). Dot colour: white: concentrations in all samples were above LOQ; grey shading: one or more concentrations were below LOQ and set to 0.5*LOQ (the darker the grey, the more concentrations were below LOQ). Numbers in brackets: cities’ rank (average over all available years). Cities in bold type participated in all 3 years and were used to calculate annual overall means (see Table 2). Cities in italic type exhibited abnormal high values in at least 1 year (see text for more details). All P-values can be found in Supporting information, Appendix S3.
Figure 5  Population-normalized 11-nor-9-carboxy-delta9-tetrahydrocannabinol (THC-COOH) loads of a single 1-week period per year. See Table 1 for more information. <LOQ: concentrations in all daily samples were below limit of quantification (LOQ). Grey dashed line: 2013 overall mean of all participating cities. Dot colour: white: concentrations in all samples were above LOQ; Grey shading: one or more concentrations were below LOQ and set to 0.5*LOQ (the darker the grey, the more concentrations were below LOQ). Numbers in brackets: cities’ rank (average over all available years). Cities in bold type participated in all 3 years and were used to calculate annual overall means (see Table 2). All P-values can be found in Supporting information, Appendix S3.
An increase in BE loads from 2012 to 2013 was observed in the Belgian and Swiss locations, while a decrease was observed in two Dutch locations (Utrecht and Amsterdam). Besides the high variation of mean BE loads observed across Europe, this study also highlights differences among locations within countries. Results from Belgium, Czech Republic, Germany, Serbia, Slovakia, Sweden and Switzerland suggest that the consumption of COC is lower in smaller towns compared to larger cities (Table 1, Fig. 1). Qualitatively, this is in agreement with studies investigating more locations within a country [17–22], although some of these rely on grab samples or single days only. The difference between Dresden and Dortmund, two cities of similar size, is attributable to their geographic location within Germany, as discussed previously.

The population-weighted mean COC consumption, calculated from BE loads (see Calculations), for locations included in all study years is similar between years and varies from 867 mg/1000 person/day in 2012 to 912 mg/1000 person/day in 2013 across Europe. This study also highlights differences among locations within countries. [17–22].

Table 2 Population-weighted overall mean loads (units = mg/1000p/d). The loads in cities with all concentration values <LOQ were set to 0. Loads range from (close to) 0 up to several 10–100 mg/1000 person/day among cities, which implies large standard deviation (SD) or 95% confidence interval (CI) for all substances’ overall means. Therefore, significance of changes cannot be meaningfully assessed for overall means and is assessed at cities’ individual levels only (see Figs 1–5 and Supporting information, Appendix S3).

<table>
<thead>
<tr>
<th>Year</th>
<th>BE</th>
<th>MDMA</th>
<th>AMPH</th>
<th>METH</th>
<th>THC-COOH</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td></td>
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<td>2013</td>
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use of amphetamine-like substances. In Dülmen and Dortmund (West), relatively high AMP and negligible METH use was observed, while for Dresden (East, proximity to Czech Republic) the opposite was found.

The weighted mean of METH loads for the cities that were included in all study years declined by 45% from 2011 to 2013 (Table 2), due to some location-specific changes. For AMP, the weighted mean of the cities included in the 3 years is similar (Table 2). In contrast to BE loads, the difference in AMP and METH loads between smaller towns and bigger cities within a country is less clear.

**MDMA**

The highest loads of MDMA were found in western European locations, while locations in northern, eastern and southern Europe presented substantially lower MDMA loads (Fig. 4). This pattern is comparable to BE and AMP, as demonstrated by the locations within Germany, with low MDMA loads in Dresden and higher loads in Dortmund.

The weighted mean of MDMA loads for the cities included in all 3 study years was stable (Table 2). No substantial changes in per capita MDMA loads between years for the individual locations were observed, with some exceptions (Fig. 4). The mass loads of MDMA from Eindhoven in 2012 and 2013 were much higher compared to 2011, and in Utrecht significantly higher loads for MDMA were observed in 2011 compared to 2012 and 2013. An explanation for these high loads in Utrecht (2011) and Eindhoven (2012) is most probably a release of unconsumed MDMA into the sewer system that was confirmed by specific enantiomeric profiling of the wastewater [30]. These outliers were not taken into account when assessing temporal changes. MDMA loads are generally higher in larger cities compared to smaller towns, as can be seen in different locations within Belgium, Finland, Germany, Serbia and Slovakia. A notable exception is St Gallen in Switzerland, which showed MDMA loads comparable to the larger city of Zurich.

**THC-COOH**

The determination of THC-COOH in wastewater poses some (pre-)analytical challenges, and as a result not all laboratories could report results for this THC metabolite. Furthermore, results from the performed inter-laboratory exercises revealed that participating laboratories that reported results for THC-COOH have comparable analytical methods (Z-scores within the limits), but because of some unknown pre-analytical losses, underestimations of the absolute amounts are probably made (de Voogt et al., unpublished). In the present study, however, this is not a real issue, because the focus lies on the relative comparison of THC-COOH loads.

In contrast to the other investigated substances, no clear geographical pattern could be observed for THC-COOH loads in the different European locations (Fig. 5). The values for Amsterdam were (expectedly) the highest, as Amsterdam is known for its coffee shops and because the Netherlands produces large amounts of herbal cannabis with a relatively high content of THC [31]. Also notable are the high loads observed in the city of Novi Sad, Serbia.

The weighted mean of THC-COOH loads for cities that were included in all 3 years showed some subtle variation, pointing out a variable cannabis use (amount or potency) between 2011 and 2013 (Table 2). No clear difference in THC-COOH loads between smaller towns and larger cities could be observed from the gathered data.

**DISCUSSION**

Comparison of wastewater results with surveillance data

Europe has an established multi-indicator system for drug surveillance that is based on standardized demand and supply information, as well as research and intelligence sources [32]. Prevalence estimates are derived from a mixture of survey results and indirect statistical methods that try to estimate the unobserved cases from registers of observed drug users, such as treatment attendees or arrestees [33]. These methods can provide information on the main classes of users, the frequency and mode of use of a drug as well as on the purity of the substances available on the market, while WWA can provide objective and timely information on the total amount of a drug used in a specific area. These methods are highly complementary and, if used together, can substantially improve the quality of information on drug use patterns.

In terms of prevalence at the population level, the findings from WWA are broadly in agreement, with respect to relative drug use levels, with existing estimates, although they are not directly comparable. The wastewater data, however, highlight the need to consider the contribution of high and low prevalence areas in the estimates of total drug use within a population. Due to differences in demographics, the ranking of the city-based estimates reported in this study do not necessarily have to agree with national survey-based estimates. This points to the need to collect contextual information for a meaningful interpretation of wastewater data. Future monitoring campaigns should therefore (i) include more cities with different demographics within a country and (ii) evaluate monitoring design strategies to find an...
optimum among feasible logistics, sufficient quality control and representativeness for an entire year [34].

The spatiotemporal data on drug use data reported are largely, but not totally, in line with what is observed from surveys and other sources. The stable levels of COC suggested by the presented wastewater data differs from other demand and supply data, which report a decline in COC use [35]. With WWA, it is currently not possible to differentiate between smaller number of people using larger amounts or vice versa, or even evaluating differences in consumption due to changes in purity. The analysis on METH and AMP accords with other data sources. The use of METH is long established in the Czech Republic, Slovakia and eastern Germany [36], and more recently supply-side data point to an increased use of METH elsewhere, especially in Scandinavian countries where it has, at times, displaced AMP. The situation appears quite dynamic and largely supply-side-driven. The wastewater data reported here accords with, and complements, the existing analysis of this situation.

For both MDMA and cannabis use, the picture is less clear. High levels of MDMA and THC-COOH might be expected in the Dutch cities sampled, but it is surprising that MDMA stands out so prominently with respect to some of the other European cities. The most recent supply-side data suggest that there is more MDMA available on the European market, and it is interesting to note that there is no evidence of this from the wastewater data reported here. The findings for THC-COOH in Amsterdam are not too surprising, as it is known for its large non-resident population using cannabis.

Uncertainty assessment

Details on estimating \( U_s \) can be found in [37,38]. Applying the same scenario as in [25]—i.e. 1% of users in the population with two relevant, substance-related toilet flushes—results in a maximum of 20% for a daily value of \( U_s \). An objective assessment of \( U_s \) was derived from inter-laboratory tests and does not exceed 30% (de Voogt et al., unpublished). Operational accuracy of flow meters (\( U_f \)) still proves to be a challenge, and in this study was assumed conservatively to be 20% [39]. Despite advances in estimating \( U_f \) [40] it remains difficult to obtain a site-specific estimate, and in our study we assume 20% (RSD) as an average [25,40]. A conservative estimate of overall uncertainty for a 7-day average based on WWA is approximately 46% (RSD) for all substances and locations (see Supporting information, Appendix S2 for more details). A sensitivity analysis reveals that reducing all four uncertainty components \( U_i \) by approximately one-quarter (\( U_s \approx U_f \approx U_r \approx 15\%, U_c = 23\% \)) has the same effect as trying to eliminate only one \( U_i \) (e.g. \( U_c = 0\% \)); in both cases the overall uncertainty would be around 33%.

In areas with leaky sewers the results from WWA may tend towards an underestimation of actual illicit drug loads. A certain fraction of the wastewater and illicit drugs discharged from households may not arrive at the WWTP. Information on the potential amount of exfiltration can be found in Table 1. Furthermore, in cases where population size is estimated from nutrient loads in the wastewater stream, the population could be overestimated if industrial contributions are not properly subtracted. This would lead to an underestimation of population-normalized drug loads. In contrast, WWA results may tend towards an overestimation of population-normalized drug loads if the residential population only was used for normalization. But a net increase on workdays is effective due to commuters. This and additional information is provided in Table 1 and Supporting information, Appendix S3 for further data interpretation.

CONCLUSIONS

By successfully increasing the number of participating cities to 42 in 2013 (2011: 19, 2012: 23), this is now the biggest application of WWA covering 24.74 million people. The wastewater from approximately 8 million people was analysed for BE, AMP, METH and MDMA during a 1-week period over 3 consecutive years (approximately 4 million for THC-COOH). As such, this study provides the most actual evidence for the quantification of spatial differences and temporal changes in the consumption of illicit drugs across European regions. Relatively stable loads for all investigated substances were observed, except for METH (apparent decline in 2012). In general, spatial differences were in agreement with surveillance data, where available. Wastewater analysis provides the possibility to collect, and report, measurements more quickly and regularly than is the current norm for national surveys. Wastewater analysis provides a unique opportunity to obtain near-real-time data on illicit drug use and for future comparison with other surveillance data, or particularly where such data are missing. Therefore, it should be considered for implementation on an annual or even more frequent basis. Systematically gathering information on catchment characteristics (sewer system and population) seems as indispensable as inter-laboratory tests for a meaningful comparison of wastewater data, which requires concerted efforts of numerous partners and disciplines.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

**Appendix S1** Questionnaire 2012 and 2013.

**Appendix S2** Uncertainty estimation.

**Appendix S3** Answers from questionnaire, all analytical data 2012 and 2013, means and P-values for changes of one week to another for all substances and locations (different spread sheets in separate Excel file).

**Appendix S4** Weekly variation of drug loads 2012 (separate pdf file).