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Wastewater-based epidemiology for illicit drugs: A critical review on global data

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ABSTRACT

Illicit drug use is complex, hidden and often highly stigmatized behaviour, which brings a vast challenge for drug surveillance systems. Drug consumption can be estimated by measuring human excretion products in untreated wastewater, known as wastewater-based epidemiology (WBE). Over the last decade, the application of wastewater-based epidemiology to monitor illicit drug loads increased and WBE is currently applied on a global scale. Studies from over the globe are evaluated with regard to their sampling method, analytical accuracy and consumption calculation, aiming to further reduce relevant uncertainties in order to make reliable comparisons on a global level. Only a limited number is identified as high-quality studies, so further standardization of the WBE approach for illicit drugs is desired especially with regard to the sampling methodology. Only a fraction of the reviewed papers explicitly reports uncertainty ranges for their consumption data. Studies which had the highest reliability are recently published, indicating an improvement in reporting WBE data. Until now, WBE has not been used in large parts of Africa, nor in the Middle East and Russia. An overview of consumption data across the continents on commonly studied drugs (cocaine, MDMA, amphetamine and methamphetamine) is provided. Overall, high consumption rates are confirmed in the US, especially for cocaine and methamphetamine, while relatively low illicit drug consumption is reported in Asia.

1. Introduction

Illicit drug use is complex, hidden and often highly stigmatized behaviour, which brings a vast challenge for drug surveillance systems. The traditional way of monitoring illicit drug use is through population surveys, consumer interviews and police seizures. These methods yield qualitative data and provide useful information such as age, sex, behaviour and the mode of use (ingestion, injection or inhalation). However, due to several limitations such as self-report bias and limited population coverage, survey-based results have difficulties in reflecting detailed spatial and temporal differences of illicit drug use. To get access to quantitative data, the human metabolic excretion products resulting from drug consumption can be measured in untreated wastewater. The measured parent compound or metabolite can be used to calculate the daily mass loads entering a wastewater treatment plant (WWTP) for these compounds. With the knowledge of human drug metabolism and excretion rates, together with in-sewer transformation rates, the relation to consumption (g/day) can be calculated from these mass loads. When dividing this by the served population at the point of measurement in the sewage system, the amount of illicit drugs consumed in g/day/inhabitant can be estimated allowing for comparisons between locations (van Nuijs et al., 2020). While this approach provides no knowledge about the behaviour of single users, it is useful for identifying the spectrum of substance use for a population serving a particular WWTP. This approach provides near real-time information for a specific city or region and gives insight about temporal trends. It is also a promising tool to estimate the illicit drug market size. Together with survey-based monitoring, wastewater-based epidemiology (WBE) can evaluate drugs abuse more comprehensively and potentially support governments in developing policies to scale down drug abuse (Lai et al., 2016).

Using WBE to detect illicit drugs was first introduced by Daughton in 2001 (Daughton, 2001) and first applied by Zuccato et al. (Zuccato et al., 2005) in 2005 to monitor cocaine use and track trends in local illicit drug use in Italy. In 2012 the first international assessment in 19 European cities was published by Thomas et al. (Thomas et al., 2012). A paper discussing the uncertainties within the WBE approach has been published in 2013 by Castiglioni et al. (Castiglioni et al., 2013) and a global overview of results was presented by Feng et al. (Feng et al.,...
2018) covering publications between 2005 and 2017. WBE has shown to be an innovative and promising tool, and sophisticated methodologies have been published for measuring a great variety of illicit drugs (Choi et al., 2018; F. Hernández et al., 2019; F. Hernández et al., 2018)

Despite the fact that WBE provides an evidence-based estimation on illicit drug use for a specific population, it brings a number of uncertainties related to the sampling methodology, the analytical procedure and the consumption calculation (Castiglioni et al., 2013; Zheng et al., 2019). One of the main challenges in WBE is reducing the uncertainty for each of these variables in order to make comparable comparisons on an international level.

Synchronising wastewater sampling and analysis will allow more accurate data (O’Brien et al., 2019). The European network of sewage analysis, Sewage analysis CORE group Europe (SCORE) coordinates and ensures quality control in international WBE studies. This way, research can be done with the same validated methods, which makes results robust and comparable. Data on illicit drugs collected under SCORE supervision is therefore used annually by the European Monitoring center for Drug and Drug Addiction (EMCDDA) (González-Marino et al., 2020). Wastewater is an important source of public health information and can be applied in many fields of expertise, like for diet and nutrition, pesticide use, public health and doping, and currently it is used to monitor the SARS-CoV-2 virus (Bivins et al., 2020).

The present paper first investigates the potential and reliability of WBE methodologies by critically looking at the literature published in the last decade. The key areas that are evaluated to determine the reliability are; the sampling methodology, the analytical accuracy and the consumption estimation, and overall reliability scores are considered. Then, an overview of consumption data on the most commonly studied drugs (cocaïne, MDMA, amphetamine and methamphetamine) is provided, evaluating spatial trends. European-wide studies are frequently published and discussed (Castagnano et al., 2018; Krizman-matasic et al., 2019; Ort et al., 2014; Thomas et al., 2012), but here we provide the first overview on a global scale, based on a large number of data from published literature on intercontinental level. Finally, suggestions to further improve future WBE studies are provided.

2. Methods

2.1. Literature search

One hundred and ten studies reporting on wastewater-based epidemiology of illicit drugs were extracted from the Scopus database and reviewed systematically (Haddaway et al., 2017, 2015; Xiao and Watson, 2019). Used search strings were ‘wastewater-based epidemiology’ or ‘sewage epidemiology’ and ‘illicit drug’ or ‘drugs of abuse’ in studies published between 2010 and 2020. Export data were filtered based on relevance; reports that did not provide new data, concerned only new psychoactive substances (NPS), did not calculate the drug consumption, or were not representative for the community, were removed (S.I.1). Searches were performed until March 2020. Fifty-two papers are included and reviewed on the estimated drug consumption and the overall reliability of the methodology.

2.2. Assessment of method reliability

The reliability of the selected papers was assessed based on factors introducing uncertainties as described by (Ort et al., 2010a; van Nuijs et al., 2018; Feng et al., 2018; Castiglioni et al., 2013) and (Fernández de Córdova and Medina, 2014). The studies are reviewed with regard to their sampling uncertainty, analytical accuracy and the consumption estimation. Each of the three main criteria was assessed based on specific sub-criteria (Table 1).

For each sub-criterion, a value of 2, 1 or 0 is assigned, which indicates the reliability of each aspect with a maximum of 6 for the sampling uncertainty, a maximum of 10 for the analytical accuracy and a maximum of 6 for the consumption estimation. The overall reliability score per study has a maximum of 22. When no information is reported in the reviewed literature for a specific criterion, ‘0’ will always be assigned. Table 2 lists the cut-off per sub-criterion, which is further explained and justified per sub-criterion in the sections below.

2.3. Comparison of international drug consumption

The selected fifty-two papers were reviewed on drug consumption. Median consumptions of cocaine, amphetamine, methamphetamine, and MDMA were used to compare consumption on an intercontinental scale.

3. Results and discussion

3.1. Reliability of methods

In this study, the reliability of literature on WBE and illicit drugs published in the last decade is critically reviewed with regard to the sampling uncertainty, analytical accuracy and consumption estimations. Over all 52 papers that are evaluated, the mean score of the studies is 14.3 out of a maximum of 22, ranging from 10 to 18 (Table 3). According to the criteria used in this study, especially with regard to the sampling and its description there are major possibilities for further improvement. Fig. 1 shows the percentages of studies with a positive score per sub-criterion, further details on assigned points per sub-criterion per study can be found in S.I.2.

3.1.1. Sampling uncertainty

3.1.1.1. Long- and short-term variations. Sampling can be a dominant source of uncertainty for the determination of illicit drugs in wastewater as both short-term variations such as diurnal patterns in consumption and human behaviour, festivals or rainfall, and long-term variations such as week-weekend and seasonal changes do occur (Ort et al., 2010, 2010a). Extreme weather changes and human behaviour will change the daily flow of wastewater to a WWTP and therefore will cause variability and dilution (Banta-Green et al., 2016; Ort et al., 2010, 2010a). The concentration of the analyte is also highly dependant on the season, due to wet and dry weather conditions (Loraine and Pettigrove, 2006). However, these sporadically extreme weather (short-term) events do not give the same uncertainty as (long-term) seasonal changes, which are more constant.

The concentration of illicit drugs can increase significantly during special events and during the weekends (Bijlsma et al., 2014; Foppe et al., 2018). This brings variability in human behaviour when it comes to drug consumption and will bias the overall consumption of a certain community. A similar bias applies to work-commuters and tourists who only take part a community for a certain amount of time. Therefore, these are important factors regarding the uncertainty (Foppe et al., 2018).

### Table 1

| Main criteria including sub-criteria to assess the quality of WBE papers. Sub-criteria that have a larger weight in the scoring system are underlined. |
|---|---|---|
| Sampling uncertainty | Analytical accuracy | Consumption estimation |
| (Max 6) | (Max 10) | (Max 6) |
| Mode of sampling | Detection technique | Stability of the drug |
| Sample Volume | Analytical Conditions | Metabolites |
| Long term variations | LOD/LOQ | Equation |
| Short term variations | Replicates | Population estimation |
| | Positive control samples | Reporting measured concentrations |
| | Negative control samples | |
| | Internal standards | |

The concentration of illicit drugs can increase significantly during
Table 2
Cut-off for assigning ‘1’ or ‘0’ for each sub-criterion, when no information is reported ‘0’ will be assigned as indicated with *.

| Sub-criterion                  | Assigned 2 | Assigned 1 | Assigned 0 |
|-------------------------------|------------|------------|------------|
| Mode of sampling              | Flow-proportional sampling mode is applied | Volume- or time-proportional sampling is applied | Grab samples are used |
| Sample volume                 | Sample volume is ≥ 1 L | Sample volume is < 1 L | Sample volume < 1 L |
| Short term variations         | Conditions during the sampling are reported regarding short term variations (diurnal patterns in consumption, human behaviour, festivals and rainfall) | * | * |
| Long term variations          | Conditions during the sampling are reported regarding long term variations (week-weekend & seasonal variations) | * | * |
| Detection technique           | High resolution mass spectrometry identification (MS/MS, QTOF, Triple Quadrupole, Orbitrap) | Analytical conditions are described in detail or referring to other paper where described in detail. | Not using mass spectrometry (i.e. UV-detection) |
| Analytical Conditions         | LOD/LQq     | Average concentrations are <10 times the LOD or LOQ | Average concentrations are >10 times the LOD or LOQ |
| Replicates                    | Number of replicates is reported > 3 | Representative replicated positive controls are reported, concentration and purity of standards used is reported | < 2 |
| Positive control samples      | The purity/concentration of the positive standard is not specified, or positive controls are lacking | * | * |
| Negative control samples      | Clearly indicated that actual sample results are corrected for blanks | Internal standard is not isotopic labelled | * |
| Stability of the drug         | Correction factors on stability are used during consumption calculation | * | * |
| Metabolites                   | Metabolites are measured and applied in consumption calculation | * | * |
| Equation estimation           | Consumption calculation is described explicitly | Parameters in equation are not explained |
| Population estimation         | Estimation of population is reported per individual WWTP and estimation-method for population is explained | Population is reported for a country, or for multiple WWTPs serving a region |
| Reporting measured concentrations | Measured concentrations before calculation are reported in paper or supplementary data | * | * |

In general, long-term variations are commonly reported (68%) whereas short term variations are reported in only 39% of the papers. This was expected because long-term variations are easier to track since these are more constant factors. To give a reliable estimate of illicit drug use by the local community, preferably measurements should be performed during a ‘normal week’.

3.1.1.2. Mode of sampling. The systematic sampling error depends on the sampling mode. The use of 24-hour composite sampling is most common in WBE. Composite sampling has a clear advantage over grab sampling with respect to local heterogeneity (Miikkinnen and Esbensen, 2009). As influent flow and composition may vary significantly over the timespan of sampling, composite sampling can be challenging (Feng et al., 2018; Ort et al., 2010b). Composite sampling can be performed by three approaches, i.e., flow-proportional, volume-proportional, or time-proportional. Flow-proportional composite sampling takes a subsample volume proportional to the flow in the sewer at a constant time interval, subsamples are weighted individually to form a composite sample. Volume-proportional sampling takes samples more frequently during higher flows and less frequently during lower flows, the sampling volume remains constant. However, this cannot provide a true average concentration since only the frequency changes and individual samples are not weighted properly according to the flow in the sewer. In time proportional sampling both frequency and sampling volume are constant and therefore does not provide a true average concentration as well. The flow-proportional mode of sampling is regarded as most reliable choice for data on illicit drug consumption and is favoured over time- and volume proportional sampling because subsamples are weighted individually. (Ort et al., 2010, 2010a).

The majority of reviewed papers use 24 h composite influent samples, while several studies used grab samples (Banta-Green et al., 2016; Feng et al., 2018; Fernández de Córdova and Medina, 2014; Ort et al., 2010, 2010a; van Nuijs et al., 2018). Whether the composite samples are volume-proportional, flow-proportional or time-proportional is not always reported. When a detailed description of the sampling methodology is specified, flow-proportional is most prevalent. In total, only 21% of the papers specify the use of flow-proportional composite sampling. Thus, lack of (description of) use of flow-proportional composite sampling importantly contributes to sampling uncertainty.

3.1.1.3. Sample volume. Low sample volumes reduce the power of a study and will increase error (Einax, 2004; Koelmans et al., 2019). Detection limits benefit from large sample volumes as extracts can reach high concentration factors. Because of the relatively low concentration of certain excreted illicit drugs in wastewater. Most common illicit drugs (cocaine, amphetamines) will be present in wastewater with relatively high concentrations but for NPS the concentration can be much lower, and therefore a larger sample volume is required. A total sample volume of 1 L for influent is considered sufficient (Ort et al., 2010). Subsamples can be taken for sample preparation and chemical analysis. More than half (58%) of the studies do not report on sample size or do not meet the requirement of collecting 1 L influent. Publishing full information regarding detailed sampling methodologies is crucial to interpret the obtained results. Together with the long- and short-term variations, the sample size was often not reported and therefore a factor in reducing the sampling uncertainty of these methods.

3.1.2. Analytical accuracy

3.1.2.1. Identification technique. Analytical uncertainty is commonly well specified in WBE studies (Ort et al., 2010a). The fact that most illicit drugs are of medium to high polarity makes LC-MS/MS the most attractive method for their identification and quantification. All papers report a sophisticated analytical method; analytical technique is described in 100% of the studies, and in 98% of the studies the technique of choice is liquid chromatography coupled to mass spectrometry (LC-MS) or tandem mass spectrometry (LC-MS/MS). One exception is analysing methamphetamine using gas chromatography coupled to mass spectrometry as the main analytical tool (GC-MS/MS) (Wang et al., 2019). LC-MS/MS is commonly used to investigate pharmaceuticals and...
### Table 3
Overview of individual and total scores of papers reporting illicit drug concentrations using a wastewater-based epidemiology approach.

| Study                  | Country          | Sampling uncertainty (max 6) | Analytical accuracy (max 10) | Consumption estimation (max 6) | Overall reliability of method (max 22) |
|------------------------|------------------|------------------------------|------------------------------|-------------------------------|----------------------------------------|
| Postigo et al., 2010   | Spain            | 1                            | 8                            | 5                             | 14                                     |
| Terziec et al., 2010   | Croatia          | 2                            | 8                            | 5                             | 15                                     |
| Karolak et al., 2010   | France           | 5                            | 8                            | 2                             | 15                                     |
| van Nuijs et al., 2011 | Belgium         | 3                            | 7                            | 5                             | 15                                     |
| Harman et al., 2011    | Norway           | 3                            | 8                            | 2                             | 13                                     |
| Irvine et al., 2011    | Australia        | 4                            | 7                            | 4                             | 15                                     |
| Baker et al., 2012     | Czech Republic   | 1                            | 8                            | 4                             | 13                                     |
| Neela et al., 2013     | France           | 4                            | 7                            | 4                             | 15                                     |
| Khan et al., 2014      | China            | 1                            | 8                            | 4                             | 13                                     |
| Devuign et al., 2014   | Martinique       | 4                            | 7                            | 5                             | 16                                     |
| Baker et al., 2014     | UK               | 3                            | 7                            | 4                             | 14                                     |
| Mackulak et al., 2014  | Slovakia         | 3                            | 8                            | 2                             | 13                                     |
| Kankaanpaa et al., 2014 | Finland     | 2                            | 6                            | 3                             | 11                                     |
| Oxtman et al., 2014    | Sweden           | 2                            | 10                           | 4                             | 16                                     |
| Reid et al., 2014      | Norway           | 1                            | 10                           | 5                             | 16                                     |
| Andres-Costa et al., 2014 | Spain       | 2                            | 8                            | 3                             | 13                                     |
| Nowicki et al., 2014   | Poland           | 1                            | 6                            | 4                             | 11                                     |
| Subedi and Kannan, 2014 | USA            | 1                            | 9                            | 5                             | 15                                     |
| Yong et al., 2015      | South-Korea      | 3                            | 9                            | 3                             | 15                                     |
| Rodriguez-alvarez et al., 2015 | Spain & Italy | 3                            | 8                            | 5                             | 16                                     |
| Palardy et al., 2015   | Canada           | 2                            | 6                            | 2                             | 10                                     |
| Baz-lomba et al., 2016 | European countries | 3                        | 6                            | 3                             | 12                                     |
| Kankaanpaa et al., 2016 | Finland     | 3                            | 8                            | 3                             | 14                                     |
| Krizman et al., 2016   | Croatia          | 3                            | 8                            | 4                             | 15                                     |
| Mackulak et al., 2016  | Slovakia & Czechia | 4                        | 8                            | 4                             | 16                                     |
| Klupcynska et al., 2016 | Poland        | 2                            | 8                            | 3                             | 13                                     |
| Bodt et al., 2016      | Slovakia         | 4                            | 6                            | 2                             | 12                                     |
| Lai et al., 2016       | Australia        | 2                            | 8                            | 4                             | 14                                     |
| Bijlsma et al., 2016   | Colombia         | 2                            | 8                            | 5                             | 15                                     |
| Causantilles et al., 2017 | Costa Rica   | 2                            | 7                            | 4                             | 13                                     |
| Manroismi et al., 2017 | Spain           | 4                            | 9                            | 4                             | 17                                     |
| F. Sodr´e et al., 2017 | Spain           | 3                            | 9                            | 4                             | 16                                     |
| Archer et al., 2018    | South-Africa     | 3                            | 7                            | 5                             | 15                                     |
| Nguyen et al., 2018    | Vietnam          | 1                            | 9                            | 5                             | 15                                     |
| F. F. Sodr´e et al., 2018 | Brazil       | 3                            | 8                            | 3                             | 14                                     |
| Castrignano et al., 2018 | European countries | 4                        | 9                            | 3                             | 16                                     |
| Love et al., 2018      | Scandinavia      | 4                            | 8                            | 3                             | 15                                     |
| Cosenza et al., 2018   | Italy            | 1                            | 9                            | 4                             | 14                                     |
| Skees et al., 2018     | USA              | 2                            | 10                           | 5                             | 17                                     |
| Foppe et al., 2018     | USA              | 4                            | 9                            | 5                             | 18                                     |
| Y. X. Zhang et al., 2019 | China         | 2                            | 7                            | 4                             | 13                                     |
| Mercan et al., 2019    | Turkey           | 2                            | 9                            | 4                             | 15                                     |
| Daglioglu et al., 2019 | Turkey          | 4                            | 7                            | 4                             | 15                                     |
| Y. X. Zhang et al., 2019 | China         | 3                            | 8                            | 4                             | 15                                     |
| Kumar et al., 2019     | New Zealand      | 3                            | 7                            | 5                             | 15                                     |
| Marino et al., 2019    | Brazil & Spain   | 2                            | 9                            | 2                             | 13                                     |
| Fallati et al., 2020   | Maldives         | 3                            | 8                            | 3                             | 14                                     |
| Deng et al., 2020      | China            | 2                            | 10                           | 3                             | 15                                     |
| Du et al., 2020        | Malaysia         | 2                            | 9                            | 5                             | 16                                     |
| Shao et al., 2020      | China            | 2                            | 9                            | 5                             | 16                                     |
| Croft et al., 2020     | USA              | 2                            | 7                            | 4                             | 13                                     |
| Kim and Oh, 2020       | South-Korea      | 4                            | 8                            | 3                             | 15                                     |

Average Minimum
| Maximum | Minimum |
|---------|---------|
| 2.6     | 1       |
| 5       | 7.9     |
| 4       | 3.8     |
| 10      | 2       |
| 6       | 14.3    |
| 18      |         |
their metabolites because of the robustness and excellent reproducibility (van Nuijs et al., 2011; Zheng et al., 2019), and therefore also a favoured technique to measure concentrations of illicit drugs. Triple quadrupole mass analysers are used most and considered the reference technique to quantify illicit drugs and their metabolites (Hernández et al., 2018). This technique is both sensitive and suitable for quantitative analysis, and selective for identification, and an excellent tool for targeted analysis. New methodologies are expected to increase in the coming years, e.g., based on mixed-mode liquid chromatography–tandem mass spectrometry (Koelmans et al., 2019), or high-resolution mass spectrometers such as orbitrap and time-of-flight (QTOF) analysers in combination with ultra-high-performance chromatography (UHPLC), which are more suitable for untargeted/suspect screening. Combined, these techniques will enhance the sensitivity of the overall method (Baz-lomba, Reid, and Thomas, 2016).

3.1.2.3. Method validation (Internal standards, replicates, positive- and negative controls). Prior to application, the analytical methodology needs to be completely validated for all analytes in terms of trueness/accuracy (evaluated by recovery experiments) and precision (as reviewed studies reported on analysing in triplicates.

### 3.1.2.2. Analytical conditions

Specification of the analytical conditions is crucial to make a reliable estimation of the accuracy. The polar/ionic analytes require specific chromatographic separation. Separation modes are usually reversed phase (RP) chromatography and hydrophilic interaction liquid chromatography (HILIC). In RP, a hydrophobic stationary phase is used for retention and a mobile phase consisting of a mixture of organic modifier and a water phase for elution. In HILIC, the analytical column is polar combined with a highly organic mobile phase in which water is introduced as the eluting solvent. The most commonly reported detection technique is mass spectrometry (MS) with electrospray ionisation (ESI). All studies report the analytical methodology used, either in the report, supplementary data or referring to previous work. Analytical conditions are reported in more detail compared to the sampling methodologies. All studies provided a detailed description of the analytical conditions. This can be related to quality control protocols which are well-developed (Krizman-matasic et al., 2019) and the fact that the analytical conditions are easier to control for researches.

3.1.2.3. Method validation (Internal standards, replicates, positive- and negative controls). Prior to application, the analytical methodology needs to be completely validated for all analytes in terms of trueness/accuracy (evaluated by recovery experiments) and precision (as reviewed studies reported on analysing in triplicates.

#### 3.1.2.3.1. Consumption calculation & metabolites.

The reliability of calculation of drug use depends on the selection of an appropriate drug target residue (DTR), which can be either the illicit drug itself or one of its metabolites. Due to the stability of the drugs in wastewater and human metabolism/excretion, it can be necessary to base consumption estimates upon metabolites. For example, the parent compound of cocaine is excreted in urine only for 1–9% of the original intake, while benzoylecgonine and eckgoninemethylester are excreted in urine for 35–54% and 32–49% of the parent compound intake (van Nuijs et al., 2011). The first formulas for the back calculation of 1) cocaine and 2) amphetamine-like stimulants were proposed by Zuccato et al. in 2008 based on the main excretion products. This could be summarized per DTR specifically as followed:

\[
\text{Consumption} \left( \frac{\text{mg}}{\text{day} \times 1000 \text{inh}} \right) = \frac{1}{\text{Stability of DTR}} \times \frac{1}{\text{Excretion of DTR}} \times \frac{\text{Load of DTR} \left( \frac{\text{mg}}{\text{day} \times 1000 \text{inh}} \right)}{\text{MW}\text{drag} / \text{MWdtr}}
\]

Where, the excretion rate of the DTR is following the use of an illicit drug of interest; stability of DTR is the ratio of DTR concentration after
in-sewer losses due to transformation and adsorption to biofilm/sewer sediment, and suspended solids to initial concentration. Biofilm and sewer sediment grow on sewer walls and can potentially change biomarkers due to chemical and microbial processes. This adds to the uncertainty of the back-estimation (Li et al., 2020).

MW Drug is the molecular weight of the drug of interest and MW DTR is the molecular weight of the DTR. However, accurate excretion rates of DTRs are not always available, due to the lack of pharmacokinetic data (Feng et al., 2018; Gracia-Lor et al., 2016), or are not determined for the applied administration route (snoring, ingestion or intravenous injection) or dose.

The equation used for the consumption estimation is in 16% of the reviewed studies not explained at all. From concentrations of the metabolite (ng/L), the flow rate (L/day) of the wastewater stream and a correction factor, parent compound loads (g/day) can be calculated. The correction factor is established based on the excretion rates and degradation in waste water for the parent drug and its metabolite (van Nuijs et al., 2011; Zuccato et al., 2008, 2005).

Amphetamine, methamphetamine and MDMA are excreted unchanged in urine up to 30, 43 and 65%, respectively (McCall et al., 2016; van Nuijs et al., 2011; Postigo et al., 2010; Zuccato et al., 2008) for cocaine, only 1–9% is excreted in urine unchanged (Gracia-Lor et al., 2016). Been et al. (Been et al., 2016) reported the estimated errors using Monte Carlo simulations resulting in excretion rates of 30.58% for benzoylecgonine, 15.78% for MDMA, 29.12% for amphetamine and 28.56% for methamphetamine.

3.1.3.2. Stability. An important factor to estimate consumption is the stability of the excretion products in the sewer system (Daughton, 2001; Zuccato et al., 2008) (Zheng et al., 2019). Ignoring losses due to sorption/ degradation of illicit drugs or the excreted metabolite in the sewer, and presumably microbial degradation of cocaine which results in the formation of BE may lead to a significant underestimation (A.K. Mccall et al., 2016; Thai et al., 2014; Zheng et al., 2019). Methamphetamine and MDMA have a relatively high stability (A. Mccall et al., 2016). Cocaine is unstable in wastewater, the degradation of cocaine could lead to benzoylecgonine, so by using benzoylecgonine as a DTR cocaine consumption could be overestimated. However, only 37% of the reviewed studies discuss sewer stability of the DTR and incorporated this in the consumption calculation.

3.1.3.3. Population estimation. An estimation of the population being served by a WWTP is a critical factor in the back calculation of drug consumption (Feng et al., 2018). Drug loads have to be normalized to the population in order to enable comparison of the data between different WWTPs. An accurate population estimate is challenging because the actual number of persons being served by a particular WWTP might vary in time due to commuting, seasonal variability, holidays, and/or special events (Feng et al., 2018; Lai et al., 2013). The determination of biological oxygen demand, chemical oxygen demand, total phosphorus

Fig. 1. Percentage of studies scoring ‘0’ (grey), ‘1’ (orange) or ‘2’ (blue) per criterion.
and nitrogen in wastewater or the measurement of a stable indicator of human metabolism have been proposed for the estimation of population served by the WWTP (van Nuijs et al., 2011; Castiglioni et al., 2013). Many of these parameters reflect human activities rather than the population size (Feng et al., 2018). Other sources such as industrial and commercial discharges may cause significant variability (Feng et al., 2018). Some studies based consumption as measured at a WWTP on the total population of the country, which is only applicable for countries with a small population like The Maldives (Fallati et al., 2020). In total, fifteen papers reported a rational estimation of the population, based on the amount of people serving a specific WWTP (Baker et al., 2012; Been et al., 2015; Bijlsma et al., 2016; Causanilles et al., 2017; Croft et al., 2020; Devault et al., 2014a; Klupczynska et al., 2016; Krizman et al., 2016; Kumar et al., 2019; Mercan et al., 2019; Reid and Thomas, 2014; Rodríguez-alvarez et al., 2015; Shao et al., 2020; X. X. Zhang et al., 2019; Y. Y. Zhang et al., 2019).

3.1.4. Critical perspective on the scoring system
The systematic scoring system approach described in this paper gives a general overview of the three main sources of uncertainty in WBE and how the literature from the last decade was dealing with these uncertainties. However, even though the criteria should be as independent as possible, some criteria might cross-affect each other. The scoring system does not correct for this issue. An example is that the sampling procedure (accurate measurement of the flow rate) affects the back-calculation, and the mode of sampling affects the sample volume uncertainty.

Another issue that is not recognized by the scoring system is the co-consumption of drugs in an area. This can affect universal correction factors based on urinary extraction.

For extreme weather events are less likely to occur in certain areas, this might explain why some papers lack information on the weather during sampling. Another potential cause of uncertainty is leakage or overflowing of the sewers since this could lead to underreporting. The scoring system did not take this into account. Another limitation of the score system is that no distinguishing is made between analyte-ILIS and non-analyte-ILIS, which is of great relevance for matrix effects correction and accurate quantification.

Some papers intentionally only show temporal trends and thus are not as dependant on the uncertainties as other reports. The scoring system does not correct for this, and these papers will most likely score lower due to underreporting, even though these uncertainties are not as applicable.

3.1.5. Overall reliability of methods
For each of the reviewed studies, quality criteria and the overall reliability is assessed (Table 3). None of the reviewed papers met the maximum achievable score of 22, one study had the highest score of 18 (Foppe et al., 2018) and two studies had the second-best score of 17 (Mastroianni et al., 2017; Skees et al., 2018). These studies were published in 2017 or later, indicating an improvement in the reporting on WBE approaches.

The average scores are 2.6/6 for the sampling method, 7.9/10 for the analytical accuracy and 3.8/6 for the consumption estimation, and 14.3/22 overall. Thus sampling uncertainty scored the poorest, in agreement with conclusions stated by Ort et al. (Ort et al., 2018a). There is inherent sampling variability due to weather variation, sporadic events, and fluctuating flows. Still, most studies fail to report sufficient details with respect to the sampling method. Sampling should be based on current knowledge, and not just be based on the available equipment (Ort et al., 2010). The analytical accuracy gave the best score. The analytical method can be controlled by researchers, whereas sample collection usually involves voluntary cooperation of treatment plant staff. For this reason, it was expected that this type of uncertainty would be reported in more detail and result in the best score.

3.2. International Drug consumption
In the last decade, the application of wastewater-based epidemiology to monitor illicit drug loads quickly increased, and the approach is currently applied on a global scale. Data on consumption of illicit drugs and their metabolites is reported for each continent except Antarctica. The variability of illicit drug consumption across the globe gives insight in substance abuse and can potentially assist health and law enforcement agencies to register and cut down drug related incidents and substance abuse (Lai et al., 2016). An overview of drug consumption per country from literature published over the last decade is shown in Table 4 for the four substances that are investigated most often. These studies evaluated illicit drug use patterns in urban and rural areas and investigated weekly patterns as well as use on specific events.

The highest number of WBE studies was conducted in Europe, from where we evaluated twenty-eight selected studies reporting in eighteen different countries (Table 4). Studies on a growing number of participating cities are now organized on yearly basis by SCORE and reported to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). Therefore, also general time trends on illicit drug use in Europe are well reported based on a certain period of sampling each year. Nowadays around 70 cities are included in this project (EMCDDA, 2020). For these Europe-wide studies by the EMCDDA the protocol to monitor drug loads is fixed, and common quality control is used in all locations which makes true comparison possible. Overall reliability scores for European-wide studies are amongst the highest (Table 3). The consumption of cocaine is most abundant in western European cities, but a new increase in eastern European cities is also reported by the EMCDDA (EMCDDA, 2020). For amphetamine, highest levels are detected in north and eastern Europe and lower in southern Europe. Methamphetamine consumption is relatively low in Europe overall, with the exception of Slovakia. Since 2019, an increase has been reported by the EMCDDA in eastern Germany, Spain and Cyprus (EMCDDA, 2020). Consumption of MDMA is the highest in The Netherlands, Belgium and Germany, but consumption peaks are also observed in England and Scandinavia (González-Mariño et al., 2020) (Table 4).

The majority of the studies in Europe show an increase of drug use during weekends compared to weekdays, with an exception for methamphetamine (EMCDDA, 2020). These trends were also observed and reported by González-Mariño et al. (González-Mariño et al., 2020).

Within the USA, illicit drug use is a major concern (Foppe et al., 2018). The first study using the wastewater-based epidemiology approach in the USA was in 2009 (Banta-Green et al., 2009). More recent studies in the USA (Croft et al., 2020; Foppe et al., 2018; Skees et al., 2018; Subedi and Kannan, 2014) and Canada (Palaray et al., 2015) followed since then. Here, we evaluated five selected studies, reporting on five different states (Table 4). A high cocaine consumption was measured in New York, as well as for use of amphetamine and methamphetamine in urban and rural areas in the midwestern United States (Croft et al., 2020). A high methamphetamine concentration can affect the amphetamine concentration due to biotransformation, the data was corrected for this issue.

MDMA loads were low for urban areas and not detected in rural areas of the midwestern States, but higher in the state of New York. In Tennessee, reported consumption data of methamphetamine and amphetamine are higher than data from New York state and Kentucky, whereas the cocaine consumption was lower (Skees et al., 2018). Illicit drug use in the midwestern United States is measured during week with special events, showing significantly increased consumption during a festive week (Foppe et al., 2018).

Compared to Western countries, WBE in South America is not as often applied in South America. We evaluated six selected studies, reporting on two different illicit drugs in four different countries (Table 4). WBE in South America has been applied in Brazil (Maritio et al., 2019; F. F. Sodré et al., 2018; F. Sodré et al., 2017), Colombia (Bijlsma et al., 2016), Costa Rica (Causanilles et al., 2017) and the island of Martinique (Devault et al., 2014b).
### Table 4
Overview of drug consumption on a global scale (in mg/day/1000 inhabitants).

| Study                        | City            | Country  | Cocaine | Methamphetamine | MDMA | Amphetamine |
|------------------------------|-----------------|----------|---------|------------------|------|-------------|
| Postigo et al., 2010         | Spain           |          | 17.93   | 0.6              | 9.19 |             |
| Tzerić et al., 2010          | Croatia         |          | 166     | 3.6              | 9.7  |             |
| Karolak et al., 2010         | France          |          | 645.0 to 979.3 | 7.2 to 15.4 |      |             |
| van Nuijs et al., 2011       | Belgium         |          | 519     | 13               |      | 76          |
| Harman et al., 2011          | Norway          |          | 20-70   | 400              | 190  |             |
| Irvine et al., 2011          | Australia       |          | -LOQ-14 | 40              | 27   |             |
| Baker et al., 2012           | Zagreb          | Croatia  |          |                  |      |             |
| Neela et al., 2013           | Paris           | France   | 111 – 130| 5 - 167         |      |             |
| Khan et al., 2014            | Beijing         | China    | 0.2-0.3 | 21.4             | 0.3  | 1.8-4       |
| Baker et al., 2014           | Shanghai        | China    | 0.2-0.3 | 35.5             | 0.2-0.4 | 5       |
| Jaroslav et al., 2014        | Guangzhou       | China    | 0.2-0.3 | 121.7            | 0.5-1.9 | 21.9   |
| Ostman et al., 2014          | Shenzhen        | China    | 0.2-0.3 | 21.7             | 0.6-1.5 | 3.7    |
| Devadut et al., 2014b        | UK              |          | 1263    | 17               | 148  | 86          |
| Jaroslav et al., 2014        | Poznan          | Poland   |          |                  | 70.8 – 13.5 |         |
| Subedi and Kannan, 2014      | Bathel          |          | 807-1380| 4.41-12.8        | 19.1-85.6 | 175-312 |
| Reid and Thomas, 2014        | Buxan           | South-Korea | 1.2-11.4|                  |      |             |
| Andres-Costa et al., 2014    | Ulsan           | South-Korea |          |                  | 2.1-15.1 |         |
| Nowicki et al., 2014         | Kimhae          | South-Korea |          |                  | 14.8  |         |
| Yong et al., 2015            | Busan           | South-Korea | 1.2-11.4|                  |      |             |
| Baltas-Lomba et al., 2016    | Sapporo         | Japan    | 151.5   | 37.7             | 294.7 |         |
| Palardy et al., 2015         | Castellon       | Spain    | 463.9   | 5.4              | 0.8  |             |
| Baz-lomba et al., 2016       | Brussels        | Belgium | 390.9   | 25.4             | 3.5  |             |
| Mastroianni et al., 2017     | Bristol         | England  | 528.7   | 86.3             | 41.6 |             |
| Mackúf ak et al., 2016       | Utrecht         | Netherlands | 299.5   | 121.5            | 52.9 |             |
| Klupszynska et al., 2016     | Milan           | Italy    | 380.9   | 15.5             | 10.4 |             |
| Bodlik et al., 2016          | Naples          | Italy    | 672.6   | 64.8             | 32   |             |
| Yin et al., 2016             | Sofia           | Bulgaria | 377-126 | 3.0-11           | 2.0-57 |         |
| Bijańska et al., 2016        | Czech Republic  |          | 1.0-3.0 |                  | 0.6-2.9 | 8.0-21 |
| Causelilles et al., 2017     | Bratislava      | Slovakia | 74-112  | 4.57             | 5.47 | 85.48      |
| Maida et al., 2017           | Brno            | Czech Republic | 8.44   | 0.9              |      |             |
| Maita et al., 2017           | Gent            | Belgium  |          |                  |      |             |
| Archer et al., 2018          | Ho Chi Minh     | Vietnam  | 342.0 to 533.0 | 675.0 to 1184.8 | 9.0 to 61.6 |         |
| Nguyen et al., 2018          | Sao Paulo       | Brazil   | 2390 ± 520| 1880 ± 395 to 2550 ± 536 mg |      |             |
| Love et al., 2018            | Barcelona       | Spain    | 2400    | 157              | 188  |             |
| Love et al., 2018            | Philadelphia    | USA      | 1900    | 155.8 to 263.8   |      |             |
| Nowicki et al., 2018         | Johannesburg   | South-Africa | 181.9 to 523.5 | 2.2 and 4.9 |      |             |
| Maita et al., 2017           | Rio de Janeiro  | Brazil   | 1900    | 777 ± 54         |      |             |
| Amer et al., 2018            | Sao Paulo       | Brazil   | 2400    | 157              | 188  |             |
| Maita et al., 2017           | Palermo         | Italy    | 1900    | 777 ± 54         |      |             |
| Nuss et al., 2018            | Bangkok         | Thailand | 1900    | 777 ± 54         |      |             |
| Nowicki et al., 2018         | Kuala Lumpur    | Malaysia | 1900    | 777 ± 54         |      |             |
| Causelilles et al., 2017     | Cidade de São Paulo | Brazil | 2390 ± 520| 1880 ± 395 to 2550 ± 536 mg |      |             |
(continued on next page)
to estimate the overall cocaine consumption for specific areas. Overall, cocaine consumption in South- and Central America is reported to be relatively high compared to Europe/globe, possibly related to the proximity to the production and the relatively high purity of street cocaine (Bijlsma et al., 2016).

During the last decade, the WBE approach became a more popular indicator for drug consumption in Asia. We evaluated thirteen selected studies, reporting on five different countries (Table 4). Studies from China (Khan et al., 2014; Jing Li et al., 2014; Shao et al., 2020), South-Korea (Kim and Oh, 2020; Yong et al., 2015), Vietnam (Nguyen et al., 2018), the Maldives (Fallati et al., 2020) and Malaysia (Du et al., 2020) have been published in the last decade. Four megacities in China (Khan et al., 2014; Jing Li et al., 2014; Shao et al., 2020), the Maldives (Fallati et al., 2020) and Malaysia (Du et al., 2020) are more popular in these places compared to the rest of Asia (Du et al., 2020), supported by the fact that drug consumption increases during the holiday season.

With regards to Australia, we evaluated four selected studies in three different states (Table 4). The first study that used WBE as a tool to estimate illicit drug use in Australia was in 2011(Irvine et al., 2011). Similar trends are observed as in Asia, the cocaine consumption is lower than consumption of methamphetamine, while consumption of MDMA is closer to European consumption data. MDMA and methamphetamine are more popular in rural areas whereas cocaine is more frequently used in urban areas. Noticeable is an increase in drug consumption during weekends for popular drugs such as cocaine, amphetamine, methamphetamine and MDMA. Daily illicit drug consumption on an annual music festival in Australia also shows an increase in MDMA compared to a normal week (Lai et al., 2013). A large investigation is described on illicit use of cocaine, methamphetamine and MDMA (Lai et al., 2016), identifying an overall increase in illicit drug consumption in both metropolitan and rural communities over a six year period. In Australia, as in Western Europe, synthetic drugs are more popular. Levels similar to those in Australia of methamphetamine and cocaine

| Study | City | Country | Cocaine | Methamphetamine | MDMA | Amphetamine |
|-------|------|---------|---------|-----------------|------|-------------|
| Stockholm | Sweden | 153 | 25.3 | 39.6 | 208 |
| Reykjavik | Iceland | 136 | 32.6 | 51.5 | 217 |
| Torshavn | Faroe Islands | 4.6 | | | |
| Cosenza et al., 2018 | Southern region | Italy | 150 - 170 | | | |
| Skees et al., 2018 | Midwestern states | USA | 938 ± 706 | 1740 ± 1190 | 967 ± 455 |
| Foppe et al., 2018 | Kentucky B | USA | 434 | 1240 | 59 | 526 |
| | Kentucky A | USA | 1970 | 3090 | 1.72 | 919 |
| Wang et al., 2019 | Dalian | China | 53.9 | | | |
| Mercan et al., 2019 | Istanbul - Beyoglu | Turkey | 754 | 449 | 632 | 46.1 |
| | Istanbul - Catalca | Turkey | 15.6 | 195 | 29.3 | 8.38 |
| Dagligolu et al., 2019 | Istanbul - Beyoglu | Turkey | 14 | 2 | 87 | 8.7 |
| Kumar et al., 2019 | Guangzhou | China | 0.9–9.5 | 14.7–470.7 | 1.7–18.4 |
| Marino et al., 2019 | Brasilia north | Brazil | 997 | | | |
| | Brasilia south | Brazil | 565 | | | |
| | Santiago de | Spain | 455 | | | |
| | Compostela | | | | | |
| Fallati et al., 2020 | Male | Maldives | 0.5 | 3 | 7.7 | 2.5 |
| Deng et al., 2020 | Changzhou | China | 0.02±0.15 | 5.89±8.74 | 0.02–0.16 | 0.84±0.62 |
| Du et al., 2020 | Kuala Lumpur | Malaysia | 9 - 4 to 14 ± 6 | 468 ± 64 to 687 ± 112 | 558 ± 373 to 850 ± 177 |
| Shao et al., 2020 | Chongqing | China | 328 ± 36 | | | |
| | Chengdu | China | 170 ± 1 | | | |
| | Guiyang | China | 249 ± 19 | | | |
| | Changdu | China | 99.7 ± 15.8 | | | |
| | Kunming | China | 133 ± 17 | | | |
| | Dalian | China | 55.7 ± 4.8 | | | |
| | Harbin | China | 96.5 ± 1.1 | | | |
| | Changzhou | China | 72.3 ± 25.2 | | | |
| | Hefei | China | 119 ± 3.5 | | | |
| | Qingdao | China | 162 ± 3 | | | |
| | Jinan | China | 68.6 ± 2.1 | | | |
| | Weihai | China | 159 ± 10 | | | |
| | Beijing | China | 88.6 ± 5.4 | | | |
| | Huhehot | China | 99.5 ± 0.7 | | | |
| | Baoding | China | 6402 ± 589 | | | |
| | Zhengzhou | China | 368 ± 11 | | | |
| | Xiangtan | China | 162 ± 8 | | | |
| | Guangzhou | China | 85.2 ± 9.8 | | | |
| | Xi’an | China | 37.6 ± 5 | | | |
| | Lanzhou | China | 229 ± 28 | | | |
| | Dingxi | China | 23.0 ± 2.6 | | | |
| | Yinchuan | China | 124 ± 13 | | | |
| Croft et al., 2020 | Kentucky Urban | USA | 3830 | 1030 | 400 |
| | Kentucky Rural | USA | 864 | 1660 | 738 |
| Kim and Oh, 2020 | Busan | South-Korea | 14.9 – 28.6 | | | |
consumption are found in New Zealand (Kumar et al., 2019), although MDMA consumption is relatively low.

The application of WBE to monitor illicit drug use is still largely lacking in Africa. So far, only two WWTPs located in Johannesburg and Cape Town, South-Africa, have been monitored to estimate drug use patterns (Archer et al., 2018). Methamphetamine is the primary substance detected, at consumption data comparable to USA and Australia. Clandestine manufacturing of illicit methamphetamine results in dumping events of chemical waste, which could be traced via spikes including the precursors used in the production process observed at the WWTP in Johannesburg (Archer et al., 2018). Cocaine consumption is found to be similar to European consumption data, while consumption data for MDMA are low compared to Australia, the USA and Europe.

Fig. 2 illustrates the global consumption distribution for MDMA (purple), methamphetamine (blue), cocaine (red) and amphetamine (orange). So far, WBE has not been used to determine illicit drug consumption in most of the African continent, the Middle East and Russia.

Overall, high consumption rates are found in the USA, especially for cocaine and methamphetamine (Fig. 3). For Asia, except for methamphetamine, lowest consumption is reported.

Cocaine production expressed as a percentage of the gross domestic product (GDP) is the highest for Colombia (2 to 3%) (INCB, 2002), while for the USA profits from drugs traffic are estimated to be 0.5% of GDP (INCB, 2002). Within Europe, the cocaine market is the second largest illicit drugs market with an estimated retail value of 9.1 billion euros in 2017 (EMCDDA and Europol, 2019). The total value for the retail market for illicit drugs in Europe was estimated at 30 billion euros in 2017 (EMCDDA and Europol, 2019). The consumption of synthetic drugs, such as amphetamine and MDMA, in Europe increased in the last decade, especially for the northern and eastern regions of Europe. Similar trends are observed in Europe’s synthetic drug market, which has rapidly grown in the past ten years (EMCDDA and Europol, 2019). Large-scale production of MDMA and amphetamine remains concentrated in the Netherlands and Belgium, while production of methamphetamine is mainly concentrated in central Europe (EMCDDA and Europol, 2019). In Asia, drug consumption is relatively low compared to other continents. According to a report by the United Nations Office on Drugs and Crime (UNODC) in Asian regions, illicit drug production in Asia is increasing for amphetamine-like substances (Liu et al., 2013; UNODC, 2008). This is proportional to the increase in methamphetamine consumption in China and South-Korea.

The reported results should be viewed with an assured degree of uncertainty. Consumption values are frequently reported without calculated uncertainty values (Ort et al., 2010a). Only a handful of the reviewed papers (Causanilles et al., 2017; Deng et al., 2020; Devault et al., 2018; Du et al., 2020; Kumar et al., 2019; Shao et al., 2020; Skees et al., 2018; F. F. Sodré et al., 2018) explicitly reported on uncertainty values for their consumption data (±xy). The complete uncertainty assessment would include the sampling uncertainty, analytical uncertainty and the uncertainty for the consumption estimation as mentioned in the previous chapter. The trueness of the final consumption data should undergo a suitable statistical propagation. Various studies have used Monte Carlo analysis (Been et al., 2015; Croft et al., 2020; Jones et al., 2014; Shao et al., 2020; Y. Y. Zhang et al., 2019; Zheng et al., 2019) to calculate the uncertainties. Fig. 3 shows the distribution of all reviewed papers per drug for each continent including the reliability of the method used to obtain the data points. For many drug/continent combinations, the majority of the data fall within one order of magnitude.

Fig. 2. Average illicit drug consumption per country for MDMA (purple), methamphetamine (blue), cocaine (red) and amphetamine (orange) based on data published over the last decade.
4. Conclusion

Based on the relatively limited number of studies that could be identified as high quality, further advancement of the WBE approach for illicit drugs is desired especially with regards to the sampling methodology. However, studies carried out in Europe within the SCORE research group, have been using a systematic analytical approach, including annual interlaboratory exercises as an important factor in making data more comparable. Notable is that over the years, the analytical methodology is rapidly improving, and the implementation of high-resolution mass spectrometry techniques will allow more efficient methodologies for wide-scope screening, identification of untargeted/suspect compounds, or for the detection of metabolites and transformation products. Due to more advanced analytical approaches in the last decades, detection limits are decreasing and became less challenging when measuring low concentrations. Publishing full information regarding detailed sampling and analytical methodologies, even if only in the supplementary data, is crucial for the interpretation of obtained results. It will be necessary to harmonize the criteria for reliable identification/confirmation and accurate quantification of compounds detected in samples, reliable sampling, and less uncertainty in population estimation. This way, data collected from different laboratories in different parts of the world would become more comparable to each other and valid conclusions can be drawn on illicit drug consumption in

Fig. 3. Boxplots showing distributions in drug consumption (mg/day/1000inh) for cocaine, MDMA, amphetamine and methamphetamine. Individual data points per reviewed study are indicated via dots in red (low reliability score 10,11,12), yellow (medium reliability score 13,14,15) or green (high reliability score 16, 17 and 18).
different communities on a global level. This study provides an overview of the available literature, reporting on data on drug consumption using the wastewater-based epidemiology approach. Overall, high consumption rates are found in the USA, especially for cocaine and methamphetamine consumption, while lowest illicit drug consumption is reported in Asia. These results agree with data reported by the EMCDDA (Europe) and the UNODC (other continents). The WBE approach can identify trends in consumption quickly which makes it extremely useful in generating data on illicit drug use.

Declaration of Competing Interest

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

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Supplementary materials

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