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Triangulating Amsterdam's illicit stimulant use trends by wastewater analysis and recreational drug use monitoring

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Abstract

Drug consumption estimates are of relevance because of public health effects as well as associated criminal activities. Wastewater analysis of drug residues enables the estimation of drug consumption and drug markets. Short-term and long-term trends of cocaine, MDMA (ecstasy), amphetamine (speed) and methamphetamine (crystal meth), were studied for the city of Amsterdam. MDMA (+41%) and cocaine (+26%) showed significantly higher weekend vs. week consumption, while no differences were observed for the other drugs. The consumption of MDMA, cocaine, amphetamine and methamphetamine significantly increased between 2011 and 2019. Weekly trends emerging from wastewater analyses were supported by qualitative and quantitative data from a recreational drug use monitoring scheme. However, information collected in panel interviews within nightlife networks and surveys among visitors of pubs, clubs and festivals only partially reflected the long term increase in consumption as registered from wastewater analysis. Furthermore, methamphetamine use was not well presented in survey data, panel studies and test service samples, but could be monitored trough wastewater analysis. This illustrates that wastewater analysis can function as an early warning if use and user groups are small or difficult to reach trough other forms of research. All in all, this study illustrates that wastewater-based epidemiology is complementary to research among user groups, and vice versa. These different types of information enable to connect observed trends in total drug consumption to behaviour of users and the social context in which the use takes place as well as validate qualitative signals about (increased) consumption of psychoactive substances. Such a multi angular approach to map the illicit drug situation on local or regional scale can provide valuable information for public health.

Key words:

Wastewater-based epidemiology (WBE), recreational drug use monitoring, drug consumption trends, illicit drugs, triangulation, MDMA, cocaine, methamphetamine, amphetamine.

Highlights:

- Wastewater analyses Amsterdam 2011-2019
- Increased consumption of MDMA, cocaine, amphetamine and methamphetamine
- Higher weekend vs. week consumption of MDMA and cocaine
- Findings wastewater analysis partially supported by recreational drug use monitor
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Introduction

Both the consumption and the regulation and/or prohibition of psychoactive substance is of all times and ages(1). In modern society use of (illicit) drugs is of relevance because of public health effects related to development of dependence, as well as criminal activities linked to procurement, production, and trade(2). Nevertheless, the estimation of the consumption and the identification of its users remains a complex challenge, since production and trade are hidden and consumption is poorly documented and performed in a variety of scenes such as nightlife, festivals, chemsex scene, specific working environments and street life.

With robust analysis of wastewater and correct calculation of census data wastewater-based epidemiology (WBE) can provide information on the illicit drug consumption on local, regional, national, and international scales(3, 4). Furthermore, its high temporal resolution allows to monitor short temporal trends (days to weeks) related to festivals or season as well as longer timeframes(3, 5). In addition, surveys, panel studies, and field testing provide valuable information on local users and characteristics of consumed drugs(6). General population surveys provide prevalence rates of drug use for age and gender strata, but not always per separate drug.

In the Antenna Amsterdam monitor – which has been following trends in recreational drug use since 1993 – annual surveys are performed among specific populations such as nightlife attendants and other groups with relatively high rates of use. In addition, a panel study is performed among lay and professional experts reporting on networks of people who use drugs in these settings(7). Together, the surveys and panel studies generate valuable quantitative and qualitative information about drug use, user characteristics, consumption patterns, inter- and intrapersonal variations in amounts and frequency of use, and changing use habits among specific user groups. In addition to user monitoring, Antenna Amsterdam also reports on testing results from the Amsterdam drug checking services. These voluntary test services, available to users in Amsterdam (and many locations in the rest of the Netherlands), analyse the quality (i.e., purity or dose of active substance) of drugs available on the market(8). Despite the wealth of information collected in Antenna Amsterdam, results cannot easily be used to quantify overall consumption in the city. This is because not all user groups are reached equally(9, 10), findings from specific groups cannot easily be generalised to wider populations, and the nature of qualitative panel studies is less suitable for quantification of consumption. Neither WBE nor the Amsterdam Antenna Monitor can fully generate general population prevalence rates for a population, but they both do yield distinct indicators that, when triangulated, can be used to reveal changing patterns of drug use.

For this paper, both long-term and short-term trends of illicit drugs have been studied for the city of Amsterdam using WBE. For this purpose, four illicit stimulants were selected, namely cocaine, MDMA, amphetamine and methamphetamine. Trends in consumption patterns were evaluated for the past decade (2011-2019)(11). The obtained figures and trends are triangulated with data collected in Antenna Amsterdam.

Materials and methods

Amsterdam wastewater sampling

Samples were collected in the Amsterdam-West Wastewater treatment plant in the Netherlands. The sewer system is characterized by means of a standardized questionnaire developed by Ort and colleagues(12). The plant has a capacity of 850.000 inhabitant equivalents. Its catchment holds 669401 residents at 1/1/2020 based on the registration of addresses (Basisregistratie Adressen en Gebouwen) situated in the catchment of the treatment plant and the registration of inhabitants associated to these addresses (Basisregistratie personen). 93.2% of these residents live in municipality of Amsterdam, 4.6% in Diemen, 1.4% in Ronde Venen, 0.8% in Ouder-Amstel and <0.5% from other neighbouring municipalities. The treatment plant covers 77% of the total Amsterdam inhabitants. The population dynamics of the city of Amsterdam was used to estimate the population dynamics of the catchment of the treatment plant. Between 2011 and 2020 the population of Amsterdam grew with 12%, while greater Amsterdam including neighbouring municipalities grew with 10%(13). Inhabitants of the waste water treatment plant catchment are listed in the Supplemental Information (Table S1). These data were used to calculate per capita drug consumption. The collection of this meta-data is essential for the correct interpretation of results.

Sample collection and storage

24 h composite influent wastewater samples were collected during seven consecutive days using an automated volume-proportional that was harvested at 8:00 AM that was sampling aliquots of 50 mL every 350 m^3, resulting in over 300 sub-samples per 24 h. The sampling was performed between March and April except for the sampling in 2017 that was performed in September. All sampling weeks did not hold public holidays and were outside holiday season. Furthermore, no large events or festivals were within or near the catchment of the wastewater treatment plant during the sampling week. Finally, during the sampling weeks, no sewer overflows were registered that could account for losses of wastewater circumventing the wastewater treatment plant. During sample collection days, samples were stored at 4°C in the auto sampler for a maximum of 24 h and were frozen (-20°C) immediately after collection. Chemical stability studies illustrated that sample storage did not lead to significant losses during storage.

Chemical analysis and quantification

Sample treatment and instrument operating conditions are summarized in the Supplemental Information and are described in more detail elsewhere(14). Sampling dates are provided in the Supplemental Information as well (Table S1). All compounds were identified using external reference standards. Annual proficiency testing in an international network of laboratories were performed to evaluate accuracy and robustness of analytical methods throughout the monitoring period(15).

Calculating consumption

Daily mass loads in mg / day / 1000 inhabitants were calculated by multiplying the concentration in each sample by the corresponding daily wastewater flows and normalizing the obtained values to 1000 inhabitants from the number registered in the catchment of the wastewater treatment plant. The daily loads were converted to drug consumption by the conversion factors obtained from literature, correcting for excretion and substance stability (Table 1). This leads to the amount of pure drug consumed per 1000 inhabitants per day over a week.

Table 1: Calculation factors to estimate drug consumption from concentrations in wastewater

Drug	*Factor applied for consumption estimation (Standard Error)*	*Ingestion route applied for calculations of consumption*	*Excretion route applied for calculations of consumption*
Benzoylecgonine (Cocaine)	3.27 (2.93-3.70)[A] 6.08 (4.65-8.79)[B]	*Snorted* *Smoked*	*Renal excretion (urine)*
Amphetamine	3.42 (3.33-3.55)[A]	*Ingested/snorted*	*Renal excretion (urine)*
Methamphetamine	3.50 (3.21-3.85)[A]	*Injected/Ingested*	*Renal excretion (urine)*
MDMA	6.34 (5.68-7.17)[A]	*Ingested*	*Renal excretion (urine)*

[A] *Conversion factors obtained from Beén et al.(16)*

[B] *Conversion factor from smoking crack cocaine obtained from Cone et al.(17)*

One should note that excretion rates can vary widely for individuals and among circumstances. However, with wastewater analysis of Amsterdam, a large population is sampled that averages out individual variations in excretion(18). Nevertheless, it should be noted that these average excretion factors are often obtained under controlled conditions with specific modes of application, defined single-drug dosages, and volunteers of defined sex and/or age groups and drug consumption history. The studied subjects, doses and circumstances might not be fully representative for the average consumer in the field. Therefore, these factors are prone to bias. However, a similar approach performed for opioids and pharmaceuticals, where consumption figures are better registered, show good agreement between registered use and measured use via concentrations in wastewater(19, 20). Furthermore, even when data might be biased, the relative comparisons between samples are not affected. Therefore, trends in consumption can be evaluated accurately.

Statistical evaluation

All statistical tests were performed using Graphpad Prism version 5.01 and p values below 0.05 were considered significantly different. Temporal trends over the course of years were evaluated by fitting a linear regression to the consumption data and evaluating the significance of the slope of the regression line. Each year, seven 24h composite samples of a consecutive week were included except for the 2011, when only four consecutive samples were obtained. Drug consumption can have a variety of temporal trends that are not represented by a simple linear regression over time. However, since no assumption can be made on the on the nature of the trend, a simple linear regression was fitted to the data.

Differences in consumption between days of the week were evaluated using a non-parametric ANOVA test (*i.e.* Kruscal-Wallis test). Before analysis all data were normalized to the weekly average of the particular year and grouped per day of the week (e.g., Mondays, Tuesdays, *etc*.). In addition, a comparison was also made between the consumption during weekdays and weekend days using an unpaired non-parametric Wilcoxon signed rank t-test was applied to compare the pooled normalized weekday data with the pooled weekend day data.

Panel study, survey and test service data used for triangulation

Methods and results of the Antenna Amsterdam monitor are described in detail in annual Dutch publications since 1993 (see Nabben and Benschop 2021 (7) and previous editions).

For the panel study, about 20-25 lay and professional experts are interviewed about drug consumption patterns in networks with trendsetting potential in nightlife. Lay experts report on scenes or groups of friends they belong to; professional experts report on nightlife visitor crowds. While these networks are linked to nightlife, recreational drug use within these networks is not necessarily limited tot nightlife settings. The composition of the panel reflects the (changing) diversity of Amsterdam nightlife. Individual panel members continue for five years on average and are replaced when they drop out or lose view of a network. Panel members are interviewed individually twice a year. The interviews are mainly qualitative in nature, using a topic list to steer the conversation. Some quantification is included where panel members are asked to estimate the extent of regular use (at least once in the past six months) within the networks in five fixed categories: 0% (none), 1-10% (a few), 11-25% (some), 26-50% (small group), 51-75% (large group), 76-100% ((almost) everyone). These estimates were converted to scores between 0 and 4 (0 = 1-10% = 0.4; 11-25% = 1; 26-50% = 2; 51-75% = 3; 76-100% = 4). Scores were averaged per year (2011-2019) for all panel members.

Prevalence data from the Antenna Amsterdam surveys used in this paper come from those conducted among club and festival attendants in 2013 and 2017(21), and among pub customers in 2014 and 2018(22). Respondents were recruited on-site by teams of fieldworkers. Those who agreed to participate in the survey were provided with a link to an anonymous online questionnaire that included yes-no questions on the use of various drugs and open-ended questions on the number of days substances were used during the past year. In each survey, more than 500 respondents completed the questionnaire (see Table 2 for exact numbers per survey and some basic demographics).

The drug testing service data used in this paper includes the number of samples submitted in 2011-2019as well as purity indicators.

Triangulation of WBE results with data from Antenna Amsterdam can only be done for cocaine, amphetamine and MDMA and not for methamphetamine. Very limited methamphetamine use is reported in the panel study, methamphetamine use was rare among respondents in the clubs and festivals and pubs surveys (< 0.5% last year use), and only a few methamphetamine samples (< 20 per year) are submitted to drug testing services.

Results and discussion

Long-term trends of drug consumption (2011-2019)

Over the past decade drug consumption was monitored by wastewater analysis one week a year. The week of monitoring was a week without events such as large festivals, public holidays, or vacation periods. This allows to evaluate the “baseline” consumption within the catchment of the wastewater treatment plant Amsterdam-West without a relevant bias of consumption related to large festivals and the visitors thereof(23, 24) as well as omitted consumption due to absence of large numbers of inhabitants as a result of holidays(25). Long-term trends in illicit drug use were analysed over the 2011-2019 period.

Figure 1 shows the per capita consumption of cocaine, amphetamine, methamphetamine and MDMA over the period 2011-2019. A simple linear regression was fitted through the data to evaluate if per capita consumption significantly changed in time. The individual datapoints represent data of seven consecutive days of sampling and include variation in consumption over the course of the week.

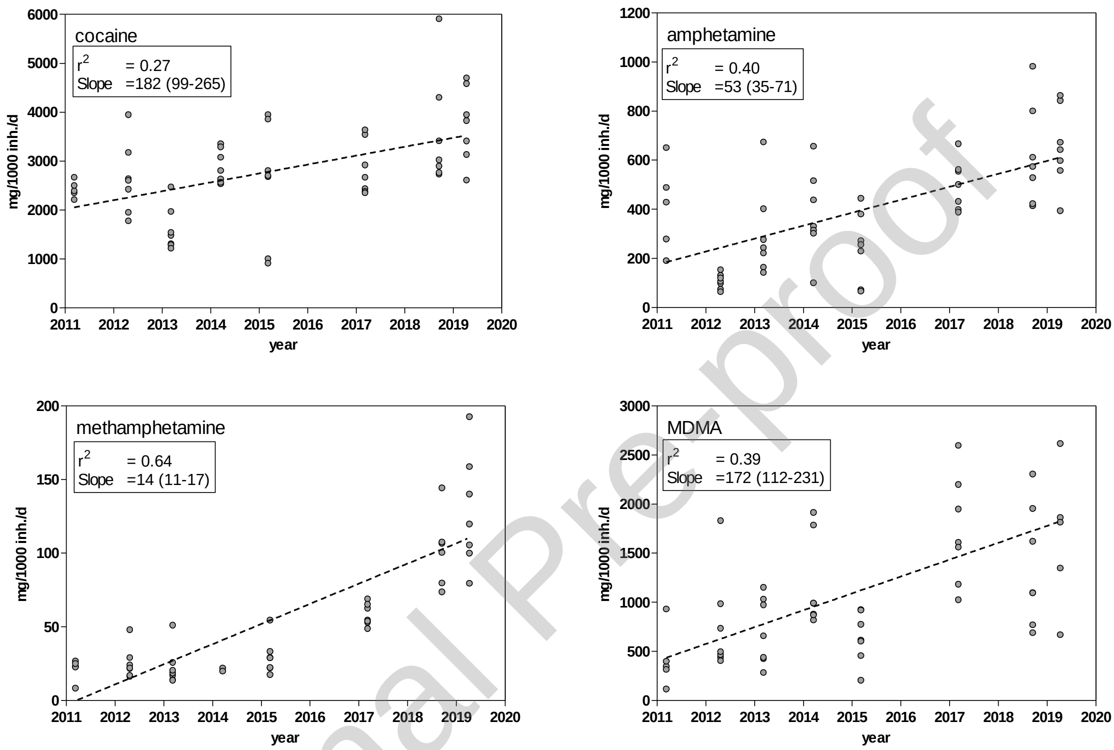

Figure 1: Long-term trend of consumption in mg/1000 inhabitants per day of cocaine, amphetamine, methamphetamine and MDMA. The coefficient of correlation (r^2) and the slope, defining the annual increase in consumption, (mg/1000 inhabitants per day) are listed. Consumption of all stimulants increased significantly (p values all below 0.0001)

Figure 1 also shows the parameters of the statistical analysis. All studied illicit drugs show a significant increase in per capita consumption over the period between 2011 and 2019. The consumption of cocaine increased with a little less than a factor two, amphetamine showed a steeper increase with a factor two to three, while MDMA increased with a factor four between 2011 and 2019. Methamphetamine showed the steepest increase of a factor five. A more careful look at the available data illustrates that the presumed linear increase does not fit methamphetamine data, as the increase in consumption mainly manifests after 2014. In addition variations during the days of the week, as discussed in section "*Short-term trends of drug consumption"* are not accounted for introducing additional variation that is linked to weekly consumption patterns.

Triangulation of long-term trends of drug consumption (2011-2019)

The trends in per capita consumption, as determined by wastewater analysis, is not reflected in all data obtained from Antenna Amsterdam.

Data from the panel study on the estimated extent of regular use in networks of trendsetters nightlife did not reveal increasing or decreasing trends between 2011 and 2019 (Figure 2).

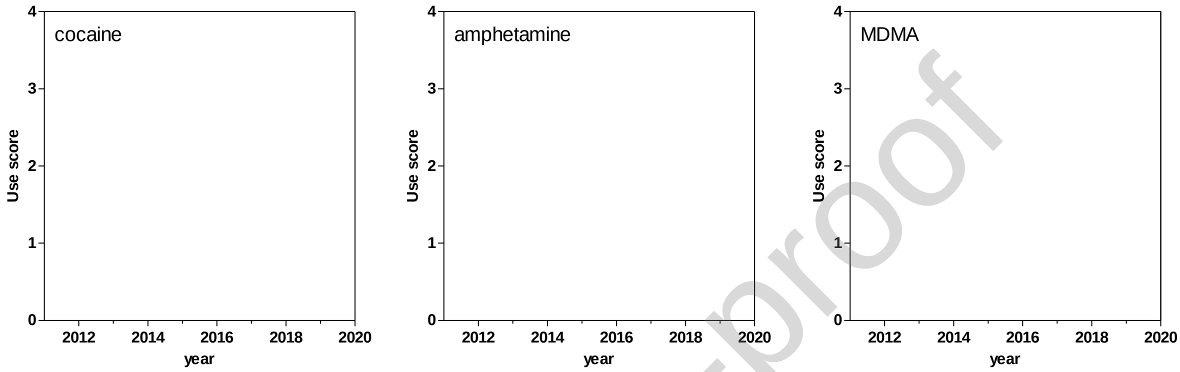

Figure 2: Trends in consumption of cocaine, amphetamine and MDMA, as derived from panel studies. The use score is based on the extent of regular use as estimated by panel members that represent various networks(7).

In the surveysamong nightlifers, it was observed that reported cocaine use significantly increased between 2014 and 2018 for pub customers, while it did not increase significantly among club and festival attendants between 2013 and 2017. Contrarily, MDMA use significantly decreased between 2013 and 2017 among club and festival attendants while it did not change among pub customers between 2014 and 2018. Amphetamine use did not show an increase in both groups of respondents. Furthermore, looking at the absolute prevalence percentages, the two groups seem to get more similar as prevalence rates are converging for all tree stimulants (Table 2).

Table 2: Survey data from club and festival attendants and pub customers

	2013 clubs and festivals	*2014 pubs*	*2017 clubs and festivals*	*2018 pubs*
N	*633*	*523*	*639*	*540*

Female %	*50.1*	*53.7*	*53.4*	*62.9*
Average Age Y (standard deviation)	*24.1 (4.9)*	*27.3 (5.6)*	*25.6 (5.8)*	*26.4 (5.2)*
Living in Amsterdam	*65.7%*	*85.7%*	*59.2%*	*83.1%*
Student	*65.7%*	*44.7%*	*52.4%*	*49.6%*
Last year prevalence rate cocaine	*34.6%*	*28.7%*[A]	*39.3%*	*38.1%*[A]
Last year prevalence rate amphetamine	*33.2%*	*19.5%*	*30.7%*	*22.2%*
Last year prevalence rate MDMA[C]	*72.8%*[B]	*50.1%*	*66.4%*[B]	*48.1%*

[A] A significant increase was observed for the prevalence of cocaine use among pub customers between 2014 and 2018 (Chi-square test, p value < 0.005)

[B] A significant decrease was observed for the prevalence of MDMA use among club and festival attendants between 2013 and 2017 (Chi-square test, p value < 0.05)

[C] MDMA prevalence data on tablets are presented. MDMA powder prevalence rates show similar trends but tablets are by far most popular. MDMA tablets and powder use is seldom mutually exclusive; both forms are used within largely the same population.

Figure 3 shows the number of samples of cocaine and MDMA presented to the Amsterdam public test services significantly correlate with the per capita consumption as derived from wastewater analysis, while for amphetamine no significant correlation was observed (p-value = 0.11). The relation appears to be strongest for MDMA. Interestingly, the number of MDMA samples exceed the other drugs by roughly a factor ten. The number of samples submitted annually might therefore be used as an indicator for consumption trends of cocaine and MDMA separately, but they are not suitable to compare the drugs as the readiness to test varies between the different stimulants.

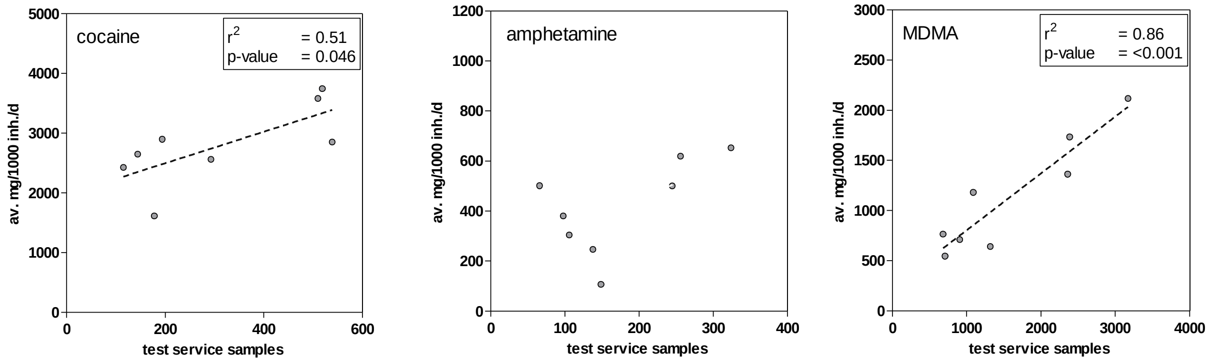

Figure 3: The correlation between samples presented to test services annually in Amsterdam and the consumption in mg/1000 inhabitants per day based on the average of one week of monitoring seven consecutive days.

Short-term trends of drug consumption

Drug loads in the sewer can show intra-weekly trends, related to differences in consumption habits, particularly between weekdays and weekends, and the subsequent excretion and collection in the sewer. Figure 4 shows the relative measured consumption per weekday as compared to the week average that is set at 100% for 7 consecutive sampling days. Data of 2011 were excluded as not all days of the week were sampled that year(11).

In order to study week trends, pooled consumption levels observed during weekdays (Tue-Fri) were compared to those of weekends (Sat-Mo). Samples of Tue-Fri are defined as weekdays and samples of Sat-Mon are considered weekend because the excretion of the drugs and transport of wastewater to the wastewater treatment plant takes time. In Amsterdam average transport of wastewater to the wastewater treatment plant takes on average 4 hours but can vary up to half a day depending on the location in the network, time of day and environmental conditions such as rain events (personal communication, Waternet). Furthermore, clinical studies show urinary excretion of benzoylecgonine peaks after 7.8 h after snorted cocaine (Cone 1998), while amphetamine, methamphetamine and MDMA peak 2-8 h (26), 1-11 h (27) and, 12.3-13.9 h (28) after oral admission, respectively. Samples collected from Saturday were included in the weekend to appoint the consumption on Friday night to the weekend.

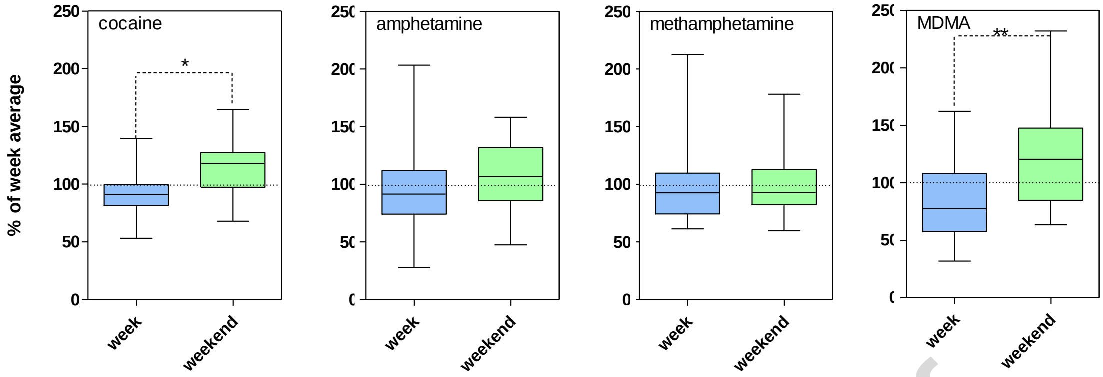

*Figure 4: The week consumption (Tue-Fri) vs. the weekend consumption (Sat-Mo) over the period of 2012-2019. Monday is added to the weekend days as delayed excretion leads to residues of drugs consumed in the weekend on Monday. Significant differences with p values of 0.01-0.05 and 0.001-0.01 are indicated with * and **, respectively.*

No significant differences were observed between week and weekend consumption for amphetamine (p value 0.20) and methamphetamine (p value 0.81) while for cocaine (through benzoylecgonine; p value 0.013) and MDMA (p value 0.0085) a significantly higher weekend consumption was observed. The consumption of cocaine in weekends is on average 26% higher than during the weekdays while the difference for MDMA is even larger with a 41% higher consumption during the three days that were considered weekend. This analysis corresponds with earlier findings of other cities with higher levels of cocaine and MDMA in wastewater during weekends(29).

Triangulation of short-term trends of drug consumption

The Antenna Amsterdam monitor does not collect separate data on week and weekend consumption to offer support for the differences found through wastewater analysis. However, the most pronounced elevated weekend consumption for MDMA does correspond to the 2018 survey data on the frequency of use, which show MDMA use is more limited with an average annual consumption frequency of 5.2 (sd 4.5) days per year as compared to amphetamine with 7.4 (sd 10.1) days per year and cocaine with 11.0 (sd 24.3) days per year(22). The proportion of users who consume more than 10 days per year is also smaller for MDMA (10.1%) than amphetamine (19.3%) and cocaine (27.6%). In addition, it also corresponds to the qualitative information from the panel interviews, where MDMA is characterized as a drug reserved for nightlife and party settings, that mainly manifest during the weekends. Cocaine has a reputation as an ‘upbeat companion’ that feels equally at home at a pub, a private party, or anywhere else where friends meet to drink and socialise. This does not necessarily limit cocaine use to the weekends, especially for those working in fields without Monday-to-Friday jobs (e.g. hospitality or creative industry). Finally, amphetamine is not only popular in nightlife, but also regarded as an aid for improving performance or staying awake on working days(30).

Discussion

The observed increase in per capita drug consumption determined by wastewater analysis between 2011 and 2019 correlates to some extent with increased prevalence rates from survey data and increased numbers of samples presented to test services. And the observed increased consumption during weekends is to some extent supported by frequency data from the survey and qualitative information from the panel study. However, trends derived from wastewater analysis are not fully reflected by the Antenna Amsterdam monitor. There can be various reasons explaining this presumed discrepancy.

First, the panel study and surveys do account for prevalence among networks in nightlife, club and festival attendants, and pub customers, but not for the size or changing composition of these groups. Total consumption will also grow if the individual consumption among a group is stable but the group expands relative to the total Amsterdam population. The growth of Amsterdam nightlife since the tens of this century can be read from the exponential growth of nightlife venues. Amsterdam currently has 40 clubs; 30 cultural venues and 60 music cafes. The dance festival sector also expanded over this period (31). In 2019 a third (150 out of 450) of all Dutch festivals were organized in Amsterdam while only 5% of the Dutch population are Amsterdam residents(32).

Second, visitors from outside the city are not accounted for in the calculation of per capita drug consumption(5). The growth of non-residents clearly exceeds the city's residential growth. Amsterdam's registered overnight guests increased with 61% from 5.7 million 2012 to 9.2 million in 2019(33) with a population increase of only 9%. While only a part of these visitors may contribute to sewer drug loads, some impact might be expected as the panel study signals an increased presence of tourists in nightlife and on the local drug market(22).

Third, it was observed that club and festival attendants and pub customers became more similar between 2013-2018 when the prevalence of stimulant data were compared. This suggests that consumption in trendsetting club and festival scenes were adopted by the wider and more generic pub audience and might be an indicator for a "normalization" of the studied stimulants among residents and visitors in Amsterdam, which corresponds to the nett increase in total drug consumption as observed by wastewater analysis.

Forth, recreational use is characterized as consumption of drugs in a recreational setting. This use is often, but not exclusively performed in nightlife during weekends. Functional use is characterized as consumption to aid staying awake or perform better in work or study, and likely, but not exclusively occurs during weekdays. Dependent use is characterised by increased frequency of use with decreased difference between use in weekends and weekdays. The panel and survey studies focus mainly on drug use associated to nightlife, which is largely of recreational nature. For cocaine and amphetamine functional and dependent drug use is sometimes reported in the panel study while this is not the case for MDMA. The number of dependent and functional users of cocaine and amphetamine, nor their total consumption is known. It is, therefore, not possible to quantitatively appoint per capita drug consumption derived from wastewater analysis to the different consumption types (*i.e.* recreative, functional or dependent).

The Dutch National Institute for Public Health and the Environment (RIVM) ranked dependency of 19 psychoactive substances. MDMA was ranked 17th, far below amphetamine (8th), cocaine (6th) and methamphetamine (5th)(34). Runner-up (2nd) on this list was crack cocaine, the smokable free base form of cocaine, listed behind heroin (1st). This means that especially crack cocaine and to a lesser extent cocaine and amphetamine are prone to dependent use. Crack cocaine use is distinct from (powder) cocaine use, it is hardly used recreative in nightlife(35). In 2009-2011 an estimated 2,524 (95% CL 2,185 to 2,977) Amsterdam residents used crack at least twice per week(36). Though a small population in comparison to nightlife / party scenes, these users may contribute significantly to (weekday) consumption. Rough estimations based on an average weekly expenditure of €135 per crack user and retail prices ranging from €40 to €109 per gram, depending on quantity sold*(37)*, result in 0.4 to 1.2 kg crack cocaine consumption in Amsterdam. Taking into account that the form of administration affect intake, metabolism and excretion(17) (Table 1) this estimated crack cocaine use would roughly account for one tenth to one third of the benzoylecgonine load in observed in Amsterdam wastewater in 2011, the year closest to the year the crack cocaine use study was performed. Fifth, drug purity or dose and price per unit might affect the amount consumed per user. Purity % (cocaine, amphetamine) and dose (MDMA tablet) data from the Amsterdam drug checking services show an increase between 2012 and 2019 (Table S2, Supplemental Information). With constant masses of drugs used, that would equate to increased intake of cocaine, amphetamine and MDMA. However, the illegal drug market of cocaine and amphetamine is 'fixed-price' rather than 'fixed-weight', as qualitative information collected in the panel study indicates that dealers compensate high cocaine powder purity through smaller packaging. For example selling 0.9 gram instead of 1.0 gram cocaine in €50 wrappers. In addition, high-dosed MDMA tablets are (partially) compensated by users through adjusting their dosage, taking only part of a tablet to keep control(7). It is therefore difficult to distinguish to what extent the availability, pricing and purity or dose affect use, and *vice versa,* to what extent the use affects availability, pricing and purity or dose.

Finally, the observed increase in stimulant consumption by wastewater analysis discussed above fit in a larger socioeconomic and cultural metamorphosis Amsterdam went through since the 1990s, changing from a blue collar community to a high-quality service and network community with a vibrant nightlife culture(30, 38). Since that time we can consider the city of Amsterdam as a stage and facilitator of the party culture. While Amsterdam is quite a bit smaller than Berlin, London, or New York, it is often mentioned in the same breath as other 'cool' cities where commercial impulses stimulated innovative urban development(39). The city's economic strength largely depends on the infrastructure of its (tele)communication and technology companies which is complemented with services, entertainment, and a thriving tourist industry according to the sociologist Castells(40). It was argued that the development of technology and the nurturing of talent and tolerance are important priorities that contribute to a city's success. Young urbanites thrive in a city with a large ethnic diversity and variety of lifestyles and where imagination and urban seduction play a vital role(41). From a cultural criminological perspective, spaces of consumption and hedonism, especially in the night economy, are closely intertwined and have great appeal to young people who are chasing the pursuit of the new in "leisure pleasure landscapes"(42). Drugs are catalysts that reinforce transgressive behaviour(43).

Methamphetamine, the great unknown?

Wastewater analysis registers a steep increase in *per capita* methamphetamine consumption after 2014. Nevertheless, in 2019, on a mass basis, methamphetamine consumption is a factor of 4, 10 and 28 lower than MDMA, amphetamine and cocaine, respectively. Furthermore, methamphetamine is up to a factor seven lower than in some other European cities, while Amsterdam's' cocaine and MDMA consumption is among the highest of Europe(44).

Despite of the observed increase of methamphetamine use through wastewater analysis, the Antenna Amsterdam monitor data point to limited methamphetamine use. Methamphetamine use is not often mentioned by panel members and survey respondents, while drug checking services obtain hardly any methamphetamine samples. However, Knoops *et al.* report on increasing methamphetamine use in the gay scene associated to sex parties (chemsex) which agree with the observed trends in wastewater(45). This example illustrates how signals from qualitative research can be verified and quantified using wastewater analysis and how wastewater analysis might trigger panel and targeted survey studies to further explain the observed trends.

Limitations and strengths

Drug consumption of a population is difficult to determine. Surveys enable to correlate consumption of certain drugs with user characteristics such as age, gender, education level, or social setting. Qualitative panel interviews allow to pick up signals and trends of various (trendsetting) user groups associated to specific sociocultural environments (scenes). Public test services provide information on availability, quality / purity and prices of drugs on the streets and enable to evaluate trends(8). Wastewater analysis provides near real time integrated figure on the volume of drug consumed(24, 25). Each of these methods has its own limitations but triangulation of these data sources can be used to evaluate findings.

First, the observed increased consumption over longer timeframes was not observed in panel studies and not clearly linked to survey data, while for MDMA and cocaine correlations were observed with the number of provided test service samples. This information might enable to formulate hypothesis such as increased popularity of the drugs outside panel networks and nightlife settings studied in the survey, thereby directing future research to expand the understanding of the use and users of the drugs.

Second, the analytical sensitivity of wastewater analysis and the fact that it samples the whole population allows it to function as an early warning of consumption of new psychoactive substances(46) or verify rumours or signals from qualitative studies that are not directly supported by survey or test service data. For example, the increased consumption of methamphetamine in Amsterdam reveals trends that were not observed in surveys and test service data.

Third, the combining of quantitative information and temporal variation of total drug use with information on different groups of users and their use habits might allow to provide a rough estimation of the number of users and their quantitative contribution to the total consumption of the city and the consumption dynamics over the days of the week. This data might also be used to distinguish recreational, functional and dependent use and subsequently relate this to, for example, figures on addiction, intoxication, and hospitalization or criminal behaviour, or evaluate harm reduction measures.

Although not all quantitative trends from wastewater analysis can be correlated with quantitative and qualitative data from panel studies, surveys and drug test services and explanations for discrepancies cannot be substantiated by empirical, the current study illustrates that the information is complementary as it enables interpretation and especially helps to formulate hypothesis for further research on both ends. Such a multi angular approach to map the illicit drug situation, combining qualitative and quantitative data on local or regional scale can provide valuable information for public health services.

CREDIT AUTHORSHIP STATEMENT

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript.

Authorship contributions

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Supplemental Information

Chemical analysis and quantification

For all samples from 2011-2016, 50 mL of sample were spiked with a mix of isotope labelled internal standards, vacuum filtered through 1 µm type A/E glass fibre filters, and then SPE extracted with Oasis HLB cartridges (150 mg, 6 cm^3). Cartridges were eluted with methanol and extracts automatically evaporated under a gentle nitrogen stream with a Barkey Optocontrol (Germany). The final extract was reconstituted to 500 µL of 10% methanol aqueous solution. All samples 2017-2019 were analysed by direct injection (without SPE extraction and reconstitution).

Compounds in the sample were separated using a water:methanol gradient (0.05% formic acid) on an XBridge C18 (2.1 × 150 mm; 3.5 µm particle size) column. The compounds were ionized by a Heated Ion Max Electrospray Ionization (HESI) and detected by a linear ion trap (LTQ) FT Orbitrap system, Thermo Electron, Bremen, Germany) that was operated in positive mode. Accurate mass spectra (m/z 100 to 600 Da) operated in full-scan mode were obtained at a resolution of 30,000 ion counts at full width half maximum (FWHM) (m/z 400). When an ion exceeded a pre-set threshold and corresponded to a pre-set target mass list, the instrument switched to product-ion scan mode. Thereby, identification and confirmation were combined in one analysis. All data were acquired and processed by Xcalibur version 2.1 software. Mass calibration was performed prior to every batch run of Polytyrosine-1,3,6 solution ([M + H]+ 182.01170/508.20783 and 997.39781). Identification and quantification were performed using the accurate mass of the protonated molecule within a mass window of 5 ppm. The compounds were identified using external reference standards. For identification both the parent and at least one nominal mass product ion was evaluated.

Table S1: Details on wastewater sampling in wastewater treatment plant Amsterdam-West

year	*Inhabitants in catchment of treatment plant*[A]	*Sampling dates*[B]
2011	*598110*	March 10-14 (N=5)
2012	*606011*	April 17-23 (N=7)
2013	*613043*	March 5-11 (N=7)
2014	*621985*	March 13-19 (N=7)
2015	*630280*	March 4-10 (N=7)
2017	*648071*	March 1-7 (N=7)
2018	*655051*	September 12-18 (N=7)
2019	*661891*	April 3-9 (N=7)

[A] Inhabitants connected to the wastewater treatment plant were calculated from the registered inhabitants in the wastewater treatment plant catchment in 2020 (ref) as and corrected for the (slightly) smaller population in Amsterdam in the previous years. This extrapolation assumes that the growth of the total Amsterdam population is parallel to the growth of the population in the wastewater treatment catchment that many consists of Amsterdam inhabitants ..% but also covers ..% of adjacent municipalities)of from statistical data of the total Amsterdam population

[B] during one week, seven consecutive days 24h composite samples were taken to obtain representative samples of the days of the week. In 2011, five consecutive samples were taken.

Table S2: Purity indicators from Amsterdam drug checking services

	Cocaine powder[A]		Amphetamine powder[B]		MDMA tablet[C]		MDMA powder[D]	
	'real'[E] %	purity % (sd, n)	'real'[E] %	purity % (sd, n)	'real'[E] %	dose mg/tablet (sd, n)	'real'[E] %	purity % (sd, n)
2012	83	65 (13, 104)	40	49 (18, 58)	94	131 (42, 528)	91	73 (8, 44)
2013	81	65 (14, 127)	59	58 (14, 56)	93	148 (42, 666)	93	76 (11, 86)
2014	85	65 (13, 135)	69	59 (14, 52)	94	150 (41, 823)	93	75 (10, 80)
2015	92	66 (14, 193)	62	56 (13, 61)	96	157 (36, 996)	92	76 (11, 64)
2016	94	72 (11, 434)	61	56 (15, 112)	91	164 (37, 1325)	92	77 (7, 142)
2017	93	71 (12, 471)	60	57 (17, 142)	96	168 (36, 1698)	94	77 (6, 154)
2018	93	69 (12, 450)	76	58 (17, 162)	88	174 (35, 1498)	96	78 (7, 269)
2019	93	73 (13, 420)	78	58 (17, 226)	94	179 (42, 2222)	97	79 (3, 349)

[A] 99-100% of the cocaine is presented as powder

[B] 95-99% of amphetamine is presented as powder

[C] 83-93% of MDMA is presented as tablets

[D] 7-16% of MDMA is presented as powder

[E] 'Real' samples consist exclusively or mainly (> 50%) of the respective substance. 'Fake' drugs, consisting mainly of other substances (e.g., caffeine) and dubious samples with unquantified compounds are excluded from the calculation of these purity figures.

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Conflict of interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. The submission is original work and is not under review at any other publication.

Graphical Abstract