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A comparison of trends in wastewater-based data and traditional epidemiological indicators of stimulant consumption in three locations

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ABSTRACT

Aims To compare long-term trends in wastewater data with other indicators of stimulant use in three locations and to test the reliability of estimates based on 1 week of sampling. **Design** Comparison of trends in quantities ('loads') of stimulants or their metabolites in wastewater with trends in other indicators of stimulant use (e.g. treatment, police, population survey data). **Setting and Participants** Populations in Oslo (Norway), South-East Queensland (Australia) and Eindhoven (the Netherlands). **Measurements** Wastewater data were modelled for MDMA (3,4-methylenedioxymethamphetamine), benzoylecgonine (a metabolite of cocaine), amphetamine and methamphetamine in Oslo; benzoylecgonine in Eindhoven; and methamphetamine in South-East Queensland. Choice of stimulants modelled in each region was primarily determined by availability of useable data. **Findings** In Oslo, wastewater data, driving under the influence of drugs statistics and seizure data all suggested increasing MDMA use between 2009 and 2017. In South-East Queensland, there was an estimated 31.1% [95% confidence interval (CI) = 29.4–32.9%] annual increase in daily loads of methamphetamine in wastewater between 2009 and 2016, compared with a 14.1% (95% CI = 10.9–17.3%) annual increase in seizures. Some of the increase in wastewater can be explained by increased purity. In Eindhoven, there was no evidence of a change in cocaine consumption from wastewater, but a reduction was observed in numbers in treatment for cocaine use from 2012 to 2017. In approximately half the cases examined in Oslo, credible intervals around estimates of annual average loads from a regression model versus estimates based on a single week of sampling did not overlap. **Conclusions** Long-term trends in loads of stimulants in wastewater appear to be broadly consistent with trends in other indicators of stimulant use in three locations. Wastewater data should be interpreted alongside epidemiological indicators and purity data. One week of wastewater sampling may not be sufficient for valid inference about drug consumption.

Keywords Bayesian analysis, long-term trends, MDMA, methamphetamine, Oslo, Queensland, sewage epidemiology.

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INTRODUCTION

Analysis of wastewater samples is a novel technique for observing patterns of community drug use [1]. The method, known as 'wastewater-based epidemiology' or WBE, was first used in 2005 to investigate illicit drug use [2] and has become an increasingly popular approach for making inferences about drug consumption in the population.

The approach involves collection of samples of raw sewage from the inlet of a wastewater treatment plant (WWTP), with the flow rate recorded for each sample. The samples are analysed for concentrations of specific drug target residues, which can be measured with great accuracy and precision [3,4]. These concentrations and flow rates are used to estimate daily loads (e.g. in g/day), which are estimates of the total amount of drug target

residue arriving at the treatment plant. These are divided by estimates of the size of the population connected to the WWTP to produce estimated population-normalized daily loads [5,6], i.e. the amount of drug target residue arriving at the treatment plant each day, per 1000 people served by the treatment plant.

An ongoing European multi-city study [7] analyses 1 week of daily wastewater samples each year from many cities across Europe. These data are published by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) as a complementary national indicator of drug consumption [8]. Very few locations with large populations have collected wastewater data over longer time-frames. There has therefore been very limited exploration of how much variation can be expected in wastewater samples over a longer time-period [9] and therefore of how representative any single week might be of 1 year.

No single measure can provide a full picture of regional drug use and current trends [10,11]. A multi-indicator approach is required, incorporating commensurate data such as population surveys and police data [12–20]. Several of the previous comparisons of wastewater data with other indicators of drug consumption have been limited by the single week of sampling issue. In this paper, we examine data from three case-study locations in which more frequent and long-term wastewater data are available.

The specific aims of this study were:

1. to compare long-term trends in loads of stimulant drug target residues in wastewater data with trends in more traditional indicators of stimulant use, in three locations; and
2. to explore whether 1 week of daily wastewater samples, typically undertaken in current surveillance exercises [7], can estimate daily average annual loads with sufficient accuracy.

METHODS

Design

We identified three sites with populations greater than 200 000 people where regular wastewater data and commensurate epidemiological data were available over several years, from which we could compare trends in stimulant use: Oslo (Norway), South-East Queensland (Australia) and Eindhoven (the Netherlands). We focused on four stimulant drug target residues: benzoylecgonine (a metabolite of cocaine [21]), amphetamine, methamphetamine and 3,4-methylenedioxymethamphetamine (MDMA). The choice of locations, and which of the four stimulants to model in each location, was primarily determined by availability of useable data.

We acquired other regional indicators of stimulant consumption that matched the catchment of the WWTPs as closely as possible. Where this was not viable, we obtained national data.

MEASURES

Oslo

We amalgamated eight Oslo wastewater data sets, some of which have been analysed previously, e.g. [22–24]. This includes the 1-week snapshots published by the EMCDDA each year from 2011 to 2017 [8], referred to herein as 'EMCDDA data'. These data sets had not previously been merged and analysed together, allowing long-term trends to be assessed. The combined data covers the period 2009–17 and relates to a WWTP serving approximately two-thirds of the population of Oslo, primarily the western side (approximately 550 000 people). We present the results for MDMA in this paper to provide a contrast to the other case studies. The results for methamphetamine, amphetamine and benzoylecgonine are given in the Supporting information. In total 246 samples were analysed for MDMA, with a median of 24 samples per year (ranging from seven samples per year in 2011 and 2013 to a maximum of 58 samples in 2016).

For each stimulant, we also examined annual numbers of people driving under the influence of drugs (DUI) recorded by the police in Oslo [25] and annual numbers of police seizures [26] in Oslo, Asker and Bærum during the same time-frame. Over similar time-frames, we examined annual national indicators of stimulant use in Norway. This included numbers of positive results from autopsy ([27], personal communications from Gerrit Middelkoop, Oslo University Hospital), numbers of people in treatment [28], prevalence estimates from general population surveys (GPS) and numbers of positive drug tests in prison (Oslo University Hospital).

South-East Queensland

In recent years indicators have consistently evidenced an increase in methamphetamine use in Australia [29–32], whereas indicators of use for other stimulants have been relatively flat [33,34]. In South-East Queensland, we therefore examined data relating to methamphetamine use only.

The wastewater data span the period 2009–17 and relate to a WWTP serving approximately 230 000 inhabitants; 598 daily samples were analysed, with a median of 49 samples per year (ranging from 12 in 2009 to 188 in 2012). Some of the earlier parts of the data set have been reported on previously (e.g. [17,34–37].

We also examined the annual number of methamphetamine seizures in South-East Queensland from 2010 to 2015 [17] and annual numbers of methamphetamine-related hospital admissions, emergency department presentations and psychiatric admissions in the state

(Queensland) from 2010 to 2015/16 [29]. Furthermore, we examined national annual numbers of methamphetamine-related deaths from 2009 to 2015 [32]. We also obtained regional purity data from seizures of methamphetamine in South-East Queensland, provided by the Queensland Health Forensic Chemistry Laboratory and Bruno *et al*. [17]).

Eindhoven

Although 'long-term' wastewater data in Eindhoven have been collected for each drug target residue of interest, direct disposals of unconsumed amphetamine and MDMA contaminated a considerable number of the daily samples [6], potentially indicating nearby production. As the quantity of each drug disposed of in this way is unknown, these could not be considered a reliable indicator of consumption [38,39]. Levels of methamphetamine in wastewater were at an extremely low level throughout the time-span of the data and there were no other indicators of methamphetamine consumption with which to compare. Consequently, we modelled only the benzoylecgonine data. The wastewater data cover the period 2012–17, and are from a WWTP serving an estimated population of 450 300 people in Eindhoven and several surrounding towns and villages. The wastewater data comprise 187 daily samples in total. However, for the years 2012–15 the data are much more limited than for the other two locations, consisting only of 7 days of EMCDDA data (15 days in 2012). In addition to the EMCDDA data from 2016 and 2017, there were consecutive daily samples for approximately 3 months from May–July 2016 and 7 weeks in July–August 2017.

We examined monthly cocaine treatment demand data for the Eindhoven region from 2012 to 2017. More specifically, the data consisted of the total number of people who attended treatment in each month with cocaine as their primary or secondary problem. This data set corresponds to a very similar geographical area to the WWTP catchment area, making comparisons with wastewater data more relevant. We also obtained cocaine-related national annual numbers of recorded DUI offences and deaths from 2013 to 2016 [40].

Statistical analysis

Modelling the wastewater data

We adopted a Bayesian statistical approach, which is well suited to modelling multiple sources of uncertainty and potentially complex hierarchical data structures. We accounted for three sources of sampling uncertainty in estimated population-normalized loads: analytical uncertainty in the concentration measurements, uncertainty in the daily flow estimates and uncertainty in the estimated population size served by the WWTP [41]. These were determined by the authorship team to be the important sources of sampling variability when considering long-term trends. We extended the approach previously described [41] to a hierarchical log-linear regression modelling approach, in which we further accounted for three sources of temporal variation:

1. systematic differences in daily population-normalized loads by day of the week;
2. differences in monthly average population-normalized loads. We fitted three alternative models to these monthly averages on the log scale:
   i. annual effects model: step change by calendar year
   ii. annual and quarterly effects model: step change by year and by quarter of the year
   iii. linear trend model: linear regression on month since first sample; and
3. an additional amount of random daily variation around the fitted trend line within each month (assumed constant).

A log-linear modelling approach was used due to positive skewness in the data and to prevent negative fitted values. The basic functional form of the model was decided a priori, based on previous evidence and consideration of the characteristics of the data. For example, systematic differences in loads by day of the week are well established in the literature [9,23,37]. Pragmatic decisions had to be made concerning modelling of systematic changes over time [models (i) to (iii) above] due to limited data availability: for example, there were insufficient data to include 'month' effects or year × quarter interaction terms in model (ii). Model (iii) was fitted specifically to facilitate comparison of long-term trends with other indicators through estimated gradients.

Models were fitted in WinBUGS [42], using all the available wastewater data. The deviance information criterion (DIC) [43] was used to compare the fit after penalizing for complexity of models (i) to (iii). This is a Bayesian generalization of the Akaike information criterion, with models with lower DIC values preferred. In the Results section, for each stimulant and location we display annual estimates based on model (iii) and the best-fitting models (i) and (ii).

More information about the regression models and the assumptions made about uncertainties in the concentration, flow and population size parameters in each location is provided in the Supporting information, S1.

Analysis of other regional and national indicators of stimulant use

Data such as annual or monthly numbers of seizures, hospital admissions, positive autopsy results, numbers in treatment and recorded offences for DUI were analysed using Poisson regression models, with time (year or month) as a covariate. A logistic regression model with

year as a covariate was fitted to annual prevalence data from population surveys. These simple models were fitted as rough approximations only, to facilitate comparison of overall trends with the wastewater data. These analyses were performed in R.

Comparison of trends

We estimated annual percentage changes in population-normalized loads of stimulants in wastewater [based on model (iii) above] and in other indicators of stimulant consumption based on the regression models with time as a covariate. We compare these percentages with caution, as we would not anticipate changes in total population consumption to manifest in the same way across indicators. For example, a doubling in total consumption would not necessarily lead to a doubling of number of individuals in treatment.

Purity-adjustment in South-East Queensland

Seizure data indicate that methamphetamine purity in South-East Queensland varied considerably across the wastewater sampling period [17]: increasing substantially from approximately 12.7% [95% confidence interval (CI) = 9.6–15.9%] purity in 2009 to 68.8% (95% CI = 67.2–70.3%) in 2015, then decreasing slightly to 60.8% (95% CI = 57.7–64.0%) in 2017. To explore the potential impact of this, we produced purity-adjusted annual population-normalized loads of methamphetamine by dividing annual estimates from the best-fitting of our wastewater models by estimated percentage purity. Our simulations-based modelling approach provides estimates with 95% credible intervals (CrIs) that account for uncertainty in estimates of percentage purity, in addition to the sources of uncertainty described above.

Comparison of annual daily averages from EMCDDA data and non-EMCDDA data

In Oslo and Eindhoven (which both contribute data to the annual EMCDDA estimation exercise), we compared results from EMCDDA and non-EMCDDA data for years in which there were 21 or more wastewater samples in addition to the EMCDDA data. We compared the following two estimates of average daily population-normalized loads in each year:

1 based on analysis of the 1 week of EMCDDA data per year in isolation, accounting for uncertainty in concentration, flow and population parameters [41]; and
2 based on the best-fitting of the three regression models above, applied to all available wastewater data *except* for the EMCDDA data. EMCDDA data were removed here to avoid biasing the comparison in favour of agreement.

We note that comparisons could only be made in Eindhoven for benzoylecgonine in 2016 and 2017, where data were available only for March to August in each year. We also compared the EMCDDA-based estimates with estimates based on any other 7-day consecutive period of sampling in the same year.

RESULTS

MDMA use in Oslo

Recorded numbers of DUI MDMA offences and police seizures in Oslo increased annually on average over the time-frame of the data (Table 1, Fig. 1). At the national level, there was also an increase in estimated prevalence of use and in annual numbers of positive results from autopsy and prison data (Table 1, Fig. 1).

Daily population-normalized loads of MDMA in wastewater (Fig. 2a) show a very large amount of variability, even among samples taken close together in time. This is particularly evident in 2014, where estimates range from 1.7 to 170.7 mg/day per 1000 people. Also plotted are the estimated daily average population-normalized loads for each year, based on models (i) and (iii). From model (iii), average daily population-normalized loads are estimated to have increased over time (Table 1), but model (i) has a slightly better fit to the data (Table 2): this estimates a general increasing trend, but with some evidence of a peak in 2015 and extremely low values in 2011.

Part of the observed variability in wastewater loads is due probably to variation by day of the week: as shown in Fig. 2b, there is evidence of loads being higher on average on weekends versus weekdays.

Use of other stimulants in Oslo

Long-term trends in methamphetamine measured in wastewater generally agreed with trends in other indicators of methamphetamine use in Oslo and Norway, all of which decreased during the time-frame of the wastewater data. There were no clear long-term trends in wastewater

Table 1 Estimated average annual percentage change (with 95% confidence intervals) in regional (R) and national (N) indicators of MDMA use in Oslo/Norway.

Indicator	*MDMA*
Wastewater (R)	55.1% (47.8, 62.8%)
Number of recorded DUI (R)	35.4% (22.2, 50.0%)
Number of police seizures (R)	49.2% (36.4, 63.3%)
Number of positive autopsy results (N)	45.4% (26.9, 66.6%)
Number of positive results in prison (N)	47.2% (34.0, 61.8%)
Prevalence (N)	39.5% (13.1, 72.0%)

MDMA = 3,4-methylenedioxymethamphetamine; DUI = driving under the influence of drugs.

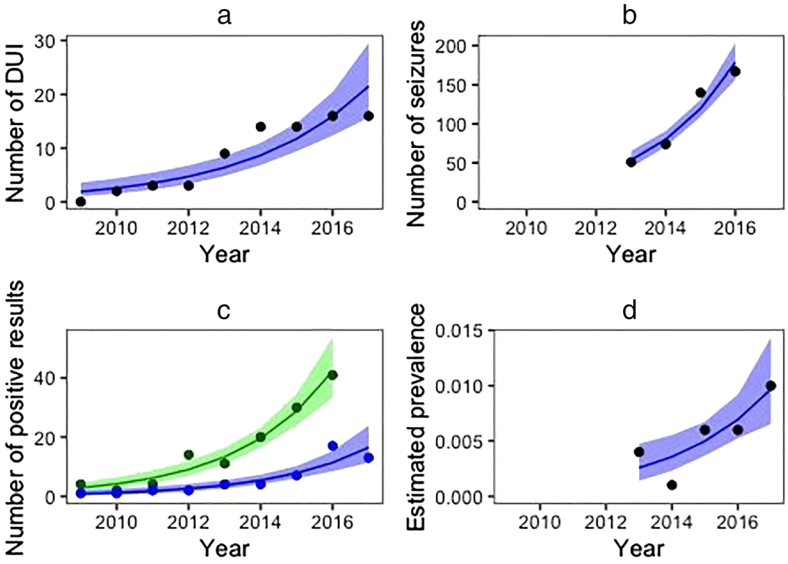

Figure 1 (a,b) Regional (Oslo) data; (c,d) national (Norway) data. Number of recorded driving under the influence offences (a), seizures* (b), positive results from autopsy (c, blue) and prison (c, green) data for 3,4-methylenedioxymethamphetamine (MDMA) from 2009 to 2017: observed data and Poisson log-linear trends with 95% confidence intervals (CIs). (d) Estimated prevalence of MDMA use in Norway among 15–64-year-olds* based on general population surveys (GPS) data and logistic regression with 95% CIs (blue). *Data were available for 2013 to 2016/17 only. [Colour figure can be viewed at wileyonlinelibrary.com]

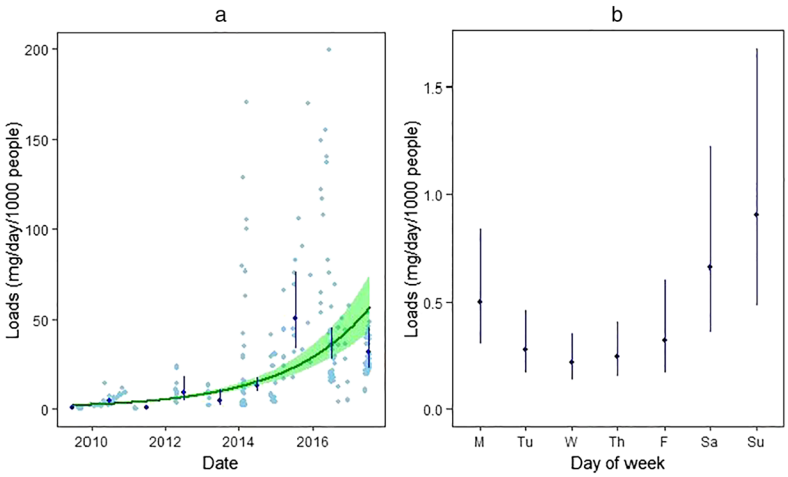

Figure 2 (a) Estimated daily population-normalized loads of 3,4-methylenedioxymethamphetamine (MDMA) in wastewater in Oslo 2009 to 2017 (light blue), with estimated averages for each year from the annual effects model (dark blue) and a trendline for the log-linear model (green), with 95% credible intervals (CrIs). (b) Estimated daily population-normalized loads of MDMA in wastewater by day of the week with 95% CrIs, calibrated to 2009. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 2 Deviance information criterion (DIC) comparison between wastewater regression models fitted to each location (and drug target residue). pD is a measure of complexity of the model, $\overline{D}$ is the posterior mean of the deviance and DIC = pD + $\overline{D}$. The best-fitting model after penalizing for complexity (model with the lowest DIC) for each location is indicated in bold type.

	Oslo (MDMA)			*SE Queensland (methamphetamine)*			*Eindhoven (benzoylecgonine)*		
	$\overline{D}$	*pD*	*DIC*	$\overline{D}$	*pD*	*DIC*	$\overline{D}$	*pD*	*DIC*
Model (i): annual effects	**394.9**	**148.0**	**542.9**	−184.4	137.7	−46.7	**−68.1**	**78.7**	**10.6**
Model (ii): annual and quarterly effects	394.6	155.4	550.0	**−178.2**	**99.8**	**−78.4**	−68.2	80.9	12.7
Model (iii): linear trend	394.3	154.6	548.9	−187.0	228.7	41.7	−69.1	111.7	42.6

MDMA = 3,4-methylenedioxymethamphetamine.

(or other indicators) for amphetamine or cocaine use. Full results for these other stimulants are provided in Supporting information, S2.

Methamphetamine use in South-East Queensland

All indicators of methamphetamine use at regional, state and national level suggested increasing use during the time-frame of the data (Table 3, Fig. 3).

The crude (unadjusted for purity) wastewater data (Fig. 4a) are consistent with a large increase in methamphetamine use from 2009 to 2016. There was also evidence of systematic variation by day of the week (Fig. 4b). Model (iii) estimates an average annual increase in daily population-normalized loads between 2009 and 2017 (Table 3). However, this linear trend model does not fit the data well (Table 2), due to strong evidence of a reduction in loads between 2016 and 2017. The more flexible model (ii) fits the data more accurately (Table 2) and estimates a 32.3% (95% CrI = 22.3–41.1%) reduction in average daily loads between these 2 years. As data from the other indicators examined are not yet available for 2017, it is not possible to ascertain whether the recent reduction according to the wastewater data is reflected in other indicators.

Estimates of the purity of methamphetamine in South-East Queensland between 2009 and 2017 are shown in the Supporting information, S1.3. After adjusting for changes in purity, the estimated trend looks quite different (Fig. 4a, red). Purity-adjusted estimates varied less across years (estimated 2.4-fold variation across annual estimates versus ninefold prior to adjusting for purity). As indicated on the plot, the total amount of (impure) methamphetamine consumed by the population may have actually reduced in 2012 and 2013 relative to 2010, subsequently rising again, with a large peak in consumption in 2016

Cocaine use in Eindhoven

There was an overall reduction in the number of people attending treatment in Eindhoven with cocaine as their primary or secondary problem between 2012 and 2017 (Table 4, Fig. 5a, although we note the large amount of overdispersion around the fitted trend line). In contrast, nationally there was an increase in numbers of recorded DUI offences per year and recorded cocaine-related deaths (Table 4, Fig. 5b).

The daily averaged population-normalized loads of benzoylecgonine plotted in Fig. 6a show a very large amount of variability, even among samples taken close together in time, and no clear temporal trend. Model (iii) provided little evidence of change over time (Table 4), but model (i) fitted the data much better (Table 2) and gave strong evidence of a reduction in daily loads on average between 2016 and 2017. There is evidence of a delayed

Table 3 Estimated average annual percentage change (with 95% confidence intervals) in regional (R), state (S) and national (N) indicators of methamphetamine use in South-East Queensland/Queensland/Australia.

Indicator	*Methamphetamine*
Wastewater (R)	31.1% (29.4, 32.9%)
Number of police seizures (R)	14.1% (10.9, 17.3%)
Number of hospital admissions (S)	63.3% (61.0, 65.7%)
Number of emergency department presentations (S)	39.6% (37.1, 42.1%)
Number of psychiatric admissions (S)	71.3% (66.0, 76.7%)
Numbers of methamphetamine-related deaths (N)	13.1% (10.4, 15.9%)

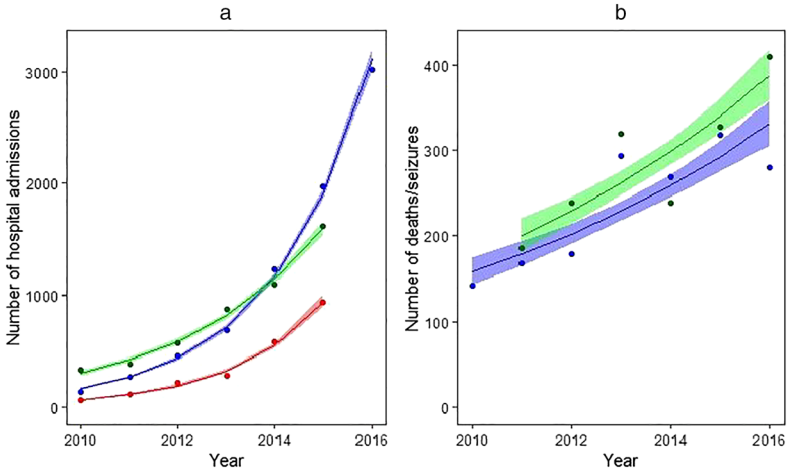

Figure 3 (a) Numbers of methamphetamine-related hospital admissions (blue), emergency department presentations (green) and psychiatric admissions (red) in Queensland from 2010 to 2016, with fitted Poisson log-linear trends and 95% confidence intervals (CIs). We note that there is some overlap between hospital admissions and emergency department presentations [29]. (b) Number of seizures (green) in South-East Queensland from 2010 to 2015 and number of methamphetamine-related deaths (blue) in Australia from 2009 to 2015, with fitted Poisson log-linear trends and 95% CIs. [Colour figure can be viewed at wileyonlinelibrary.com]

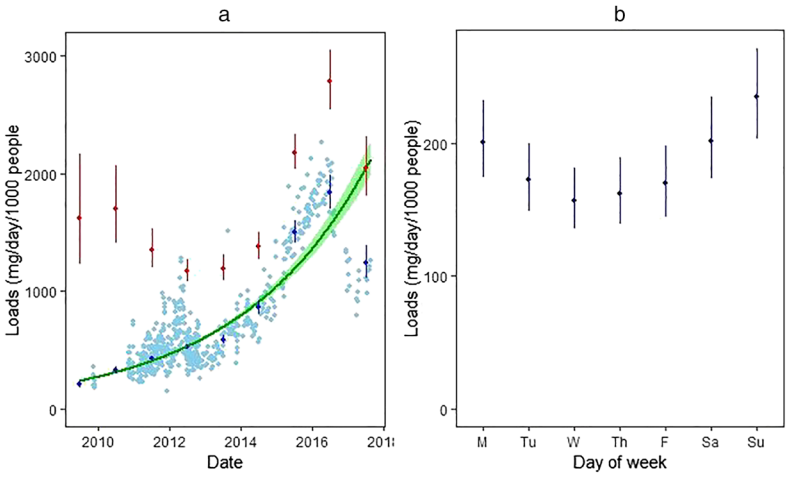

Figure 4 (a) Estimated daily population-normalized loads of methamphetamine in wastewater in the South-East Queensland region from 2009 to 2017 (light blue), with estimated averages for each year from the annual and quarterly effects model (dark blue) and a trendline for the log-linear model (green), with 95% credible intervals (CrIs). Purity-adjusted estimated yearly averages are displayed in red with 95% CrIs. (b) Estimated daily population-normalized loads of methamphetamine in wastewater by day of the week, with 95% CrIs calibrated to the first quarter of 2009. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 4 Estimated average annual percentage change (with 95% confidence intervals) in regional (R) and national (N) indicators of cocaine use in Eindhoven/the Netherlands.

Indicator	*Cocaine*
Wastewater (R)	1.9% (−1.0, 4.9%)
Treatment demand—primary (R)	−7.8% (−8.6, −6.9%)
Treatment demand—secondary (R)	−12.3% (−13.1, −11.6%)
Numbers of recorded DUI (N)	16.8% (9.2, 25.1%)
Number of recorded cocaine-related deaths (N)	20.4% (2.8, 41.1%)

DUI = driving under the influence of drugs.

weekend effect (Fig. 6b): the WWTP has advised us that this is due probably to the retention time in the system prior to reaching the treatment plant.

Estimating annual loads from 1 week of sampling

Estimates of annual average daily wastewater loads based on EMCDDA and non-EMCDDA data are displayed for Oslo in Fig. 7. The two sets of credible intervals (red versus green) did not overlap in approximately 50% of the cases. Furthermore, the credible intervals from the EMCDDA data (red) did not overlap with other weekly averages from the same year (blue) in approximately 40% of the cases. For Eindhoven, in 2016 and 2017 the EMCDDA versus non-EMCDDA-based credible intervals overlapped (see Supporting information, Fig. S3.1, Appendix S3).

DISCUSSION

Main findings

In Oslo, long-term trends in wastewater data were broadly consistent with evidence from more traditional epidemiological indicators: in particular, suggesting an increase in MDMA use between 2009 and 2017. Loads of methamphetamine in wastewater increased drastically in South-East Queensland between 2009 and 2016, consistent with large increases observed in numbers of methamphetamine-related deaths, hospital admissions and seizures. Observed increases in methamphetamine

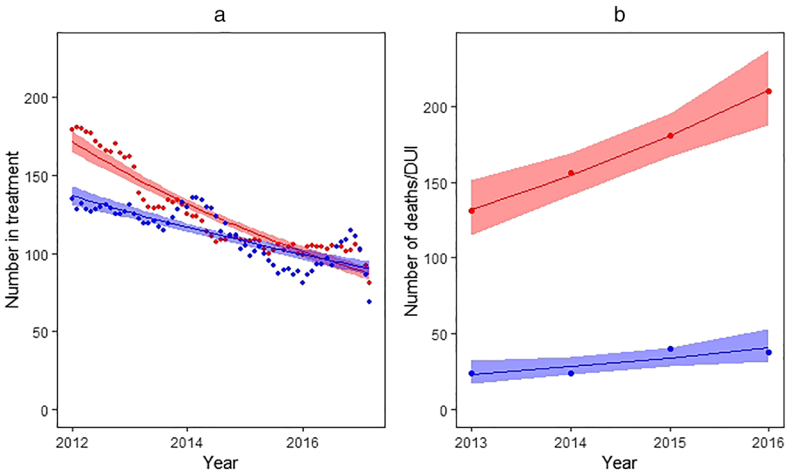

Figure 5 (a) Total number of people attending treatment in each month with cocaine as their primary problem (blue) or secondary problem (red) in the Eindhoven region from 2012 to 2017: observed data and fitted Poisson log-linear trend, with 95% confidence intervals (CIs). (b) Annual numbers of driving under the influence of drugs (DUI) (red) and deaths (blue) due to cocaine in the Netherlands from 2013 to 2016. [Colour figure can be viewed at wileyonlinelibrary.com]

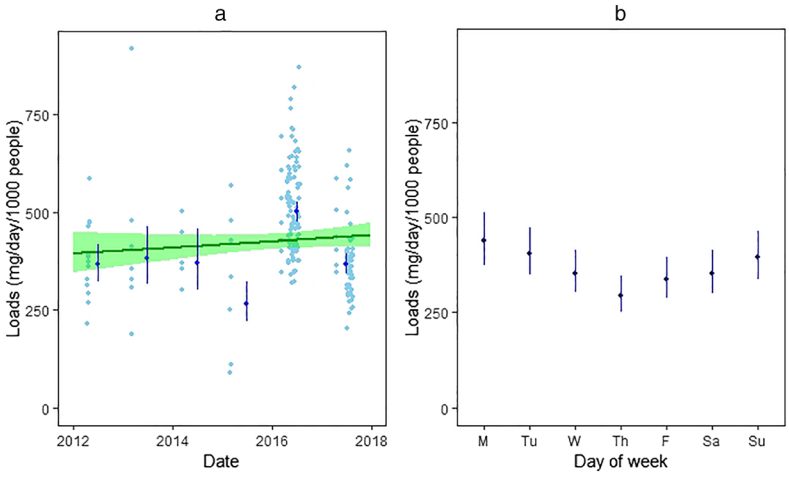

Figure 6 (a) Estimated daily population-normalized loads of benzoylecgonine in wastewater in Eindhoven from 2012 to 2017 (light blue), with estimated averages from the annual effects model (dark blue) and a trendline for the log-linear model (green), with 95% credible intervals (CrIs). (b) Estimated daily population-normalized loads of benzoylecgonine in wastewater by day of the week, with 95% Cr Is calibrated to 2012 [Colour figure can be viewed at wileyonlinelibrary.com]

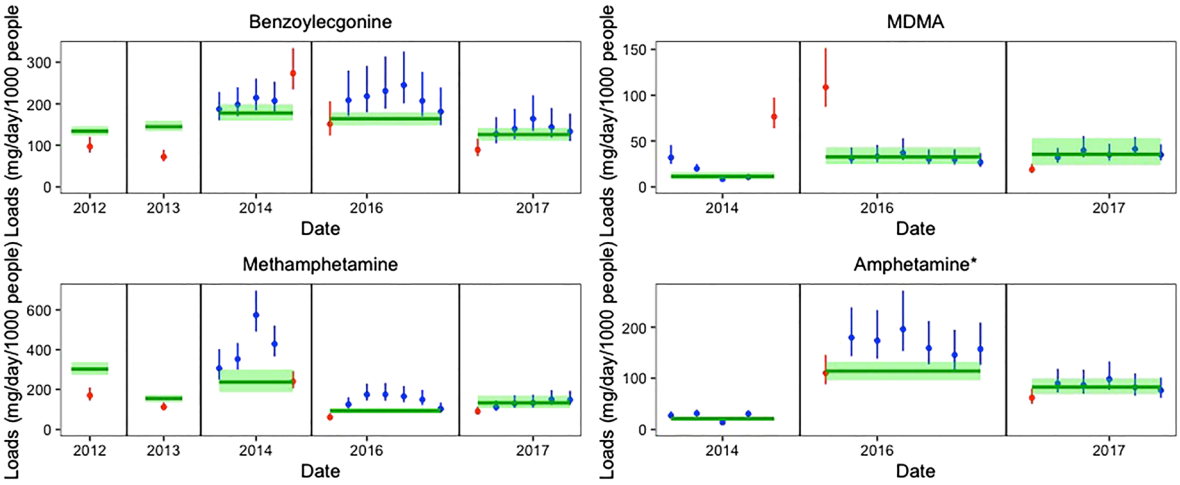

Figure 7 Estimates of average daily wastewater loads per year in Oslo from European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) data (red) versus non-EMCDDA (green) and all other weekly averages from the same year (blue) with 95% credible intervals (CrIs), for benzoylecgonine, 3,4-methylenedioxymethamphetamine (MDMA), methamphetamine and amphetamine. *There were no EMCDDA data (red) for amphetamine in 2014, but there were other 7-day consecutive periods of sampling in 2014 (blue). [Colour figure can be viewed at wileyonlinelibrary.com]

loads in wastewater appear to be partly driven by changes in purity, which may also be an important driver of increases in methamphetamine-related harms (hospital admissions and deaths). In Eindhoven, where the wastewater data are much more sparse in time, wastewater data did not evidence a clear trend in cocaine consumption, whereas there was a large reduction in treatment demand for cocaine problems during the same time-period.

Throughout all three locations that we studied, there was a large amount of variability in daily population-normalized loads of stimulants in wastewater. Although some of this variability can be explained by weekend effects (particularly for MDMA), there was clear residual variation beyond this. One or two weeks of wastewater sampling can raise hypotheses concerning differences in drug use by geographical area. However, based on our comparisons of estimates based on only 7 days ('EMCDDA data') and estimates based on longer-term sampling in Oslo and Eindhoven, we cannot be confident that inferences based on only 1 week are robust.

Strengths and limitations

We compared long-term trends in wastewater data with other indicators of stimulant use in three locations during a time-frame of up to 9 years, much longer than previous studies. We developed and applied a Bayesian hierarchical regression model that allows for uncertainty in concentration, flow and population parameters and also multiple sources of temporal variation in loads. We fitted log-linear or linear trend models as approximations for all indicators to facilitate comparison of long-term trends across data sets. We compared fit with some slightly more flexible models for the wastewater data, but not for the other

indicators, such that estimated coefficients (Tables 1, 3 and 4) should be interpreted with caution. The linearity assumption was clearly violated in some specific instances (e.g. Supporting information, Fig. S2.3: seizures and prison data).

We note that it was difficult to identify suitable locations for this study, as there are few wastewater data sets with more than 1–2 weeks of samples per year over a number of years. Further, wastewater data generally relate to a local level (city, or some fraction of a city served by a particular treatment plant), for which other indicators of stimulant use are not necessarily available. We therefore had to use national data to compare trends of some indicators with wastewater data; these comparisons should be treated with caution, as it is difficult to assess how representative these selected cities are for the country as a whole. In addition, other indicators are often available only as annual counts and are not always stimulant-specific. We also acknowledge that epidemiological data also can give uncertain, incomplete and biased perspectives on drug use trends in the population—but we lacked sufficient information to identify and adjust for inconsistencies in the evidence. For example, information was not available on levels of police activity, changes in which could affect trends in DUI and/or seizure data. We could not adjust wastewater loads for purity in Oslo or Eindhoven, as regional purity data were not available.

Estimated population-normalized loads of drug target residues in wastewater will be biased if inaccurate population size estimates are used in the standardization. We used population-size estimates provided by the WWTPs, usually based on census data. The level of uncertainty that we allowed for in these estimates (see Supporting information, S1) may not be sufficient to allow for the bias. More accurate estimates of the size of the population served by a WWTP could be obtained through mobile phone, ammonia or biomarker data [35,44–46]. Future research should continue to investigate cost-effective approaches to accurately estimate *de-facto* population size, to minimize the use of inaccurate census-based estimates in wastewater calculations.

Comparison with other evidence

Other studies that have used a multi-indicator approach [12–20] have also found a general agreement between trends in drug target residues in wastewater and trends in other indicators of drug consumption. Our study was conducted over a much longer time-frame and accounts for multiple sources of uncertainty, such as the concentration measurements, the daily flow estimates and the estimated population sizes, through our Bayesian hierarchical regression model.

Our finding that 1 week of wastewater sampling may not be sufficient is in agreement with the study of Ort *et al.* [9], which presented an analysis of 1369 consecutive days of sampling in a German village with approximately 7160 inhabitants. They reported an approximate 60% relative error in estimates of annual means based on any 1 week of samples [9]. To date, no formula has been derived to determine the minimum number of samples required for robust inference across all scenarios.

Bruno *et al.* [17] noted that changes in purity of methamphetamine may be a key driver of observed increases in loads in wastewater in South-East Queensland, which we extended to provide purity-adjusted estimates over a longer time-period. We included new data which show that both purity and wastewater loads of methamphetamine in South-East Queensland have very recently reduced. It will be interesting to see whether such a reduction is later reflected in other indicators of use and harm and, if so, how much of a time lag there is before such a reduction can be detected from other time–series data. We note that analysis of Finnish data has previously suggested that wastewater analysis could provide an 'early warning' of changes in drug consumption, before such changes are evident from other indicators [18].

Implications

Changes in street purity could be a key driver of observed changes of drug target residues in wastewater and, indeed, of changes in other indicators of use. Where possible, trends in purity data should be assessed and, if appropriate, adjusted for.

Further research is required to determine the minimum sampling period for wastewater data to be meaningful as an annual indicator of drug consumption. The issue is complicated by the fact that this will vary by the prevalence and frequency of drug use in the population studied and the ratio of episodic to dependent use [47], in addition to the drug target residue (due to varying excretion profiles) and the size of the population served by the WWTP [9].

With regular, long-term sampling, wastewater data could reliably estimate the direction of trends in stimulant use. However, while the current focus is on much sparser sampling, it is unlikely that wastewater data will be robust enough to be the sole information on consumption trends. Further, local information (e.g. on purity and patterns of use) is required to interpret the evidence. Our case study in Eindhoven illustrated the difficulty in assessing long-term trends with sparse wastewater data and few other regional indicators of stimulant consumption. For robust comparisons of wastewater data with other indicators, sampling should be targeted at locations known to have commensurate epidemiological data on drug use and

where other indicators of stimulant use can be mapped approximately to the catchment of the WWTP.

Declaration of interests

None.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.