Addiction

METHODS AND TECHNIQUES

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Can cocaine use be evaluated through analysis of wastewater? A nation-wide approach conducted in Belgium

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ABSTRACT

Aims Cocaine is the second most-used illicit drug world-wide and its consumption is increasing significantly, especially in western Europe. Until now, the annual prevalence has been estimated indirectly by means of interviews. A recently introduced and direct nation-wide approach based on measurements of the major urinary excreted metabolite of cocaine, benzoylecgonine, in wastewater is proposed. **Design** Wastewater samples from 41 wastewater treatment plants (WWTPs) in Belgium, covering approximately 3 700 000 residents, were collected. Each WWTP was sampled on Wednesdays and Sundays during two sampling campaigns in 2007–08. Samples were analysed for cocaine (COC) and its metabolites, benzoylecgonine (BE) and ecgonine methylester (EME) by a validated procedure based on liquid chromatography coupled with tandem mass spectrometry. Concentrations of BE were used to calculate cocaine consumption (g/day per 1000 inhabitants) for each WWTP region and for both sampling campaigns (g/year per 1000 inhabitants). **Findings** Weekend days showed significantly higher cocaine consumption compared with weekdays. The highest cocaine consumption was observed for WWTPs receiving wastewater from large cities, such as Antwerp, Brussels and Charleroi. Results were extrapolated for the total Belgian population and an estimation of a yearly prevalence of cocaine use was made based on various assumptions. An amount of 1.88 tonnes (t) per year [standard error (SE) 0.05 t] cocaine is consumed in Belgium, corresponding to a yearly prevalence of 0.80% (SE 0.02%) for the Belgian population aged 15–64 years. This result is in agreement with an earlier reported estimate of the Belgian prevalence of cocaine use conducted through socio-epidemiological studies (0.9% for people aged 15–64 years). **Conclusions** Wastewater analysis is a promising tool to evaluate cocaine consumption at both local and national scale. This rapid and direct estimation of the prevalence of cocaine use in Belgium corresponds with socio-epidemiological data. However, the strategy needs to be refined further to allow a more exact calculation of cocaine consumption from concentrations of BE in wastewater.

Keywords Belgium, benzoylecgonine, cocaine use, national survey, prevalence, wastewater, sewage epidemiology.

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INTRODUCTION

Cocaine (COC) is used illegally by various administration routes (e.g. intranasally, intravenously or by smoking) [1] and has important actions in humans: direct blocking of fast sodium channels, interference with the reuptake of neurotransmitters such as epinephrine, serotonin and dopamine and vasoconstriction of blood vessels [2,3]. Moreover, it has direct important physiological effects on the human body such as central nervous system stimulation, risk of cardiac syndromes, pulmonary complications, altered serotonin levels and addiction [4–6]. In humans, COC is hydrolyzed rapidly to benzoylecgonine (BE) and ecgonine methyl ester (EME) and degradated further into some minor metabolites [3]. Only a small fraction of COC is excreted in urine as the parent compound, while the largest amount is excreted as BE, the most important metabolite, and EME [7–9].

In 2007, the United Nations Office on Drugs and Crime (UNODC) estimated that 16 million people worldwide, corresponding with 0.4% of the population aged 15–64 years, have used cocaine [10]. Since 2005 cocaine use has increased significantly in western Europe, especially in recreational settings and among young people (aged 15–34 years), resulting in the fact that cocaine is now the second most-used illicit drug after cannabis [10–12]. The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) estimated that approximately 4.5 million European residents aged 15–64 (1.3%) used cocaine in 2007; in Italy, Spain and the United Kingdom the prevalence of last-year cocaine use was higher than 2% [11]. In Belgium, only limited information is available about cocaine consumption [13]. Based on existing prevalence data from the surrounding countries, the UNODC estimated in 2004 an annual prevalence of 0.9% for Belgians aged 15–64 [14].

The trends in cocaine use are derived from population surveys, consumer interviews, individual medical records and crime statistics [15]. These are subjective and indirect indicators, and a more precise estimate of cocaine use is not always feasible with this approach because surveys and interviews with consumers themselves often do not represent their true cocaine use [16]. Furthermore, such studies cannot be executed in a short period of time, and the studied population is not always representative for a complete region or country.

Zuccato *et al.* [16] proposed a more direct and objective method of evaluating cocaine consumption, based on the measurement of urinary excreted cocaine and its metabolites in wastewater, collected when it enters the wastewater treatment plants (WWTPs) [16]. Several papers have been published since then, assessing wastewater analysis for illicit drugs from different perspectives [17–24]. In the present study, we investigated if this real-time and in-field approach (Fig. 1) can be applied to estimate cocaine use, not only at a local scale but now also nation-wide. Furthermore, we compared the calculated estimates of cocaine use with previously published socio-epidemiological data of cocaine consumption to demonstrate the potential of the wastewater approach.

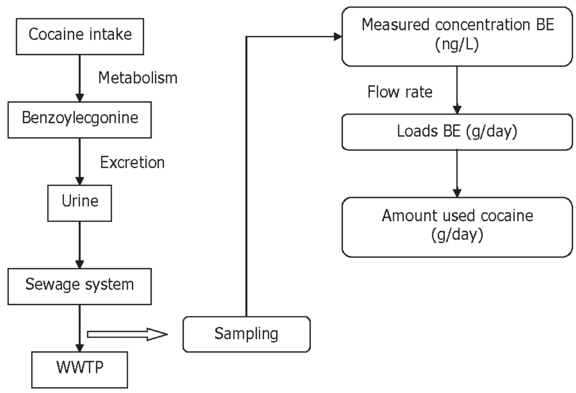

Figure 1 Schematic overview of the wastewater approach. WWTP: wastewater treatment plant; BE: benzoylecgonine

METHODS

Sample collection

Influent wastewater samples were collected from 41 WWTPs across Belgium. Sampling was executed with 24-hour flow-dependent automatic samplers. These devices mix hourly a well-defined aliquot of influent wastewater in a glass bottle, depending on the flow rate of the water stream. This procedure is repeated during the whole day and, as a consequence, a sample representative for 24 hours is acquired. Two samples were collected for each WWTP, one at the weekend (Sunday) and one during the week (Wednesday), to evaluate differences in cocaine use during the week. Two sampling periods, one in the summer of 2007 (sampling campaign I, SC I) and one in the winter of 2007–08 (sampling campaign II, SC II), were included in the study. For two WWTPs (Lier and Tessenderlo), we could collect samples only in sampling campaign II because of logistical problems. The 41 WWTPs were chosen based on the amount of residents they serve (>10 000) and on their geographical location, so that a general idea of the cocaine consumption in Belgium could be given. These WWTPs cover approximately 3 700 000 inhabitants (~35% of the total Belgian population). After collection, water samples were stored at pH 2 and at −20°C to prevent degradation of COC, BE and EME between collection and analysis [18].

Sample analysis

Concentrations of COC, BE and EME in wastewater samples were measured following a previously validated procedure [18]. Samples (100 ml) were filtered over a glass filter, followed by a concentration and purification step with solid-phase extraction (SPE) on Oasis HLB® cartridges (Waters, Milford, MA, USA) and centrifugation. The resulting extract (100 µl) was then analysed for COC, BE and EME with an Agilent 1100 series high-pressure liquid chromatography system coupled to an Agilent 1100 Series MSD ion trap mass spectrometer (Palo Alto, CA, USA) with electrospray ionization (ESI) operating in positive ionization model. The results were processed with an HP Chemstation for MS control and spectral processing (Palo Alto, CA, USA). Quantification was performed with deuterated internal standards (COC-d_3, BE-d_3 and EME-d_3) using multi-level calibration curves. Quality control has been described in detail previously [18,24], but in summary consisted of the analysis of a procedural blank and a spiked water sample with each batch of seven samples. The recoveries for COC, BE and EME in all spiked samples were within the control limits of 3 × standard deviations (SD). Limits of quantification (LOQ) were 1 ng/l, 0.5 ng/l and 20 ng/l for COC, BE and EME, respectively.

Calculations

Because EME was undetectable in all water samples (<20 ng/l) and COC is proven to be not stable in water [18], only the measured BE concentrations (in ng/l) were used to back-calculate into an amount of used cocaine (in g/day). Moreover, BE is stable in water [18] and it is the major metabolite of COC. For this back-calculation, several parameters need to be known: (i) the flow rate of the wastewater stream (litres/day) to transform concentrations of BE (ng/l) into mass loads (expressed in g/day); (ii) the relative amount of a cocaine dose excreted as BE to make a back-calculation from mass loads into a total amount of used COC (in g); (iii) the molecular masses of COC and BE; and (iv) the number of inhabitants that are served by a WWTP.

Calculations are thus based on BE concentrations in wastewater, using an already reported formula [16]: cocaine (g/day) = BE (ng/l) × flow rate (l/day) × 2.33. The 2.33 factor results from the different molecular masses of COC and BE (303 g/mol and 289 g/mol) and from the fact that a cocaine dose is excreted on average for 45% as BE [7–9].

Statistical analysis

Statstical analysis was performed with SPSS software version 15 for Windows (SPSS, Inc., Chicago, IL, USA). Values are given as an arithmetic mean with a standard error (SE) or with a 95% confidence interval (95% CI). The Kolmogorov–Smirnov algorithm was used to determine whether each variable had a normal distribution. The parametric paired Student's t test and the non-parametric Wilcoxon signed-rank test were used for evaluating measurements of the same variable (cocaine consumption) at different time-points (sampling campaigns I and II, Sunday and Wednesday).

RESULTS

Table 1 and Fig. 2 summarize the cocaine consumption of all WWTPs for the four different sampling events. Figure 3 shows the geographical distribution of the calculated amount of cocaine that is consumed for the Sunday samples from 41 WWTP regions in Belgium in sampling campaign II (in g/day per 1000 inhabitants). The raw data used to calculate cocaine consumption for the wastewater samples presented in Fig. 3 are shown in Table 2. A statistically significant increase in cocaine consumption of 0.12 g/day per 1000 inhabitants during the weekend (95% CI 0.07–0.18, $P < 0.0001$) is observed when the amount of cocaine used on a Sunday (weekend day) is compared with the amount used on a Wednesday (weekday). This trend of higher cocaine use during weekends is present in both separate sampling campaigns (SC I: 0.07 g/day per 1000 inhabitants, 95% CI 0.01–0.13, $P = 0.046$; SC II: 0.18 g/day per 1000 inhabitants, 95% CI 0.09–0.27, $P < 0.0005$). There is no statistically significant difference in cocaine consumption between the Sunday samples from each sampling campaign ($P = 0.062$); nor does the cocaine consumption calculated for the Wednesday samples from SCs I and II differ ($P = 0.203$).

The highest level of cocaine use is observed in both Sunday samples from WWTP Antwerp South (1.83 g/day per 1000 inhabitants), which receives wastewater mainly from the centre of Antwerp. Other high values are found for WWTPs receiving wastewater from other large cities such as Charleroi (0.86 g/day per 1000 inhabitants

Table 1 Summary of cocaine consumption estimates for the 41 wastewater treatment plant regions in Belgium.

	Sunday I (g/day per 1000 inh)	*Wednesday I (g/day per 1000 inh)*	*SC I (g/year per 1000 inh)*	*Sunday II (g/day per 1000 inh)*	*Wednesday II (g/day per 1000 inh)*	*SC II (g/year per 1000 inh)*
Mean	0.46	0.39	148.19	0.53	0.35	145.60
Median	0.36	0.27	108.32	0.45	0.30	116.81
SE	0.05	0.05	17.30	0.06	0.03	13.49
95% CI	0.35–0.56	0.29–0.49	113.10–183.28	0.40–0.64	0.28–0.42	117.41–172.10
Range	0.04–1.83	0.09–1.27	42.81–520.17	0.05–1.83	0.05–0.84	20.30–391.70

SC: sampling campaign; I: sampling campaign during summer 2007; II: sampling campaign during winter 2007–08; inh = inhabitants; SE: standard error; CI: confidence interval.

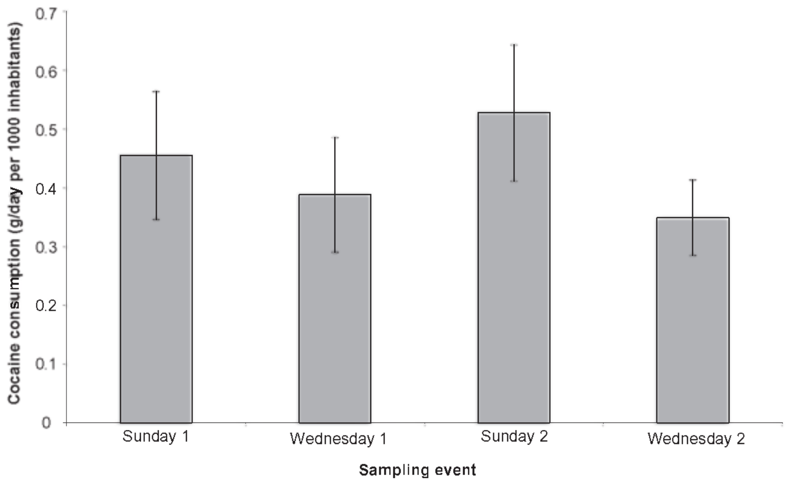

Figure 2 Average cocaine consumption for the four sampling events (1 = summer 2007, 2 = winter 2007–08). Error bars represent 95% confidence intervals

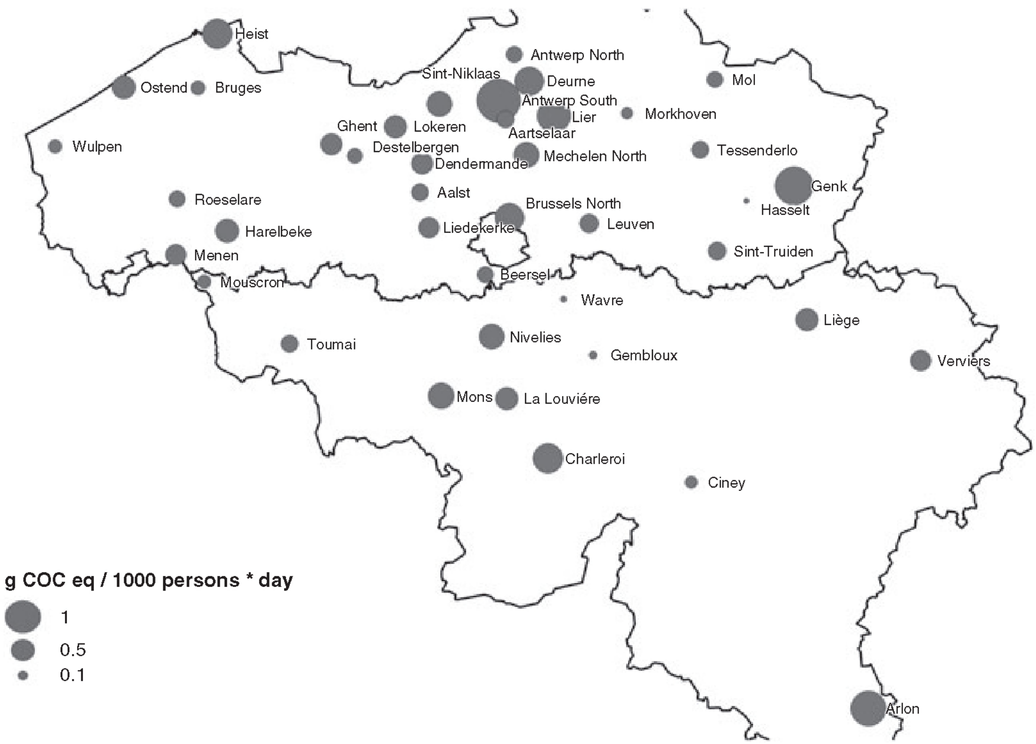

Figure 3 Geographical distribution of cocaine (COC) consumption for Sunday samples (sampling campaign II) from 41 wastewater treatment plant regions in Belgium; g COC eq/1000 people × day = amount of cocaine used in g/day per 1000 inhabitants

for Sunday sample in SC II) and Brussels (0.84 g/day per 1000 inhabitants for Sunday sample in SC II).

The concentration of COC and the COC/BE ratio in each sample was measured to exclude the presence of COC and BE in wastewater from dumping of large amounts of cocaine. If the latter occurs, the ratio COC/BE increases due to the absence of *in vivo* metabolization and because the potential microbial transformation of COC into BE in the sewage system will take place only slowly and gradually. Because cocaine is excreted as unchanged COC (1–15%) and as BE (20–60%) [7–9], the cut-off value for the evaluation of 'abnormal' COC/BE ratios can be set at 0.75 (representing the limits of 15% COC and 20% BE). The COC/BE ratio for all samples is below this value, suggesting that virtually all measured COC and BE resulted from human consumption.

To evaluate cocaine use in Belgium, the results obtained from the 41 WWTP regions are extrapolated to the total Belgian population. Table 3 gives a summary of the official population statistics of Belgium in 2007

Table 2 Calculation of cocaine consumption for Sunday samples (sampling campaign II) from 41 wastewater treatment plant regions in Belgium.

WWTP	*No. inhabitants*	*conc. BE (ng/L)*	*Conc. COC (ng/l)*	*Flow rate (m^3/day)*	*Loads BE (g/day)[a]*	*Loads COC (g/day)[a]*	*COC consumption (g/day)[b]*	*COC consumption (g/day per 1000 inhabitants)*
Aalst	89 847	410	158	29 768	12.21	4.71	28.438	0.317
Aartselaar	61 520	286	101	31 288	8.95	3.17	20.860	0.339
Antwerp North	69 668	248	100	34 280	8.49	3.42	19.788	0.284
Antwerp South	157 268	2130	693	57 932	123.39	40.16	287.444	1.828
Arlon	16 043	640	169	12 553	8.03	2.13	18.709	1.166
Beersel	63 531	692	273	11 614	8.04	3.17	18.733	0.295
Bruges	178 987	196	61	100 776	19.70	6.10	45.895	0.256
Brussels North	850 000	1306	453	233 303	304.69	105.69	709.785	0.835
Charleroi	138 000	1297	545	39 329	51.01	21.41	118.835	0.861
Ciney	10 000	140	70	6 000	0.84	0.42	1.955	0.196
Dendermonde	68 276	578	218	25 000	14.44	5.45	33.638	0.493
Destelbergen	57 999	392	174	17 912	7.03	3.12	16.369	0.282
Deurne	198 569	1245	394	57 088	71.07	22.49	165.568	0.834
Gembloux	37 131	160	38	8 400	1.34	0.32	3.131	0.084
Genk	68 924	863	363	45 540	39.28	16.52	91.509	1.328
Ghent	206 109	918	350	47 744	43.81	16.69	102.066	0.495
Harelbeke	111 515	803	244	33 292	26.74	8.12	62.299	0.559
Hasselt	63 333	37	9	38 712	1.43	0.35	3.337	0.053
Heist	18 123	642	284	9 770	6.27	2.77	14.611	0.806
La Louvière	29 800	549	195	12 134	6.66	2.37	15.518	0.521
Leuven	113 015	832	321	22 288	18.55	7.15	43.213	0.382
Liedekerke	92 465	648	247	27 392	17.75	6.76	41.355	0.447
Liège	26 300	1061	319	5 773	6.12	1.84	14.267	0.542
Lier	28 866	891	321	14 800	13.19	4.75	30.719	1.064
Lokeren	37 199	288	101	28 440	8.18	2.88	19.052	0.512
Mechelen North	87 452	1550	683	15 180	23.53	10.37	54.807	0.627
Menen	62 574	361	133	28 892	10.43	3.84	24.287	0.388
Mol	47 538	338	145	18 188	6.14	2.63	14.300	0.301
Mons	82 350	625	217	39 294	24.57	8.51	57.246	0.695
Morkhoven	38 211	171	67	19 358	3.31	1.29	7.711	0.202
Mouscron	27 831	228	73	11 045	2.52	0.81	5.861	0.211
Nivelles	27 000	515	133	14 400	7.42	1.92	17.279	0.640
Ostend	106 737	596	208	42 096	25.11	8.77	58.487	0.548
Roeselare	62 438	231	110	33 296	7.70	3.65	17.948	0.287
Sint-Niklaas	44 443	620	228	19 756	12.25	4.50	28.533	0.642
Sint-Truiden	44 131	393	159	16 590	6.52	2.63	15.188	0.344
Tessenderlo	41 761	350	117	16 710	5.85	1.96	13.624	0.326
Tournai	29 000	516	173	4 325	2.23	0.75	5.203	0.179
Verviers	95 000	554	161	33 355	18.48	5.36	43.046	0.453
Wavre	80 000	132	52	15 703	2.07	0.82	4.812	0.060
Wulpen	57 495	287	67	16 070	4.62	1.08	10.759	0.187

WWTP: wastewater treatment plant; conc: concentration; BE: benzoylecgonine; COC: cocaine. [a](concentration × flow rate)/10^6; [b]loads BE × 2.33.

[25]. The weekly cocaine consumption for each WWTP region in each sampling campaign is calculated based on the assumption that a week consists of 2 weekend days and 5 weekdays and that the Sunday samples are representative for a weekend day and the Wednesday samples for a weekday. The annual cocaine consumption for each WWTP region is calculated further through multiplying the weekly consumption by 52. The sum of the annual cocaine consumption from the 41 WWTP regions is then made for each separate sampling campaign. To estimate the annual cocaine consumption for the whole of Belgium, the results are extrapolated from 3.7 million Belgians (from which wastewater was collected) to 10.5 million Belgians (the total population). This results in an annual cocaine consumption of 1.94 tonnes (t) for SC I and 1.83 t for SC II, suggesting that an average amount of

Table 3 Official population statistics of Belgium in 2007 [25] and calculated annual cocaine use prevalence.

Age class	*Population number*	*Calculated annual cocaine use prevalence (SE)*
All	10 584 534	0.53% (0.02%)
15–64	6 976 743	0.80% (0.02%)
15–44	4 230 029	1.32% (0.04%)

SE = standard error.

1.88 t [standard error (SE) 0.05 t] cocaine is used yearly in Belgium.

On the assumption that an average administered dose consists of 100 mg cocaine [13], an average cocaine user consumes 0.769 g and 0.532 g cocaine per week according to Everingham & Rydell [26] and Cohen & Sas [27], respectively. In further calculations, we use the arithmetic mean of these two values (0.650 g/week). Our calculation of 1.88 t (SE 0.05 t) cocaine per year corresponds then with an estimated number of 55 770 (SE 1623) [$(1.88 \times 106)/(0.650 \times 52)$] cocaine users in Belgium. Depending on the size of the population which may be considered as potential cocaine users, this corresponds to an annual prevalence of cocaine use of between 0.53% (SE 0.02%) and 1.32% (SE 0.04%) (Table 3). The low estimate assumes all members of the population are potential users, a medium estimate [0.80% (SE 0.02%)] assumes that people aged 15–64 are potential users, and the high estimate assumes that people aged 15–44 are potential users. The 15–64 age range was chosen to compare with existing survey-based estimates, and the 15–44 range was chosen to reflect the previously defined demographics of the core population of cocaine users [14].

DISCUSSION

The observed trend of higher cocaine consumption during weekends can be explained by the fact that since 2005 cocaine use in Europe has increased in recreational settings (discotheques, parties, etc.) and among young people [11]. The downward trend in the price for cocaine since 2000, resulting in the substitution of amphetamines by cocaine as a 'party drug', is a reasonable explanation [11]. Higher cocaine use at weekends was also reported in other studies evaluating local cocaine use through wastewater analysis [19,23].

The UNODC estimated in 2004 a yearly prevalence of cocaine consumption of 0.9% for the Belgian population aged 15–64, corresponding with 61 370 cocaine users in Belgium [14]. Our calculations result in a yearly prevalence of 0.80% for the population aged 15–64, demonstrating that our estimations are in agreement with existing socio-epidemiological information. The EMCDDA estimates an average yearly prevalence of 1.3% of the population aged 15–64 in the European Union (EU) and Norway, with values ranging from 0.1% to 3.0% [11]. The UNODC also proposes an average yearly prevalence of 1.24% for the population aged 15–64 in western and central Europe [10]. If one takes this reported situation of cocaine consumption in Europe and our estimate for Belgium into account, one can place Belgium into the European context as a country with medium cocaine use. However, the estimates calculated in the present study are based on certain assumptions and are subject to a degree of uncertainty. Moreover, the present study emphasizes the usefulness of the 'sewage epidemiology' approach, a term proposed first by Zuccato *et al.* [23], to provide more precise and rapid estimates of cocaine consumption, but also that this methodology should be used in parallel with and complementary to socio-epidemiological studies.

Everingham & Rydell [26] and Caulkins [28] defined a 'heavy' cocaine user as a person who uses at least weekly cocaine, and a 'light' user as all other users. Both studies reported an average use of 0.3 g/week for a 'light' user and 2.3 g/week for a 'heavy' user. From this information, our estimate of yearly cocaine consumption in Belgium (1.88 t for 55 770 users) corresponds with 83% 'light' [from formula: $(0.3 \times 52 \times A) + [2.3 \times 52 \times (55\,770 - A)] = 1\,880\,000$, where A is the number of light users and A/55 770 the percentage of light users] and 17% 'heavy' users. Everingham *et al.* [29] reported in 1990 that 78% of all cocaine users in the United States were 'light' users. Because the recreational use of cocaine has increased since 2005 [11], a shift from 'heavy users' to 'light users' should occur: a conclusion reflected in our findings. A different pattern of cocaine use in the United States compared with Europe could also be a possible explanation for the greater proportion of 'light' cocaine users in Belgium. Cohen & Sas [27] have conducted a study on cocaine use in Amsterdam (the Netherlands). In this study, cocaine users were divided into three groups: low (<0.5 g/week), medium (0.5–2.5 g/week) and high (>2.5 g/week) users. The low user group can be compared with the group of 'light' users in the study from Everingham & Rydell [26] that was deemed responsible for 86% of the cocaine use in Amsterdam. This percentage of 'light' users from Cohen & Sas' study [27] also agrees with our calculations of 83% 'light' users in Belgium.

To the best of our knowledge, the present study is the largest survey yet of illicit cocaine use and provides an important basis for further sociological and epidemiological research. However, the shortcomings of our methodological approach are acknowledged, as is the fact that our findings are probably underestimates. Currently, the fate of BE in wastewater between excretion and sampling is not known precisely. Degradation in wastewater or adsorption onto solid particles or the sewage system could occur, resulting in an underestimate of the true concentrations excreted. Future experimental and field work is required to evaluate this. In our calculations, we extrapolated the yearly cocaine comsumption from only 4 sampling days, by assuming that cocaine consumption is stable throughout the year. However, no information about this is available in the literature, and hence future field experiments with more intensive sampling are required to characterize more clearly the temporal variations (daily, weekly and monthly) in cocaine consumption. Furthermore, it is worth mentioning that the consumption of 0.650 g/week cocaine for an 'average' user is derived from two studies in the 1990s in the United States and Amsterdam. New sociological and epidemiological research should be conducted to evaluate the validity of this value. To conclude, this study demonstrates the potential utility of the wastewater approach as a tool for evaluating the prevalence of cocaine use in Belgium.

The advantages of this nation-wide and large-scale 'sewage epidemiology' approach are multiple. Specifically, it provides: (i) a more direct and objective way of evaluating and mapping cocaine use; (ii) the possibility of obtaining results in a short period of time (e.g. within a week) and in a relatively cheap fashion compared with socio-epidemiological studies; (iii) identification of hot spots of cocaine use; and (iv) a clear picture of cocaine use at local, regional and national levels. This may lead to the establishment of focused actions in regions where high cocaine consumption is observed. 'Sewage epidemiology', together with socio-epidemiological studies, can provide a more precise and complete picture of drug abuse on both local and national scales. In view of increasing cocaine consumption and its deleterious effects on human health, 'sewage epidemiology' appears to provide an alternative longitudinal means of monitoring cocaine use. However, further study is required to optimize this approach fully.

Declarations of interest

None.

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