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Research paper

Substances detected in used syringes of injecting drug users across 7 cities in Europe in 2017 and 2018: The European Syringe Collection and Analysis Project Enterprise (ESCAPE)



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ABSTRACT

Background and aims: Injecting drug use is a matter of public health concern, associated with risks of overdoses, addiction and increased risk of bloodborne viral transmissions. Self-reported data on substances injected can be inaccurate or subject to bias or drug users might be oblivious to their injected substances or adulterations. Gathering of robust analytical information on the actual composition of substances injected might provide better information about the drugs that are being used. Therefore, this study aimed to analyse the residual content of discarded syringes collected across 7 European cities, collectively called the European Syringe Collection and Analysis Project Enterprise (ESCAPE).

Methods: Used syringes were collected at street automatic injection kit dispensers or at harm-reduction services in Amsterdam, Budapest, Cologne, Glasgow, Helsinki, Lausanne and Paris. Two sampling periods were executed thus far, in 2017 and 2018. Qualitative chemical analysis of the content of used syringes was performed combining gas chromatographic (GC) and ultra(high)performance liquid chromatographic ((U)HPLC) analytical techniques with detection by mass spectrometry (MS).

Results: Substances detected most frequently across both campaigns were cocaine, heroin, buprenorphine, amphetamines and synthetic cathinones. In Amsterdam, Cologne, Lausanne and Glasgow heroin and cocaine were the psychoactive substances most often detected, often in conjunction with each other. Helsinki showed a high presence of buprenorphine and amphetamines. In Budapest and Paris, synthetic cathinones were frequently detected. Less synthetic cathinones and cocaine was detected in 2018, whereas buprenorphine was detected almost twice as much. Inner-city variations were found, probably reflecting the types of people who inject drugs (PWID) in different areas of the city.

Conclusion: Overall, laboratory-confirmed local data on injected substances showed resemblance to national surveys done among PWID. However, the ESCAPE data also showed some interesting differences, showing it can be used for local interventions and complementing existing monitoring data.

Introduction

Injecting drug use is a matter of public health concern, associated with risks of overdoses, addiction and increased risk of bloodborne viral

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transmissions (Degenhardt et al., 2017; Nelson et al., 2011; Stone et al., 2018). Overall, it seems that prevalence of injecting drug use has declined in the European Union (EMCDDA, 2015). However, there are also signals that it may be on the rise in certain groups at risk, including people in prison, homeless people and people with a substance dependence (EMCDDA, 2017a). In addition, injecting drug use is also more prevalent in men or women who engage in risky sexual behavior, mainly in the gay community (Heinsbroek, Glass, Edmundson, Hope, & Desai, 2018). In many parts of the world, this has led to a phenomenon, known as “slamming” whereby several different drugs are taken at a time, often also injected. “Slamming” during “chemsex” is more often associated with hepatitis-C (HCV) and HIV infections in men who have sex with other men (MSM) (Ireland et al., 2017; Maxwell, Shahmanesh, & Gafos, 2019), supported by an increase in the incidence of HCV and HIV over the last decade (Hagan, Jordan, Neurer, & Cleland, 2015; Vaux et al., 2019). These people are generally difficult to reach by harm reduction services and little is known about the substances they inject.

Furthermore, there is also the considerable risk of overdosing and death after injecting drugs, especially opioids. In the past, it was mostly heroin that was responsible for overdose casualties, nowadays many other opioids have emerged as dangerous substances that are being injected, as is apparent from recent studies (Handanagic, Bozicevic, Sekerija, Rutherford, & Begovac, 2019; Karila, Marillier, Chaumette, Nicolas, & Amine, 2019; Rose, 2018; Schneider, Park, Allen, Weir, & Sherman, 2019).

Knowledge on which substances are being injected in a city or country is pivotal in guiding treatment strategies. Whereas data on the substances injected by users are based on self-reports or ad-hoc surveys (Wenz et al., 2016), these data are available with some delay and can be inaccurate or subject to bias. Only in methadone or heroin substitution centres, where users are getting therapeutic prescription doses, it is exactly known what people are injecting at that moment (Gervasoni, Balthasar, Huissoud, Jeannin, & Dubois-Arber, 2012; Van Den Brink et al., 2003; Wittchen et al., 2008), but in many healthcare facilitated drug consumption rooms people are able to bring their own drug purchases. Therefore, people who inject drugs (PWID) might be oblivious to the composition of the substances they inject and hardly anything is known about drugs injected by people that are not reached by these drug user services.

To address this gap in knowledge, a European research group developed a direct and innovative approach in obtaining information about injected drugs, i.e. by analysing the residual content of discarded syringes collected from the bins of street automatic injection kit dispensers (AIKD) or at harm-reduction services (Lefrançois, Augsburger, & Esseiva, 2018; Néfau et al., 2015; Péterfi et al., 2018). Previous findings reported correlations between self-reported data from clients at harm reduction services and what was found in the analysis results of used syringes, but also discrepancies were found (Péterfi et al., 2018). In the present study, this method was further refined and expanded with a number of other European partners, collectively called the European Syringe Collection and Analysis Project Enterprise (ESCAPE).

The study will provide an overview of the main findings of the 2017 and 2018 ESCAPE campaigns. ESCAPE was established in 2017 by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), and led by the French Monitoring Centre for Drugs and Drug Addiction (OFDT), it comprises a network of some major European cities: Amsterdam, Budapest, Cologne, Glasgow, Helsinki, Lausanne and Paris. The study aims to identify which drugs are injected in these cities by the chemical analysis of the residual content of used syringes. Results and limitations are discussed and implications for harm reduction strategies are reflected upon.

Materials and methods

Study design and sample collection

The first syringe collection campaign was conducted from August to November 2017 in Amsterdam, Budapest, Glasgow, Helsinki, Lausanne and Paris. The second syringe collection campaign was conducted from March to June 2018 in Budapest, Cologne, Helsinki, Lausanne and Paris. During a month, each city aimed at collecting a minimum of 150 syringes across different needle and syringe exchange services in each city. In some cases it was not possible to collect syringes during the exact same month in each city, so therefore the collection month sometimes differed per city. Depending on availability of locations per city, a range of different collection sites were selected in each city to maximise geographical coverage and representation of syringes per city. This led to 24 collection sites across all 7 cities in total. In Lausanne, only street bins could be chosen as an option. In Budapest, Glasgow and in Helsinki low threshold facilities with embedded NSP (Needle and Syringe Program) threshold facilities were sampled. In the rest of the cities, sample collection consisted of a combination of street bins and sites where NSP is realized. Syringes were collected routinely each week for one month. Syringe collection and shipment was handled by professionals working at the NSP and by the leading scientists participating in ESCAPE. Table 1 provides an overview of all participating cities of ESCAPE and the different services they provide for PWID. Sharp safe disposable bins in which syringes were collected, were sealed and labelled with date and time of collection, were then transferred to the laboratory for analysis. Bins were stored at -20 °C prior to analysis to avoid degradation of compounds.

Sample preparation

Once at the laboratory, disposal boxes were unsealed and the content was placed on a flat surface. Syringes were laid in rows and selected at random; every second syringe on the surface was picked out for sample preparation, for a second disposal box every first syringe was chosen and so on. Appropriate safety measures were mandatory, when handling the syringes: tweezers, thick laboratory coats, goggles, face masks and thick nitrile or double latex gloves. The syringe samples preparation procedure has previously been published elsewhere (Néfau et al., 2015). Briefly, the content of used syringes was recovered by purging the syringes five times with 1 mL of methanol (used syringes were filled and emptied five times). The methanolic solutions were filtered using sterile syringes and then transferred into suitable vials for instrumental (hyphenated mass spectrometric) analysis.

Chemicals, reagents and materials and instrumental analysis

Laboratory participants were: Toxicology Laboratory of the Institute of Forensic Medicine of the University of Debrecen, Hungary; University of Paris Sud, France; University of Lausanne, Switzerland (School of criminals' laws and University Centre of Legal Medicine collaboration); Forensic Toxicology Unit of the Finnish Institute for Health and Welfare; Forensic Medicine and Science of the University of Glasgow, Scotland and the Institute of Forensic Medicine at the Medical Center – University of Freiburg, Germany. The prepared syringe samples from the Netherlands were shipped to and analyzed by the University of Lausanne.

All of the laboratory analytical methods performed herein are also further detailed elsewhere (Gjerde et al., 2020; Lefrançois et al., 2016; Néfau et al., 2015; Péterfi et al., 2018). Compared to these previous studies, this study has aimed to improve on technical aspects and lower

Table 1

The scale of the cities participating in the ESCAPE study, estimated population size, number of syringes collected and type of services available for people who inject drugs (PWID).

City	Population	Estimated size of PWID population	Number of sterile syringes distributed	Syringe collection sites	Number of syringes analysed	
					2017	2018
Amsterdam	860,000 (density of 5042/km ²)	150–200		2017: Three NSP services and two drug consumption rooms. The latter is located in the Red Light District and also provides sterile syringes. It is the only drop-in centre with a shelter for women. Another one is located near the centre and also aims at clients that are homeless and often economic refugees from other countries in the EU. Clients of these services are aged between 22 and 71 years and are socially vulnerable. Self-reported substance use includes heroin, cocaine, methadone, amphetamine, cannabis and alcohol.	112	na
Budapest	2,000,000 (density of 3314/km ²)	6000	In 2017: an estimated 115,500 syringes were distributed in Budapest	2017–18: One face-to-face NSP. This low-threshold service is located in a poor neighbourhood, where there is a concentration of homeless people and sex workers. The area is also popular among tourists.	300	150
Cologne	1,081,701 (density of 2700/km ²)	6600		2018: five NSP services. Two are in the city centre where there is an open drug scene, clients are mostly homeless people. Another one is located in a mixed business/residential area and clients are PWID more inserted. The two other NSP services are located in two different residential area characterized by a high rate of unemployed people.	na	167
Glasgow	621 020 inhabitants (3 555/km ²)	5500	In 2017: 350 436 needles and syringes were provided from all outlets in Glasgow city centre	2017: Two NSP services. One service is located at the edge of the city centre in a largely industrial area and includes a rehabilitation residential service. The other is located in the city centre in a mixed retail/residential area, close to social services for the homeless.	300	na
Helsinki	643,272 (density of 3002/km ²)	8500	In 2017: 3 of the 5 NSP provided a total of 1732,462 needles and syringes.	2017: five NSP; 2018: six NSP. A first site is located in the eastern part of downtown Helsinki, an area with social and health services for PWID, known for drug trade and drug users. A second site is located in the northern part of downtown Helsinki, in a housing unit with 100 residents who suffer from substance abuse and/or mental health problems. A third site is located close to the city centre, near a similar housing unit. Two sites are located further East, one in a business and residential area with an open drug scene and trade, and the other in a residential area with higher than average concentration of government tenant housing complexes. The sixth site (2018) is located in north-eastern Helsinki.	307	425
Lausanne	144,597 inhabitants (density of 3395/km ²)		In 2015: 100,000 syringes were distributed.	2017–2018: There is only one bin of AIKD in neighbourhood of Lausanne served by two metro station. During daytime, people from diverse socio-economic background use this area. In the evening, it has significant nightlife activity and hosts marginalised groups.	297	150
Paris	2,220,445 (density 21,067/km ²)	26,328 for the whole Paris region (Ile-de-France)	In 2015: 656,000 syringes were distributed	2017–2018: five bins of AIKD. Three sites are located next to train stations. In one of these sites, users of AIKD include low-income and homeless PWID. The other two stations are busy public transport hubs frequented by people from diverse socio-economic backgrounds. The remaining two sites are located near metro stations in affluent neighbourhoods with well-integrated populations. One of the latter is famous for its nightlife.	360	96

PWID = People Who Inject Drugs; AIKD = Automatic Injection Kit Dispensers; NSP = Needle and Syringe Program; na = not applicable.

the limits for quantification (LOQ) of substances. All laboratories used validated methods to analyse these substances, as they are used routinely to detect illicit and licit substances in (forensic) research. The laboratories employed gas chromatography (GC), high performance liquid chromatography (HPLC) or ultra-high performance liquid chromatography (UHPLC) to separate the eluents of the syringes. For identification of substances in the eluents, laboratories employed mass spectrometric (MS) techniques, like tandem mass spectrometry (MS/MS) or quadrupole time-of-flight mass spectrometry (QTOF-MS). Existing up-to-date forensic databases were used to match mass-to-charge (m/z) ratios of compounds. Supplemental Table 1 gives all technical details of the hyphenated mass spectrometric techniques employed by the various laboratories for the syringe analysis.

Target compounds

At least 151 compounds were tested for, depending on the analytical method used (see supplemental Table 2 for target compounds and descriptive text). These included metabolites, degradation products and adulterants. Inactive compounds, like mixing compounds (like sugars), or biological compounds (e.g. blood) were not tested in this study. LOQ ranges of target compounds are given in supplemental Table 2 for UHPLC, according to previous described methodology (e.g. Gjerde et al., 2020). As for analysis with GC, for all compounds characterised, peak areas were integrated and LOQ was determined to be 1–5 ppm. When a peak integration (normalised by IS) was lower than the LOQ, the results were not considered (see also Lefrançois et al., 2020).

Data treatment and statistical analysis

For this study, descriptive data analysis was used for the main results, using basic Microsoft Excel software (Microsoft Office Professional Plus 2016) and Tableau software (version 10.4.19). Data that was obtained by mass spectrometric analysis was compiled into worksheets and the results were rearranged by individual drug (cocaine, heroin, morphine, buprenorphine, methadone, ketamine) or by group of drugs (amphetamines, fentanils and related substances, other opioids, synthetic cathinones, synthetic cannabinoids, benzodiazepines, phenidates, MDMA, other medications, amphetamine-like drugs and other drugs) (Supplemental Table 2). For the purpose of clarity, for Fig. 1 and Table 4 substances were depicted by occurrence of detection of a single substance, so percentages do not necessarily add up to 100%, since co-detection of more than one substance in a syringe occurred frequently. Only the syringes that tested positive for at least one substance (excluding metabolites and adulterants) were included for further analysis.

RESULTS

Depending on the availability, between 1 and 6 collection sites were selected per city. A total of 2664 syringes were collected across seven cities in the two sampling campaigns of 2017 and 2018. For various reasons (e.g. blocked syringes, contents could not be purged) some extractions failed, and therefore, analysis was conducted for 2476 syringes (93%) with at least one drug was detected in 2177 (88%). Table 2 summarises all numbers. Reasons for the absence of any known substance may be related to pharmacologically inactive substances being injected, washed/ empty syringes or substances which were undetectable with the used drug screening procedures, because of higher detection limit or a substance was not included in the subsequent methodology.

Substances detected across two sampling campaigns 2017–2018

Overall, drugs most commonly detected were heroin, cocaine, synthetic cathinones, buprenorphine, amphetamine and methamphetamine (Fig. 1). In total, across both sampling campaigns, 77 different substances and metabolites were detected. Heroin was detected in 95% of

syringes in Amsterdam, in 49% of syringes in Glasgow, 69% in Cologne and 37% of syringes in Lausanne. Buprenorphine was detected in 61% of syringes in Helsinki. Benzodiazepines were primarily found in syringes from Lausanne and Helsinki.

In addition to opioids, traditionally associated with injecting, all participating cities showed a remarkably high proportion of syringes that tested positive for stimulants, like cocaine (Amsterdam: 43%, Cologne: 69%, Glasgow: 80%, Lausanne: 70%), synthetic cathinones (Budapest: 66%, Paris: 45%) and amphetamines (Helsinki: 47%, Budapest: 16%). Across both sampling campaigns, cocaine was the most prevalent substance detected (31%), followed by heroin (24%), buprenorphine (21%) and then synthetic cathinones and amphetamines (both 17%) (see also Table 3). Furthermore, cocaine was often co-detected in syringes alongside heroin.

Whereas in 42% of all analysed syringes a single pharmacologically active substance was detected, 36% of syringes contained a combination of two substances and in another 10% a combination of three substances was found (Fig. 2). Frequencies in which combinations of substances occur in the syringes per city and per sampling campaign are given in Supplemental Figure 1. The combination most often found was heroin and cocaine. This combination was mainly found in four cities: Glasgow (44%), Amsterdam (38%), Cologne (37%) and in Lausanne (10%). Furthermore, 14% of the heroin and heroin-cocaine syringes also tested positive for benzodiazepines in Lausanne. In Helsinki, buprenorphine was co-detected with traces of amphetamines, in Paris, buprenorphine and cocaine were co-detected and in Budapest, heroin and synthetic cathinones. Some of the most common combinations are depicted in Supplemental Figure 2.

Most commonly detected synthetic cathinones were *N*-ethylhexedrone, 4-chloro- α -pyrrolidinovalerophenone (4-Cl- α -PVP) in Budapest, and 3/4-Methylmethcathinone (3-MMC/4-MMC) and 4-Methylethcathinone (4-MEC) in Paris. 3-MMC could not be distinguished from 4-MMC, but based on seizure information from France, 3-MMC seems most likely (EMCDDA, 2017b). In a large part proportion of the syringes containing a synthetic cathinone there were also traces of other drugs. In most cases, another cathinone was detected. Less frequently, they were also found in combination with other substances. They were co-detected with amphetamines and opioids (Helsinki) or new psychoactive substances (Budapest). In fact, combinations of more than one stimulant appeared in 10% of syringes. In Helsinki, 32% of syringes contained residues of a mixture of stimulants, mostly of amphetamine and methamphetamine.

Injecting benzodiazepines seems to be largely confined to Helsinki (in 2017 11% and in 2018 4% of syringes tested positive) and Lausanne (in 2017 23% and in 2018 29%). In Lausanne, midazolam accounted for almost all benzodiazepine-positive syringes, but for less than half of the benzodiazepines in Helsinki, where alprazolam, clonazepam, diazepam, oxazepam and temazepam were also detected. In syringes from Helsinki, half of the syringes containing benzodiazepines also tested positive for methamphetamine. Other medicines were generally not detected, only in Helsinki where they were detected in one out of five syringes (19%), with pregabalin (9%) and gabapentin (5%) most often detected.

The other most abundant pharmacologically active substances or adulterants, were levamisole, phenacetin and paracetamol. Among the cocaine positive syringes collected in Lausanne, levamisole was present in 55%, followed by phenacetin (32%) and caffeine (20%). However, in other cities the percentages of adulterants present in cocaine positive syringes was much lower to almost absent.

Differences between the first and the second collection campaign

Notably less synthetic cathinones (14% vs. 24%) and cocaine (26% vs. 34%) was detected in the second sampling campaign, whereas buprenorphine was detected almost twice (29% vs. 15%) as much in the second sampling campaign (Table 3). The increase of buprenorphine almost entirely traces back to Helsinki and an overall increase

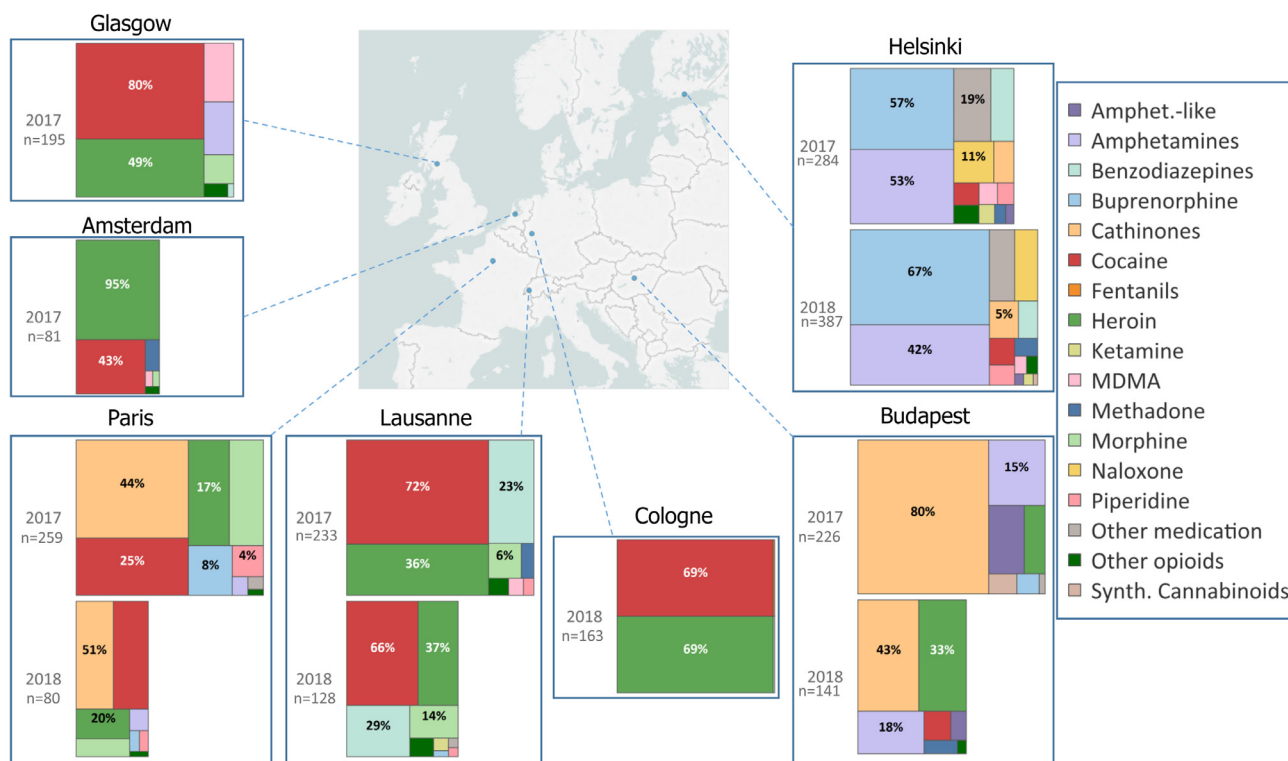


Fig. 1. Substances (in %) in used syringes that tested positive for at least one psychoactive substance across two sampling campaigns 2017–2018 in the seven cities participating in ESCAPE. Amphet.-like = amphetamine-like; Synth. Cannabinoids = synthetic cannabinoids.

Table 2

The numbers of syringes that were collected across the seven cities during the first and second sampling campaigns, numbers of syringes analysed and syringes wherein psychoactive substances were detected are indicated.

		Amsterdam Netherlands	Budapest Hungary	Cologne Germany	Glasgow Scotland	Helsinki Finland	Lausanne Switzerland	Paris France	Total
2017	Syringes Collected	112	300		300	307	297	360	1676
	Analysed	112	227		232	301	297	352	1521
	Containing Substances	81	226		195	284	233	259	1278
2018	Syringes Collected		150	167		425	150	96	988
	Analysed		150	164		401	150	90	955
	Containing Substances		141	163		387	128	80	899
Total	Syringes Collected	112	450	167	300	626	447	456	2664
	Analysed	112	377	164	232	702	447	442	2476
	Containing Substances	81	367	163	195	671	361	339	2177

of buprenorphine use in most parts of the city, from 57% of all syringes in 2017 to 67% in 2018 (Table 4). On the other hand, the decreased occurrence of synthetic cathinones in the second campaign was due to a reduction of almost half of synthetic cathinones detected in the number of syringes from Budapest, from 80% to 43%. Interestingly, in Budapest, a substantial increase of heroin was detected, from 6% in 2017 to 33% in 2018. Occurrence of cocaine dropped, partly because Glasgow did not analyse syringes in the second campaign and Amsterdam did not participate. In both Helsinki and Budapest, hardly any cocaine was detected across both sampling campaigns. Furthermore, no heroin was detected in both 2017 and 2018 campaigns in Helsinki.

Substances detected in different city regions

There were differences found between city regions. In Helsinki, differences were found between the downtown area, western and the east-

ern part of the city. In the downtown and western areas, primarily amphetamines were detected in syringes, whereas in the eastern part, buprenorphine was the drug detected most. In Paris, also an inner-city variation was seen in substances. Near the train station and in the northern part, areas frequented and inhabited by impoverished users, mostly opioids (often buprenorphine or diverted morphine medicines) were detected in syringes collected. By contrast, synthetic cathinones, but also cocaine, were primarily found in the syringes sampled across the west and east side of the city, boroughs that are frequented by more affluent and socially integrated users. In Cologne, mainly a division between areas where cocaine was detected was seen, whereby in the south and centre there was much more cocaine detected than in the rest of the city. In the centre of Amsterdam mainly heroin was detected, but hardly any cocaine, whereas in the other parts of the city and the vicinity most syringes contained cocaine alongside heroin. The other participating cities

Table 3
Types of substances detected in injecting syringes across two sampling campaigns between 2017–2018.

	2017 campaign (N = 1278)		2018 campaign (N = 899)		TOTAL (N = 2177)	
	Occurrence	Proportion	Occurrence	Proportion	Occurrence	Proportion
Cocaine	436	34%	236	26%	652	31%
Heroin	312	24%	197	22%	503	24%
Buprenorphine	189	15%	261	29%	441	21%
Cathinones	309	24%	123	14%	365	17%
Amphetamines	206	16%	192	21%	365	17%
Benzodiazepines	87	6.8%	51	5.7%	138	6.6%
Other medicines	56	4.4%	36	4%	92	4.4%
Morphine	55	4.3%	29	3.2%	71	3.4%
Naloxone	32	2.5%	32	3.6%	64	3%
MDMA	34	2.7%	4	0.4%	38	1.8%
Other amphetamines	25	2%	6	0.7%	31	1.5%
Piperidines	19	1.5%	13	1.4%	32	1.5%
Other opioids	19	1.5%	11	1.2%	29	1.4%
Methadone	13	1%	12	1.3%	25	1.2%
Ketamine	6	0.5%	2	0.2%	8	0.4%
Synthetic cannabinoids	5	0.4%	1	0%	6	0.3%

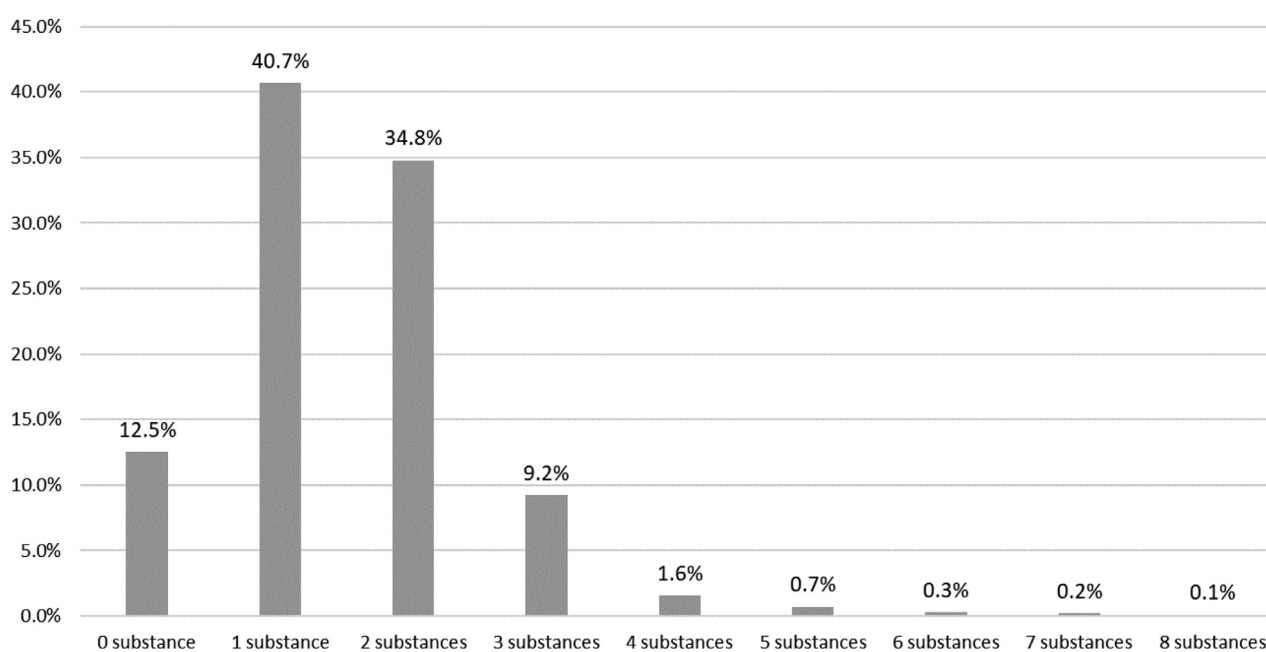


Fig. 2. Percentages of syringes in which none, one or more substances were (co-)detected.

did not cover enough geographical spread in the sampling sites to uncover regional differences.

Discussion

This study was undertaken to provide some insight into patterns of drug injection among PWID across some major European cities. It expands on previous efforts undertaken to gain local and regional insights (Lefrançois et al., 2018, 2016; Néfau et al., 2015; Péterfi et al., 2018), and this study is novel in that it covers 7 major European cities with very different cultural backgrounds. The current study identified trends and patterns in injecting substance use in a unique way and data like this is otherwise very difficult to obtain by using conventional methods, like subjective questionnaires for instance, therefore the results of this study might help to further tailor specific regional harm reduction programmes. For instance, the high prevalence of stimulant injection that was found in this study has implications for public health, as it is associated with a higher frequency of injection, thereby resulting in possible cardiovascular diseases and psychiatric comorbidities. While another issue that has been associated with stimulant use is unsafe sexual behavior

(Cavazos-Reh et al., 2009), such as outbreaks of HIV or HCV that have been described among PWID in some cities (Giese et al., 2015). So, harm reduction services might address this issue by emphasizing on avoiding reuse of needles, handing out ample new syringes and providing specific information on risks of stimulant use, such as the tendency to inject these substances more frequently than opioids. In addition, the high incidence of polydrug use found, is associated with a higher risk of drug-related harms, so harm reduction and drug treatment services need to address this by providing specific information about risks of these combinations of substances.

Substances detected most frequently in both campaigns were cocaine, heroin, buprenorphine, amphetamines and synthetic cathinones. Generally, profound differences were found between some European cities, whereas other cities showed similarities in substances injected. In Glasgow, Amsterdam and Cologne heroin and cocaine were the psychoactive substances most often detected, often in conjunction with each other. Lausanne showed a similar pattern, but this city also showed a notable presence of benzodiazepines. In Budapest, opioids and synthetic cathinones were primarily detected, depending on the city area. Paris also showed a more diffuse pattern of substances, depending on city

Table 4
Types of substances detected (in %) across the participating cities of ESCAPE across both syringe collection campaigns.

City	Amsterdam		Budapest		Cologne		Glasgow		Helsinki		Lausanne		Paris	
	2017	2018	2017	2018	2017	2018	2017	2018	2017	2018	2017	2018	2017	2018
Year														
Substances	%		%		%		%		%		%		%	
Amphetamines	-		15	18			10		53	42	-	-	1	5
Cocaine	43		-	5	69		80		4	3	72	66	25	49
Heroin	95		6	33	69		49		-	-	36	37	17	20
Morphine	1		-	1	1		2		-	-	6	14	14	13
Buprenorphine	-		2	-	-		-		57	67	-	1	8	3
Naloxone	-		-	-	-		-		11	8	-	-	-	-
Methadone	5		-	3	-		-		1	2	2	-	-	-
Fentanils	-		-	-	-		-		-	-	-	-	-	-
Other opioids	1		-	1	-		2		3	1	2	4	-	1
Synthetic cathinones	-		80	43	-		-		6	5	-	-	44	51
Synthetic cannabinoids	-		2	-	-		-		-	-	-	-	-	-
Benzodiazepines	-		-	-	-		1		11	4	23	29	-	-
Piperidines	-		-	-	-		-		2	3	1	1	4	3
MDMA	1		-	-	-		11		3	1	1	1	-	-
Ketamine	-		-	-	-		-		2	1	-	-	-	-
Other medicines	-		-	-	-		-		19	8	-	1	2	-
Amphetamine-like substances	-		10	3	-		-		1	1	-	-	-	1
Pharmacologically active adulterants	98		29	69	59		10		1	1	89	79	-	-

Percentages have been rounded off.

area. Helsinki was characterized by a high presence of buprenorphine, mainly in the eastern part of the city, and amphetamines were found mainly in the other areas of the city. Both campaigns showed some differences, notably less synthetic cathinones and cocaine was detected in 2018, whereas buprenorphine detection increased substantially in 2018. This is partly due to some cities that did not partake in 2018, but very likely also reflects changes in the drugs used by people who inject drugs (PWID) in some cities.

Inner-city variations in detected substances likely reflect the different socio-demographic profiles of PWID across the sites and stability of the demand and supply market. In Paris, for example, cocaine and opioids were most commonly found near areas frequented by marginalized and impoverished users, whereas synthetic cathinones were detected near neighbourhoods frequented by more affluent and socially integrated users. In a 2014 study, cocaine was the only substance detected in syringes collected from the western site (Néfau et al., 2015). Synthetic cathinones were found in 98% of the syringes collected in 2017 from the same site, indicating a new local trend, demonstrating that the current method of syringe sampling can quickly detect temporal and spatial changes and inform services that may need to address them.

In general, it has to be noted that the number of syringes collected does not reflect the number of individuals providing them, but some of the regional trends observed are in accordance with surveys done by addiction treatment centres. In Finland, buprenorphine (66%) and amphetamines (30%) were the most reported substances (2019), in the Netherlands, 80% of clients entering drug treatment in 2015 reported heroin as their primary drug (Wisselink, Kuijpers, & Mol, 2016), and in Hungary, self-reported data from NSP services has shown synthetic cathinones use among clients (reported by 80% in 2015) and this was confirmed by analysis of syringe residues (Péterfi et al., 2018). In Glasgow, unpublished 2018 data from NSP services showed heroin and cocaine were injected by most clients (82% injecting heroin, 77% cocaine, and 26% a combination of both). Syringe residues from Paris do not reflect national treatment data from France, where heroin was reported by the majority of clients in 2017 (EMCDDA, 2017b). In the present study, heroin came third, after synthetic cathinones and cocaine in Paris. This discrepancy may be partially explained by the Parisian regional differences compared to the national situation. Moreover, in Paris, syringes were collected almost exclusively from street bins and not NSP services, which is in contrast to the self-reported data obtained from those treatment services. So, it is likely that other populations, not in treatment,

in Paris are covered by the ESCAPE study, possibly predicting treatment demands in the future.

Historically, heroin was the substance injected in most Western European cities (Morgan, 2014). However, the present study showed a remarkably high proportion of syringes testing positive for stimulants. It cannot be ruled out that traces of blood containing substances consumed via other modes of administration prior to injection are drawn into the syringe during injection. Globally, several studies have expressed concern about the increasing trend of injecting stimulants and the relationship to disease (Cepeda et al., 2020; Farrell et al., 2019). An increase in cocaine injection, alone or in combination with heroin, was reported in 2018 in France, Germany and Switzerland (EMCDDA, 2018b). A high prevalence of synthetic cathinone injection among PWID of low-threshold programmes in Hungary was reported in 2014 (>50%) (Kapitány-Fövényi & Rácz, 2018). Likewise, PWID in Finland reported injection as the main route of amphetamine administration (2019). This high prevalence of stimulants in syringes could be associated with a higher injecting frequency leading to more used syringes, typical of stimulant use (Rigoni, Brecksema, & Woods, 2018). In Glasgow, there was a HIV outbreak among PWID in 2015 that was associated, among others, to injecting cocaine (McAuley et al., 2019).

Synthetic cathinones were found in a large proportion of syringes in Paris and Budapest. Synthetic cathinones first appeared as substitute substances in Budapest after a heroin shortage in 2011, and have since then presented a significant problem (Péterfi, Tarján, Horváth, Csesztregi, & Nyírády, 2014; Tarján et al., 2015). Among other things, the replacement of heroin with synthetic cathinones was associated with an increased frequency of use, reuse and sharing of syringes, leading to a higher HCV prevalence among PWID. Some of the main synthetic cathinones reported on in Hungary were pentadone and methylenedioxypropylrovalerone (MDPV). However, analysis of syringe residues has shown distinct temporal changes in the occurrence of different synthetic cathinones (Péterfi et al., 2018). In agreement to these temporal changes, the current study did not find any syringes containing either pentadone or MDPV. Most frequently found synthetic cathinones in Budapest were *N*-ethylhexedrone and 4-Cl- α -PVP. By contrast, in Paris, 3-MMC (or 4-MMC, also called mephedrone) and 4-MEC were the synthetic cathinones detected in used syringes.

Overall, a substantial proportion of the syringes tested contained traces of two or more drugs, indicating that polydrug use appears quite common among PWID. This is a worrying trend, since polydrug use is generally associated with increased psychopathology, more risk

behaviours, lower treatment adherence and worse health outcomes (Connor, Gullo, White, & Kelly, 2014). The simultaneous injection of heroin and cocaine is known as 'speedballing' (or 'snowballing' in Scotland), and seemed to occur most in Glasgow, Cologne, Lausanne and Amsterdam. Co-injection of cocaine and heroin increases the risks of cardiovascular effects of cocaine, while cocaine masks the sedative effects of opioids, thereby increasing the risk of delayed overdose (EMCDDA, 2018b). In addition, combining heroin and cocaine leads to poorer compliance with opioid substitution treatment (DeFulio et al., 2012; Rowan-Szal, Lois, Chatham, 2000). The combination of opioids and benzodiazepines increases the risk of overdose and severe respiratory depression (McClure, Niles, Kaufman, & Gudin, 2017). Also, in Helsinki, buprenorphine was occasionally detected with amphetamines (17%). It has to be stressed that the detection of multiple substances does not necessarily imply intentional polydrug use by injection. First, drugs consumed earlier may enter into the syringe via blood drawn by the user during injection, differentiating it from simultaneous polydrug use. Secondly, detection of multiple substances could also be the result of unintentional adulterations. Amphetamines or synthetic cathinones are used by dealers to adulterate more expensive drugs (Giné, Espinosa, & Vilamala, 2014). Also, reuse of syringes by one or more users could result in a higher number of detected substances. Finally, detection of multiple substances might also be indicative of syringe reuse, whereby traces of the previously injected substance are co-detected with the substance injected after. A recent study from Paris indicated that reuse is practiced by 19% of PWID (Torres-Leguizamon, Reynaud, Néfau, & Duplessy, 2020). Of PWID from Budapest about 20% indicated they reused or shared their syringes (Gyarmathy, Neaigus, Mitchell, & Ujhelyi, 2009).

Buprenorphine was the most frequently detected opioid in Helsinki, and only found sporadically in syringes from Paris and Budapest. This is in line with national data on drug treatment services. In Finland, buprenorphine use is the main reason for opioid users to seek drug treatment (2019), where 80% of opioid users entering treatment in Finland in 2016 reported use of buprenorphine, whereas this was 10% in France and none in the Netherlands (EMCDDA, 2018a, 2020). Interestingly, in Helsinki, about 20% of the syringes positive for buprenorphine contained traces of naloxone. This may be explained by use or diversion of Suboxone — a mixture of buprenorphine with the opioid antagonist naloxone, in order to discourage injection, which is prescribed to 62% of opioid substitution clients in Finland. Suboxone detection indicates that it is used and injected, and that co-injected naloxone does not entirely antagonize the effect of buprenorphine (Alho, Sinclair, Vuori, & Holopainen, 2007; Johnson et al., 2000).

Misuse of benzodiazepines among PWID has been an acknowledged phenomenon both in Europe and worldwide (Bach et al., 2016; Kerr et al., 2010; Ross, Darke, & Hall, 1997; Strang, Griffiths, Abbey, & Gossop, 1994). Common benzodiazepines (alprazolam, clonazepam, diazepam and midazolam) were tested in all cities, some new benzodiazepines, which may reflect illegal sources, were detected in Amsterdam, Budapest, Glasgow, Helsinki and Lausanne. Injecting benzodiazepines was most prevalent in Helsinki and Lausanne. Benzodiazepines, alone, may be used recreationally or in order to modify the effects of other drugs (Jones, Mogali, & Comer, 2012). Use of benzodiazepines is predominantly linked to opioid users, both via oral administration as injection, and this was the case in Lausanne, where benzodiazepines were co-detected in syringes with heroin. In Helsinki, buprenorphine was often co-detected with benzodiazepines. Benzodiazepines are used to increase or prolong the effect of the opioid substitution medication (Gudin, Mogali, Jones, & Comer, 2013). However, combining benzodiazepines with buprenorphine increases the risk of respiratory depression and overdose (Reynaud, Tracqui, Petit, Potard, & Courty, 1998).

Levamisole, the major adulterant of cocaine, can be linked to a weakened immune system and other pathophysiological effects (Brunt, van den Berg, Pennings, & Venhuis, 2017). Likewise, phenacetin, another common adulterant, has neurotoxic and carcinogenic adverse

effects (Solimini et al., 2017). Whereas cocaine is known as the most adulterated drug (Kudlacek et al., 2017), no adulterants were detected in half of the syringes containing cocaine. This seems to be in accordance to the rise in purity of cocaine over the last years (EMCDDA, 2018b). The presence of synthetic cathinones alongside other drugs in syringes may very well reflect adulteration, rather than intentional polydrug use (Giné et al., 2014), since these substances are generally cheap and easy accessible through the internet.

Limitations

Several limitations regarding the analysis of the content of used syringes as a monitoring tool have already been reported (Lefrançois et al., 2020; Lefrançois et al., 2016; Néfau et al., 2015; Péterfi et al., 2018). In the first place, the number of syringes collected and tested in this study does in no way reflect the actual number of PWID across the various cities. A small number of users might actually contribute a disproportionately large number of syringes, if users handed in syringes in bulk for example. Therefore, the ESCAPE approach should not be seen as a method to estimate prevalence of the different substances used by all PWID. For instance, injecting stimulants at a higher frequency than depressants results in relatively higher amounts of syringes containing stimulants. Because several laboratories were participating, limits of detection of substances were sometimes depending on the method used, however the partnership of multiple laboratories led to the identification of more than 150 compounds, whereas this was 23 in a previous study of a single city (Néfau et al., 2015). Also, the sites of syringe collection were chosen on the availability of NSP services or automated injection kit dispensers (AIKD) bins in the various cities, this limits the results in geographical spread, as areas that are not covered by NSP services or AIKD bins are probably underrepresented. Secondly, a drug detected in a syringe may come from traces of blood originally drawn into the syringe during injection (Gjerde et al., 2020). So, there is no definitive way of differentiating drugs taken prior to injection and the actual drug injected, which could partly confound results found on polydrug use. Reusing syringes might also affect results found on polydrug use. Only if a human metabolite is detected, it was likely to have been taken prior to injection, but some metabolites are not distinguishable from degradation products (e.g. heroin metabolite 6-monoacetylmorphine (6-MAM)). In this study, presence of 6-MAM together with either morphine or codeine was classed as a heroin syringe.

Conclusion

Overall, the ESCAPE approach provides information that can be used for local interventions and complements existing monitoring data, like surveys, but does not replace them. Laboratory-confirmed local data on injected substances and injection patterns as provided by the current ESCAPE project adds in helping guiding local responses. Furthermore, analysis of syringes from anonymous street bins provides information about PWID that are probably not reached by health services. Repeating ESCAPE campaigns will ultimately enable countries to analyse trends over time and detect changing patterns of injecting. Future campaigns shall aim at collecting syringes from more diverse settings and will include more cities, to provide a representative picture of the European situation and to advance knowledge on local injecting practices.

Contributors

Authors Tibor Brunt, Thomas Nefau and Elodie Lefrançois designed the study. All the authors and partners collected the data and Tibor Brunt and Elodie Lefrançois analysed the data and Elodie Lefrançois designed most of the graphs in collaboration with staff from the EMCDDA. Tibor Brunt wrote the manuscript and did the bibliography and formatting. All authors critically reviewed the draft, send their contributions and approved the final version.

Role of funding sources

The EMCDDA provided the funding for collection and chemical analysis of the syringe samples.

Supplementary data

Supplementary data associated with this article can be found, in the online version.

Declarations of Interest

All authors declare that they have no conflict of interest.

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Supplementary materials

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