European Monitoring Centre
for Drugs and Drug Addiction

TECHNICAL REPORT

Drug-related hospital emergency presentations in Europe: update from the Euro-DEN Plus expert network

February 2020

Legal notice

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About this report

This report presents the latest findings on drug-related hospital emergencies from a network of sentinel hospitals across Europe. Almost 24 000 emergency presentations were recorded at 32 sentinel hospitals over the first 4 years of the project. The data reveal that the substances most commonly involved in acute drug toxicity presentations include heroin, cocaine and cannabis. Prescription medicines are frequently reported. The report also sheds light on other aspects of drug-related emergencies such as clinical features, geographical variation, outcomes, demographics and time patterns.

About the EMCDDA

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is the central source and confirmed authority on drug-related issues in Europe. For over 20 years, it has been collecting, analysing and disseminating scientifically sound information on drugs and drug addiction and their consequences, providing its audiences with an evidence-based picture of the drug phenomenon at European level.

The EMCDDA's publications are a prime source of information for a wide range of audiences including: policymakers and their advisors; professionals and researchers working in the drugs field; and, more broadly, the media and general public. Based in Lisbon, the EMCDDA is one of the decentralised agencies of the European Union.

European Monitoring Centre
for Drugs and Drug Addiction

Praça Europa 1, Cais do Sodré, 1249-289 Lisbon, Portugal
Tel. +351 211210200
info@emcdda.europa.eu | www.emcdda.europa.eu
twitter.com/emcdda | facebook.com/emcdda

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At a glance

- Hospital emergency data can provide a unique insight into acute health harms related to drug use.
- Euro-DEN Plus uses a sentinel centre model to collect data on emergency department presentations with acute drug toxicity; at the time of the latest Euro-DEN Plus meeting in Lisbon (end 2018), there were 32 sentinel sites in 22 countries. Before the Euro-DEN project started, there was limited systematic collection of data on acute drug toxicity in Europe.
- There were 23 947 acute drug toxicity presentations reported by the Euro-DEN Plus centres over the 4-year period January 2014 to December 2017, representing a median of 0.3 % of all emergency presentations to the sentinel hospitals.
- More than 7 in 10 people presenting with acute drug toxicity arrived by ambulance, which has pre-hospital resource implications.
- Three quarters of those presenting were male, and presentations were most common among those aged 20-39 years.
- Three quarters of patients were discharged directly from the emergency department, and almost half were discharged within 4 hours. However, almost 1 in 5 of those discharged from the emergency department self-discharged, entailing lost opportunities for brief intervention, referral and care in the community.
- Although only a minority of patients were admitted to hospital, one quarter of those admitted required admission to the critical care unit because of severe clinical features.
- Opioids, and heroin in particular (the latter accounting for 22 % of all presentations), were the drugs most frequently encountered in acute drug toxicity presentations. Cocaine and cannabis were also prominent; these drugs were involved in 19 % and 17 % of presentations respectively.
- New psychoactive substances (NPS) were seen in 9 % of presentations over the 4-year period. There was significant geographical variation in the involvement of NPS in presentations, and the type of NPS that was predominant changed from cathinones in 2014-15 to synthetic cannabinoids in 2016-17.
- More than one quarter of all presentations involved the misuse of at least one prescription medicine, most commonly opioids and benzodiazepines such as methadone, diazepam and clonazepam.
- Presentations with acute drug toxicity constitute a significant burden on emergency health services; agitation and aggression are common features, and presentations are more common at weekends, in the late evening and at night.

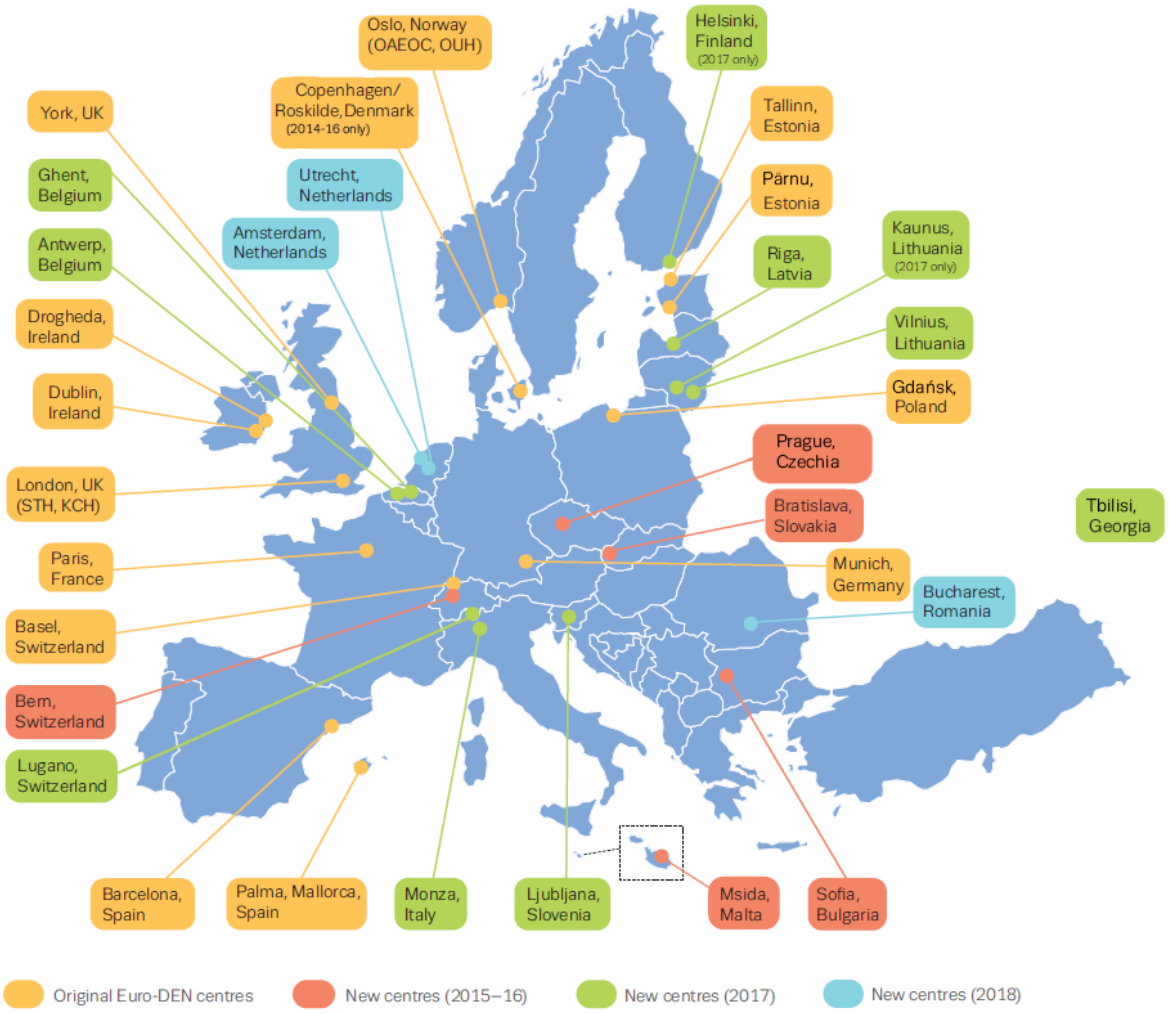
Introduction and objective of this report

There is a significant, multifaceted and rapidly changing social and health burden related to illicit drug use in Europe (EMCDDA, 2019). To monitor this phenomenon and to support evidence-based policies, data are systematically collected and reported to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) on a number of key indicators related to drug use in Europe, including prevalence, both among the general population and of problematic forms, admission to treatment infectious diseases and deaths. The data on these epidemiological key indicators are supplemented with information from data sources that have been developed in recent years to broaden the scope and coverage of the information available. These additional information sources include wastewater analysis (EMCDDA, 2016a, 2018a), internet surveys, forensic and pill testing, trendspotter studies (EMCDDA, 2018b,c) and data on hospital emergencies provided by Euro-DEN Plus (Wood et al. 2014a; Dines et al. 2015a, EMCDDA, 2016b).

The European Drug Emergencies Network (Euro-DEN) was established in October 2013 as a 2-year project funded by the European Commission Directorate-General for Justice, with the aim of improving knowledge at European level on acute established illicit/recreational drug and new psychoactive substance (NPS) toxicity (Wood et al., 2014a). The project has continued with the support of the EMCDDA as the Euro-DEN Plus project since April 2015. Euro-DEN Plus has expanded from the original 16 sentinel centres in 10 European countries in October 2013. In 2018, there were 31 active Euro-DEN Plus sentinel centres collecting data in 21 countries (Figure 1). While two centres (Helsinki in Finland and Kaunas in Lithuania) stopped reporting after 2017, three centres (Amsterdam and Utrecht in the Netherlands and Bucharest in Romania) started to report data for the year 2018. Active recruitment of centres continued in 2019. The methods and added value of the network are described in the box ‘Methods and added value of the Euro-DEN Plus database’.

This report summarises the Euro-DEN Plus data for the 4-year period from 1 January 2014 to 31 December 2017 from the 32 Euro-DEN Plus centres in 21 countries that were collecting data during that period (see Appendix 1). The analysis presented here also draws on scientific presentations (references provided on page 32) and round-table discussions at a 2-day meeting of Euro-DEN Plus researchers, hosted by the EMCDDA in Lisbon on 4 and 5 December 2018.

FIGURE 1
Euro-DEN Plus centres by year of joining, 2013-18



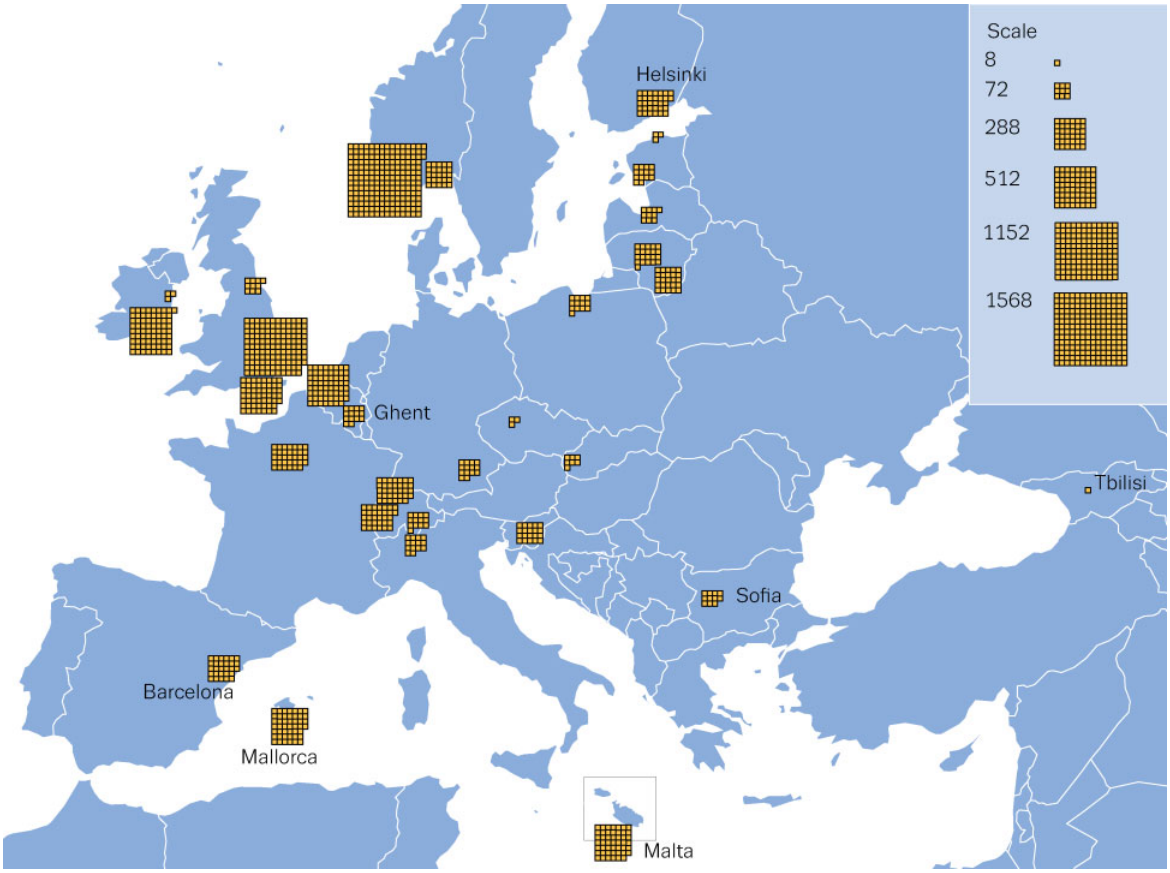
Note: Centres are also located in the non-EU countries of Switzerland (Basel, Bern and Lugano) and Georgia (Tbilisi). Abbreviations — KCH, King's College Hospital, London; STH, St Thomas' Hospital, London; OAEOC, Oslo Accident and Emergency Outpatient Clinic; OUH, Oslo University Hospital.

Methods and added value of the Euro-DEN Plus dataset

Euro-DEN developed a minimum dataset to capture the key demographic, clinical and outcome variables in presentations with acute drug toxicity to emergency departments (Wood et al., 2014; EMCDDA, 2016b). This dataset currently contains 38 data variables. A purpose-designed Microsoft Excel spreadsheet is used to collect these, with pre-formatted variables and drop-down menus to ensure consistency. Each centre has appropriate local ethical approval from their institution for the collection and sharing of the data. The data are collected on all presentations to each sentinel centre's emergency department with acute drug toxicity. Data are collected from information recorded in medical records, and the Euro-DEN Plus data collection sheets are returned every 2 months to the lead centre in London for collation and further analysis.

The recording of the drugs involved in each presentation is based on the patient's self-report and/or the clinical interpretation of the drugs by the clinicians managing the patient and collecting the Euro-DEN Plus data in each centre. If drug screening is undertaken as part of routine clinical care, the results of the screening are collected, but toxicology investigation is not undertaken specifically for the project. This follows international best practice in the management of acute drug toxicity, whereby patients are

FIGURE 2
Number of presentations to Euro-DEN Plus centres, 2017



treated on the basis of the clinical pattern of toxicity and the drugs that the patient reports having used, rather than on the basis of analytical confirmation of the drugs involved.

The criteria used for case definition are set out below.

- Inclusion criteria: presentations are included if the patient has a history of use or clinical features consistent with acute toxicity directly related to illicit drug or NPS use, or if the presentation relates to misuse of a prescription/over-the-counter medicine.
- Exclusion criteria: drug-related presentations are excluded if they are not directly related to acute established illicit/recreational drug or NPS toxicity (e.g. cases of trauma, infection or drug withdrawal) or are the result of self-harm. Cases of alcohol intoxication on its own are also excluded, but data on whether or not alcohol has been co-used in an acute drug/NPS toxicity presentation are collected.
- Of the 16 original Euro-DEN centres, 15 provided data for all 4 years (Roskilde in Denmark was unable to collect data in 2017); five additional centres contributed data for 2016 and 2017, and 10 for 2017 only (Appendix 1). Importantly, the centres have different capacities, catchment areas and locations, as described in the appendix to Euro-DEN's initial report (Euro-DEN, 2015). The number of acute drug toxicity presentations per centre in 2017 is illustrated in Figure 2. There were 4 large centres with 500 or more presentations in that year, 9 centres with 200-499 presentations, 9 with 100-199 presentations and 8 smaller centres with fewer than 100 presentations in 2017.
- The Euro-DEN Plus project monitors, with a high degree of sensitivity, acute drug toxicity presentations to sentinel emergency departments across Europe. Previous studies, including studies from Euro-DEN Plus, have shown that routine hospital statistics significantly under-represent acute drug toxicity presentations; therefore, current national data on acute drug-related harm are likely to underestimate the extent of the problem and provide a biased picture (Wood et al., 2011;

Heyerdahl et al., 2014). The enhanced case-based surveillance provided by Euro-DEN Plus yields a rich core dataset, enabling analysis of geographical variations and time trends in the drugs involved in the presentations and of the patterns of toxicity and the morbidity and mortality associated with these presentations. Euro-DEN Plus data reflect local patterns of drug use and drug-related harm, providing a powerful and valuable triangulation tool at city level. One limitation of this approach is that findings cannot be extrapolated to other cities or to the country in question as a whole. However, the expansion of the network to include multiple centres in some countries has helped to reduce this limitation.

The Euro-DEN Plus dataset provides a unique insight into the drugs responsible for acute drug toxicity in Europe. It is of particular value given the weaknesses of and limited systematic data from other sources on this topic, and has been contributing to EMCDDA-reporting on the drug situation in successive European Drug Reports since 2015. It provides a foundation for developing a better picture of the overall public health implications of drug use in Europe and helps to fill the gaps in our knowledge of the drugs responsible for and the scale of the issues related to acute drug toxicity in Europe. It also adds information that can be triangulated with other indicators. Considering the Euro-DEN Plus results alongside information from wastewater analysis, general population surveys and web survey data enables a greater understanding of the overall public health impact of drug use at population level.

Euro-DEN Plus 4-year dataset: overview

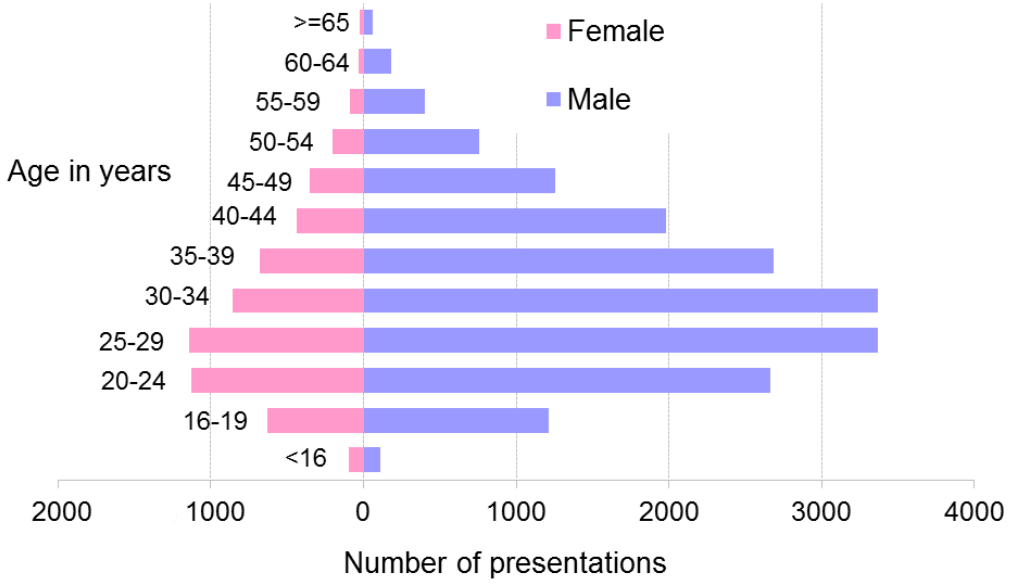
Overview of characteristics of acute drug toxicity presentations in Europe

There were 23 947 acute drug toxicity presentations to the 32 Euro-DEN Plus centres in 21 countries over the 4-year period from 1 January 2014 to 31 December 2017. The burden of these acute drug toxicity presentations as a proportion of all presentations to emergency departments varied across centres. Where the proportion of all emergency department presentations that related to acute drug toxicity was known (26 centres), it ranged from 0.1 % to 3.5 % (median 0.3 %; interquartile range, IQR, 0.2-0.8 %). Overall, 17 066 people presenting with acute drug toxicity (71.3 % of the total) arrived by ambulance, which has clear resource implications.

Demographics

There was a predominance of males among those presenting in all age groups: 76.2 % of Euro-DEN Plus presentations over the 4-year period involved male patients (Figure 3). The majority of those presenting were aged 20 to 39 years (67.0 % of presentations); the median age was 31 years (IQR 25-39 years), with a range of 10-90 years and a modal age of presentation of 25 years. The Euro-DEN Plus cohort is several years younger than the population entering drug treatment — although this differs depending on the drug involved — and much younger than those who die of an illicit drug overdose (the mean age of those dying drug-related deaths in Europe is 39 years) (EMCDDA, 2019). This suggests that there are opportunities to intervene in hospital emergency settings, to assess the risk of drug problems and to offer brief intervention, harm reduction and referral for drug treatment where appropriate. However, the age range of those presenting is wide, and the needs of those older people presenting with acute drug toxicity are likely to differ from those of people in the younger age groups. This is discussed in more detail in the section ‘Acute drug toxicity presentations among those at opposite ends of the age spectrum’, which describes a study highlighting the high proportion of presentations related to cannabis among teenagers.

FIGURE 3
Euro-DEN Plus presentations by age and gender, 2014-17 (*n* = 23 718)

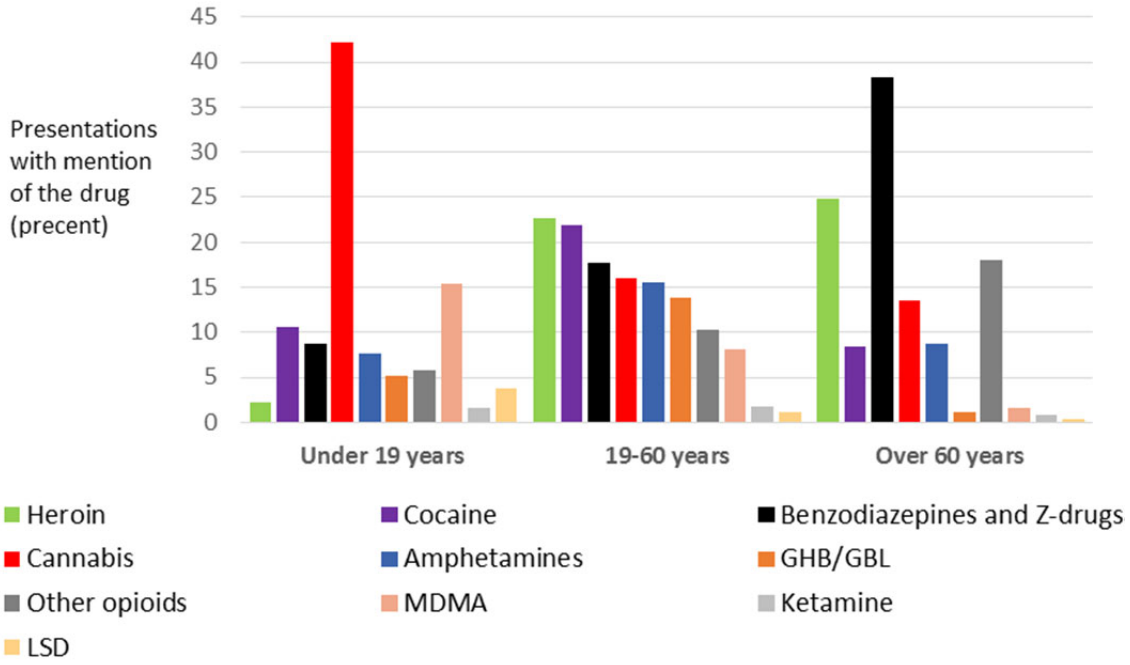


Acute drug toxicity presentations among those at opposite ends of the age spectrum

While there is global interest in drug use by both younger and older individuals, there are few European studies looking specifically at this area and none examining differences in the drugs involved in acute toxicity presentations to emergency departments. Euro-DEN Plus data were analysed to describe acute drug toxicity presentations amongst the youngest and oldest age groups, as this information can inform prevention and harm reduction strategies targeting people of different ages and at different stages in their drug-using history. Presentations reported in the 4-year Euro-DEN Plus dataset were categorised into three age groups — (i) 18 years and under, (ii) 19-60 years and (iii) over 60 years — to examine the demographics of and drugs used by the two extreme age groups, with the middle age group used as a reference comparator.

Of the 23 947 presentations, 1 384 (5.8 %) were by people aged 18 years or under, and 250 (1.0 %) were by people aged over 60 years; in 226 presentations (0.9 %), the age was not recorded. The proportion of females (36.7 %) was significantly higher in the youngest age group than in the middle (23.1 %) and oldest (20.4 %) age groups ($p < 0.05$ based on a chi-squared test). In the youngest age group, the percentages of presentations that involved cannabis (42.2 %), MDMA (15.5 %) and LSD (3.8 %) were significantly higher than in the middle age group, whereas in the oldest age group significantly more of the presentations involved medicines such as benzodiazepines (38.4 %) and opioids other than heroin (18.0 %) (Figure 4). Presentations in both the youngest and oldest groups were less likely to involve cocaine or GHB than those in the middle age group. Members of the youngest group were also less likely to come to the emergency department by ambulance and more likely to be medically discharged from the emergency department (Waring et al., 2020).

FIGURE 4
Proportions of people within each age group reporting each drug in Euro-DEN Plus presentations, for selected substances, 2014-17



Note: A presentation can be associated with more than one drug and thus the total for each age group may be greater than 100 %. The drugs are ordered according to frequency in the middle age group.

These differences between the age groups are consistent with data on the prevalence of use in the general population, which show a decreasing prevalence of cannabis and MDMA use with age and a higher average age of starting using cocaine and heroin. The findings are also consistent with data from drug treatment settings and on drug-related deaths, which both point to an ageing cohort of opioid users who typically are in their 40s and have problematic use of heroin, other opioids and other medicines including benzodiazepines and Z-drugs (EMCDDA, 2019).

Time-trend analysis shows that, in the 15 centres for which data were available for all 4 years, cannabis and benzodiazepines were increasingly involved in presentations in the youngest group over time. These initial findings warrant further analysis and triangulation with other datasets, and they also illustrate the value of continued monitoring over time.

More generally, this analysis shows that while, at the individual level, treatment and referral to care may essentially be determined by the drug causing the acute toxicity, which drugs are most likely to be involved may vary by age. Monitoring and analysis of the demographic characteristics of the presentations can reveal findings that have implications for and can inform the design of harm reduction activities targeted at different groups.

Time patterns in presentations

As shown in Figure 5, there is seasonal variation in presentations to emergency departments for drug toxicity, as well as differences by day of the week and time of day. There were more presentations in the summer months (10.2 % of presentations were in August) than in the winter months (6.6 % of presentations were in February). During the week, a greater proportion of presentations per day were seen at the weekend (17.7 % and 17.5 % of presentations occurred on a Saturday and on a Sunday respectively) than on other days of the week (12.4 % to 14.1 % occurred per day from Monday to Friday). Presentations were also more common in the evening and in the early hours of the morning than during 'core' working hours, which has important implications for the staffing of emergency departments for the management of these presentations. Taken as a whole, these time patterns in presentations to the emergency department with acute drug toxicity suggest that a significant proportion of presentations relate to recreational patterns of drug use, which are more common at these times.

FIGURE 5

Proportions of presentations to the Euro-DEN Plus centres by time of the day (top), day of the week (bottom left) and month of the year (bottom right), 2014-17

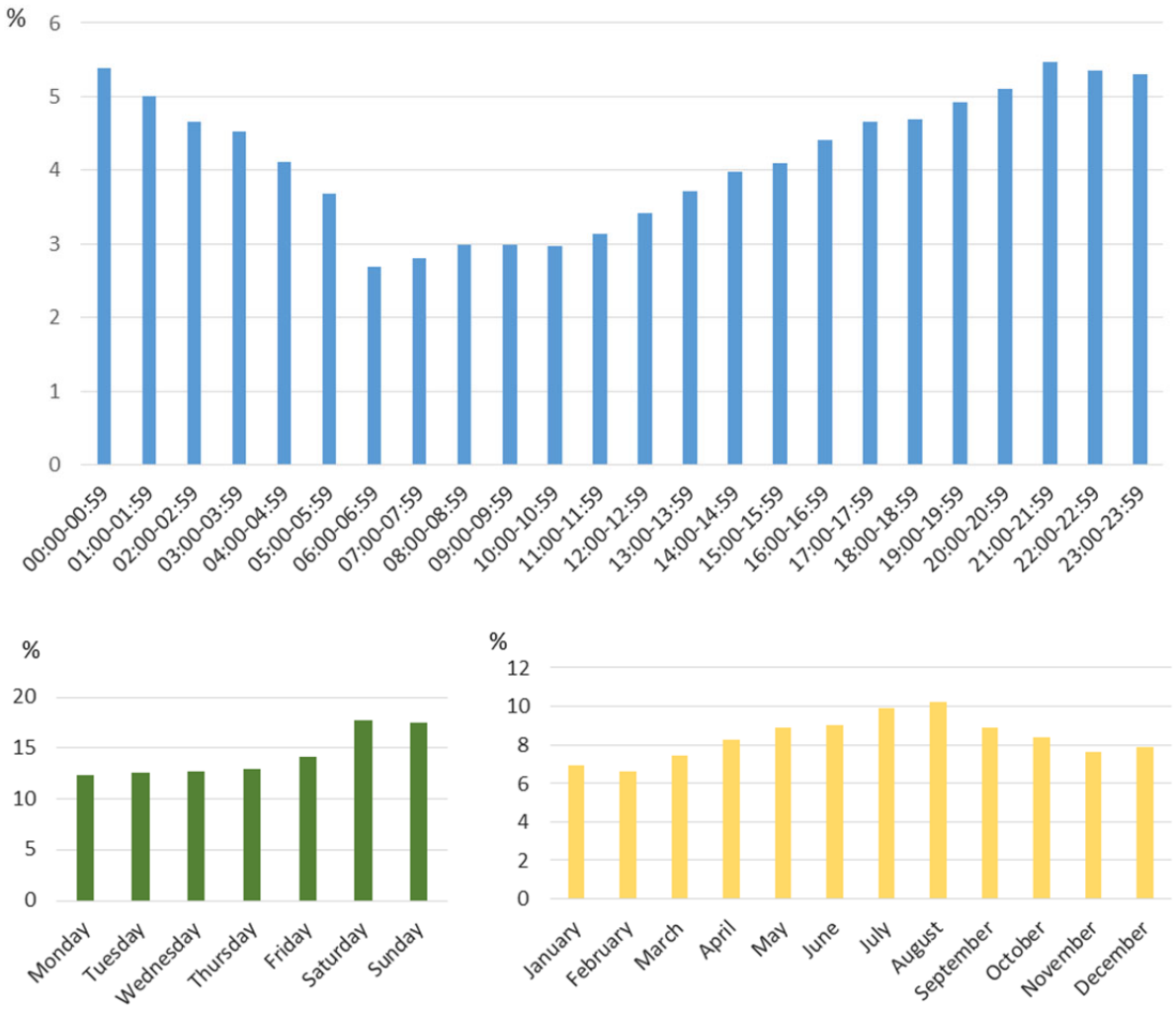
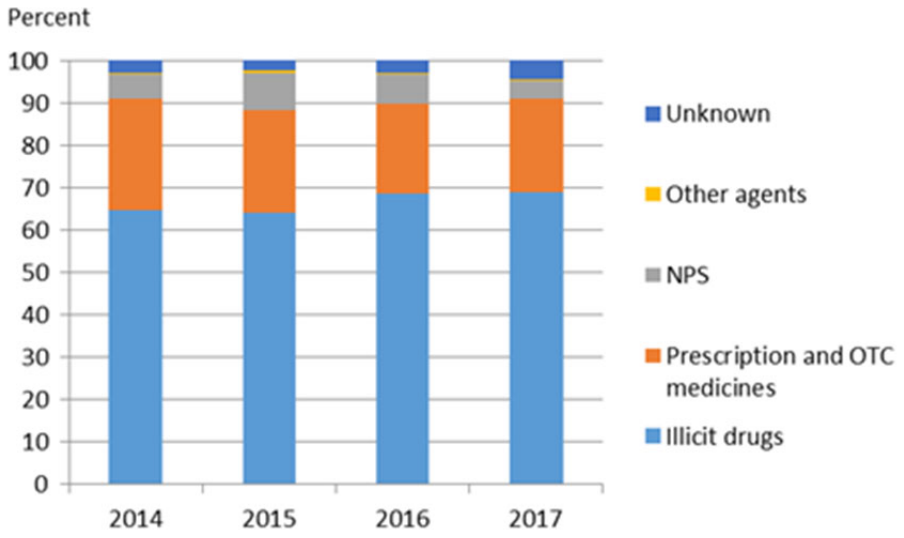


FIGURE 6
Frequency distribution of the main drug groups among all drugs identified in Euro-DEN Plus presentations, 2014-17



Drugs involved in emergency department presentations

The majority of the 23 947 presentations over the 4 years of data collection involved one (63.4 %) or two (25.7 %) drugs; only 8.0 % involved three drugs; and 2.9 % involved four or more. Overall, there was a mean of 1.5 drugs (standard deviation, SD, ± 0.8 drugs) (excluding alcohol) per presentation. Whether or not alcohol was involved in the presentation was not recorded in a little under one third of presentations; in the 16 860 presentations (70.4 % of the total) for which this information was recorded, alcohol had been used in 59.0 %.

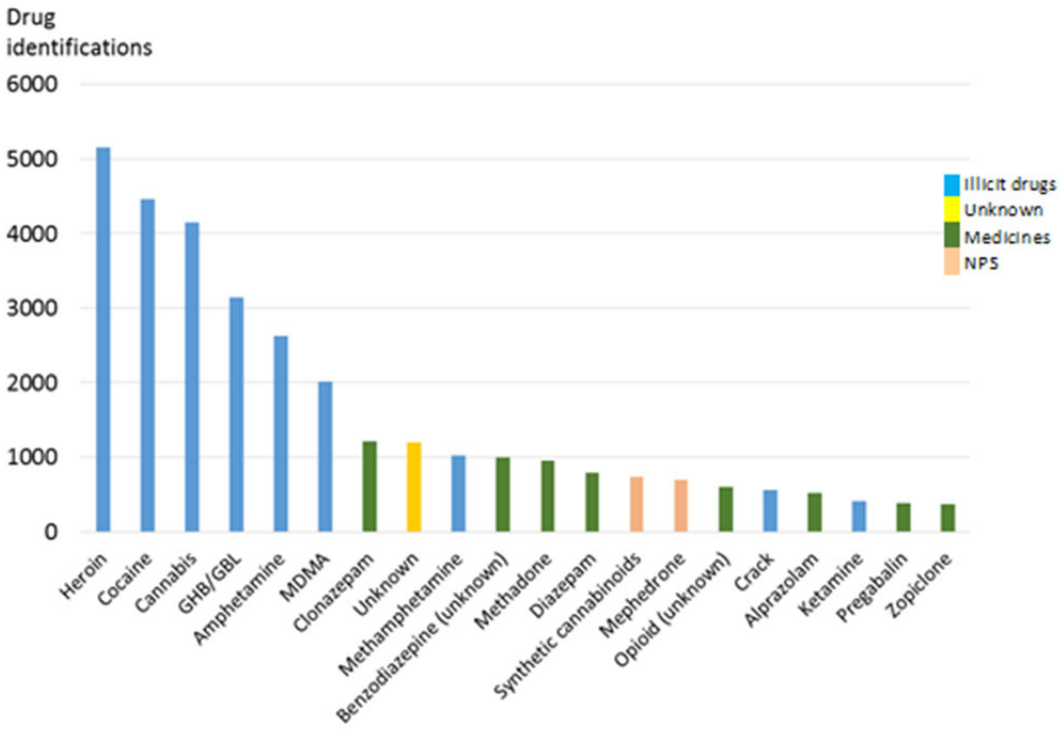
Drug categories

As shown in Figure 6, the drugs involved in the presentations were predominantly established illicit drugs (66.9 % of drugs identified in presentations) or prescription/over-the-counter (OTC) medicines (23.0 %). It is important to note that prescription/over-the-counter medicines are included only if the presentation involved misuse of the drugs. NPS accounted for only 6.2 % of the drugs involved in the presentations. When comparing years, it is important to remember that the centres reporting varied from year to year, which may have had an impact on the substances involved in presentations because of geographical variations in drug use.

Top 20 drugs

Overall, heroin, cocaine, cannabis, GHB/GBL, amphetamine and MDMA are the most frequently reported drugs (Figure 7). This reflects both the health risks associated with use of these drugs (heroin in particular) and also the high prevalence of use (for cocaine and cannabis). GHB/GBL is the fourth most frequently reported drug, although, according to the available data, the prevalence of its use in the general population is low. However, it is important to note that most cases are reported by one London centre. This centre serves an extensive area of nightlife activity, where the drug is more commonly used, and this is reflected in the type of acute toxicity episodes seen in the centre. Amphetamine and MDMA are the fifth and sixth most frequently reported drugs, but, as with other drugs, their frequency varies by centre.

FIGURE 7
Top 20 drugs involved (number of reports) in Euro-DEN Plus presentations, 2014-2017



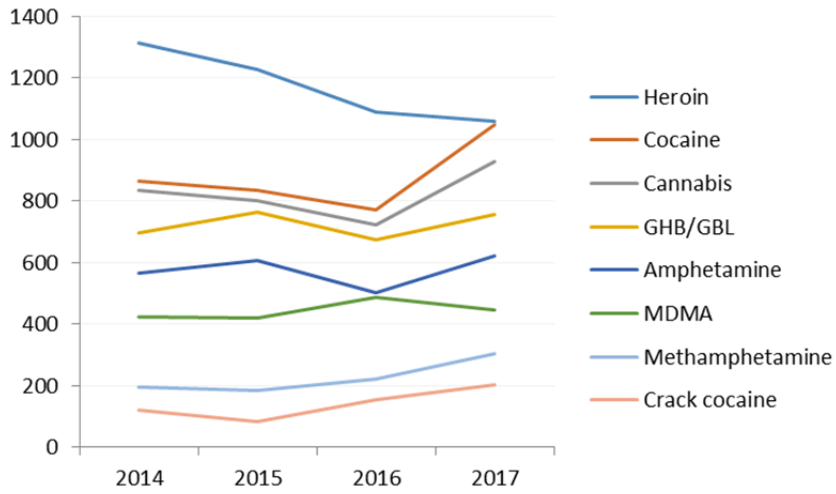
Note: Out of 36 232 drugs reported (excluding alcohol) involved in 23 947 presentations.

Of the 20 most frequently reported drugs, 4 are benzodiazepines (clonazepam, 'benzodiazepine unknown or unspecified', diazepam and alprazolam), with a total of 3 513 reports, and clonazepam is the seventh most frequently reported drug (Figure 7). This shows the importance of this group of medicines with regard to drug-related acute poisonings. Other medicines, including methadone but also pregabalin and zopiclone, are frequently reported as well. Two NPS feature in the list of the most frequently identified drugs: mephedrone and synthetic cannabinoids.

The profiles of acute toxicity presentation vary by hospital, as described later in this report with a focus on four large centres that represent half of all presentations in 2017 (see 'Geographical variation and city profiles', page 20). This complements and provides local-level insights into the top 20 drugs for the 4-year dataset shown in Figure 7.

An analysis of trends in the most common substances seen in the 15 centres reporting data for all 4 years from 2014 to 2017 (Figure 8) shows a variety of trends: reports of heroin declined over the whole period (but with perhaps early signs of flattening out in 2017); reports of cocaine powder and cannabis declined slightly up until 2016 but then increased in 2017; reports of crack cocaine and methamphetamine declined or were stable early on but have increased since 2015; reports of GHB/GBL, amphetamine and MDMA have fluctuated year on year but have overall remained fairly stable. These findings are consistent with other indicators suggesting a rebound in the powder and crack cocaine market and associated use and harm over recent years in Europe (EMCDDA, 2018c); with regard to heroin, this change is consistent with other indicators on treatment demand (EMCDDA; 2019).

FIGURE 8:
Number of presentations involving selected drugs to the 15 Euro-DEN Plus sentinel hospitals that have reported data since 2014



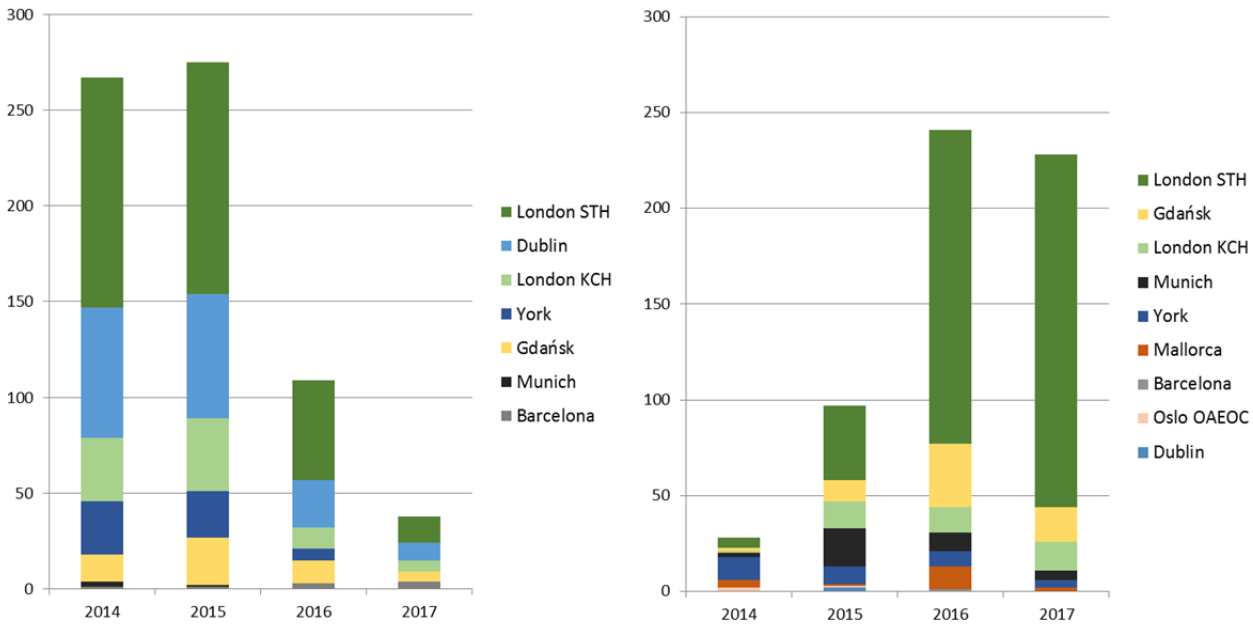
In the following subsections, more detailed consideration is given to patterns of presentations for NPS, prescription medicines, MDMA, cocaine and GHB/GBL. These substances were the subject of contributions at the 2018 Euro-DEN Plus meeting in Lisbon in December 2018, and those contributions have been used as the basis of the analysis included in this report.

New psychoactive substances

Overall, NPS were involved in only 9.1 % of all 23 947 presentations (accounting for 6.2 % of all drug identifications), but there was significant geographical variation, with 6 centres reporting no presentations involving an NPS, 16 centres reporting less than 5 % of presentations involving an NPS and 6 centres reporting more than 20 % of presentations involving an NPS.

The two most common categories of NPS involved in the presentations were cathinones and synthetic cannabinoids; however, as shown in Figure 9, among the 15 centres reporting data for all 4 years from 2014 to 2017, these presentations were concentrated in a small number of centres, with only 8 centres reporting presentations involving mephedrone (the most commonly reported cathinone, involved in 71.1 % of all cathinone presentations) and 9 centres reporting presentations involving synthetic cannabinoids. London, Dublin and York reported most mephedrone presentations, while London, Gdańsk and Munich reported most synthetic cannabinoid cases. There was an overall shift towards a decrease in the number of mephedrone cases and an increase in the number of synthetic cannabinoid cases from 2014 to 2017. The shift was visible mainly in the two London centres and — although the numbers were smaller — in the Gdańsk centre (Figure 9).

FIGURE 9:
Presentations related to mephedrone (left) and synthetic cannabinoids (right) in the 15 hospitals that reported every year from 2014 to 2017



Note: KCH, King's College Hospital; OAEOC, Oslo Accident and Emergency Outpatient Clinic; STH, St Thomas' Hospital.

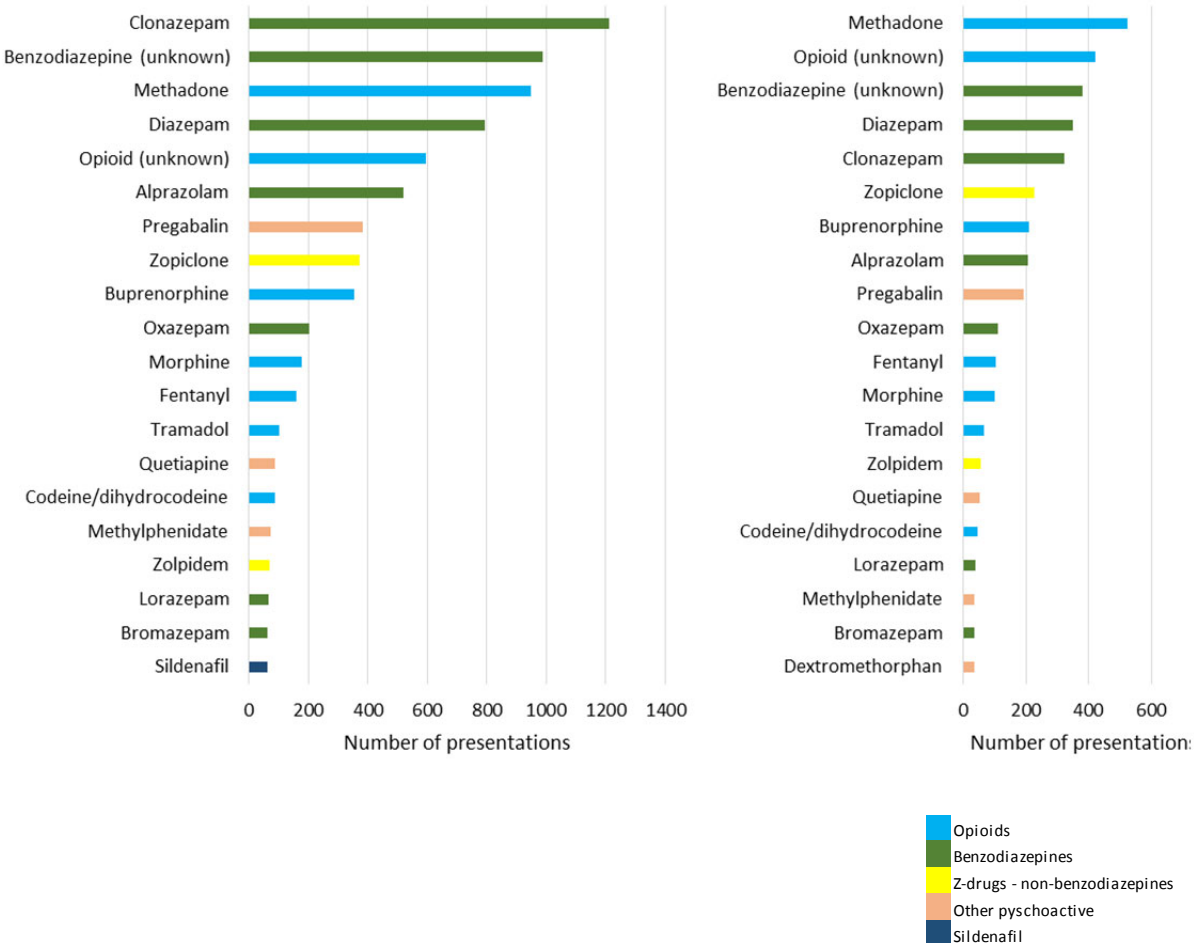
There was a significant change in the proportions of presentations involving these two NPS categories over the 4-year period. In 2014, 76.9 % (400) of the 520 NPS presentations involved a cathinone, with only 5.4 % involving a synthetic cannabinoid; conversely, in 2017 only 17.2 % (82) of the 476 NPS presentations involved a cathinone, while 69.5 % involved a synthetic cannabinoid. The number of presentations related to synthetic cannabinoids increased markedly from 28 cases in 2014 to 228 cases in 2017 among the 15 centres reporting data for all 4 years from 2014 to 2017 (Figure 9, bottom panel). While these two substances are plotted together, it is not likely that the change in NPS involved in Euro-DEN Plus presentations relates to the same population switching NPS, particularly as there has been a change in the geographical distribution of presentations (Figure 9). It is more likely that this relates to differences in the NPS used among different sub-populations, with use of synthetic cannabinoids more common among those who are socially marginalised, for instance prisoners and homeless drug users.

Prescription medicines

Some prescription and over-the-counter registered medicines (hereafter referred to as prescription medicines) have potential for misuse. They are included in the Euro-DEN Plus dataset only if they are identified as having been misused and involved in Euro-DEN Plus presentations.

Of the 23 947 presentations in the 4-year Euro-DEN Plus dataset, 6 207 (25.9 %) involved at least one prescription medicine, and of these almost half (2 876; 46.3 % — 12 % of all presentations) involved only prescription medicines, with no other established illicit/recreational drug or NPS. The people presenting with toxicity in which only prescription medicines were involved were slightly older (median age 34 years, IQR 28-43 years) than those presenting overall (median age 31 years, IQR 25-39 years), and the proportion of women was higher (31.6 % in the prescription-only group, compared with 23.8 % for all Euro-DEN Plus presentations). There was considerable variation between Euro-DEN Plus centres in the proportion of presentations involving only prescription medicines, with these making up less than 10 % of presentations in nine countries (Belgium, Bulgaria, Italy, Malta, Poland, Slovakia,

FIGURE 10
Top 20 prescription medicines involved in 'any prescription medicine' presentations (left) and 'prescription medicine only' presentations (right), Euro-DEN Plus, 2014-17



Spain, Switzerland and the United Kingdom) and more than 25 % of presentations in five countries (Czechia, Estonia, Finland, Germany and Latvia).

There were 209 different prescription medicines involved in Euro-DEN Plus presentations; the most common were benzodiazepines (51.3 % of the 2 876 presentations involving only prescription medicines and 6.3 % of all 23 947 Euro-DEN Plus presentations), opioids (50.1 % and 6.1 %), Z-drugs (9.8 % and 1.2 %) and GABA-ergic drugs (7.3 % and 0.9 %) (Figure 10).

MDMA

The MDMA market in Europe has changed in recent years, and there has been an increase in higher-dose pills and concentrated powders (EMCDDA, 2016c,, 2019). The characteristics of and changes in presentations involving MDMA to Euro-DEN Plus over the 4 years from 2014 to 2017 need to be viewed in this context. Overall, over this period, 2 013 (8.4 %) of the 23 947 Euro-DEN Plus presentations involved MDMA. The proportion of presentations involving MDMA varied across the centres, from over 10 % in Belgium, Czechia, Denmark, France, Slovakia and the United Kingdom to less than 5 % in Bulgaria, Finland, Germany, Latvia, Lithuania, Norway and Poland.

On average, those who presented with MDMA-related acute toxicity tended to be younger and were more likely to be female: the median age of those presenting with MDMA-related toxicity was 24 years (IQR 20-29 years), compared with 32 years (IQR 25-40 years) for the overall dataset, and 28.7 % were female, compared with 23.8 % in the overall dataset. Almost all MDMA intoxications occurred in the context of polysubstance use; only 4.4 % of presentations involving MDMA involved use of MDMA

alone, whereas 36.4 % of all presentations in the dataset involved use of one substance on its own. In the cases associated with polysubstance use, alcohol was by far the most common substance co-ingested with MDMA (70.4 % of MDMA presentations involving other substances), followed by cocaine (25.6 %), cannabis (14.6 %) amphetamine/methamphetamine (14.1 %), benzodiazepines/Z-drugs (7.2 %), GHB/GBL (6.8 %) and ketamine (5.3 %). Acute MDMA toxicity was characterised by sympathomimetic effects: agitation/aggression (32.7 %), anxiety (26.4 %), palpitations (14.1 %), hypertension (8.8 %), chest pain (8.5 %) and hyperthermia (2.4 %) (Noseda et al., 2020).

When the presentations to the 15 centres that reported data for all 4 years are considered, the overall proportion of MDMA presentations remained constant between 2014 and 2015 (8.2 % and 8.3 % respectively), increased to 10.4 % in 2016 and returned to 8.2 % in 2017 (see Figure 8).

Powder cocaine and crack cocaine

In recent years, there have been indications of increasing cocaine availability in Europe as well as pockets of increasing crack cocaine use in some parts of the region (EMCDDA, 2018c). An in-depth study of the 17 371 Euro-DEN Plus presentations between October 2013 and December 2016 found that 3 002 (17.3 %) involved cocaine (powder cocaine, 2 600; crack cocaine, 376; both, 26) (Miró et al., 2019). The demographics, the clinical picture and emergency department management for these presentations were analysed, and the clinical features seen in the powder and crack cocaine presentations were compared using multivariate adjustment to control for the co-ingestion of alcohol and other drugs.

Overall, the people presenting with acute toxicity associated with cocaine use had a mean age of 32 years (SD ± 9 years) and 23 % were female. The proportion of presentations involving cocaine varied significantly between countries (> 30 % of presentations in Denmark, France, Malta and Spain), and only centres in France, Ireland, Malta, Poland and the United Kingdom reported crack cocaine cases. There were differences in the drugs that were co-ingested with powder cocaine and with crack cocaine and in the clinical features of the presentations involving these two substances (Table 1). Patients who presented with crack cocaine toxicity were more likely to have used other drugs, particularly opioids, while they were less likely to have ingested alcohol.

TABLE 1
Numbers of cases with and frequencies of (i) co-ingestion of certain substances and (ii) occurrence of certain clinical features, for presentations related to powder cocaine and crack cocaine (Euro-DEN Plus presentations between October 2013 and December 2016)

	All presentations involving cocaine *n* = 3 002 (%)	**Powder cocaine *n* = 2 600 (%)**	**Crack cocaine *n* = 376 (%)**	**Adjusted odds ratio; 95 % confidence interval**
Co-ingestion				
Co-ingestion of alcohol	1 759 (58.6)	1 557 (59.8)	189 (50.3)	
Co-ingestion of any other drug (apart from alcohol and cocaine)	1 705 (56.8)	1 431 (55.0)	248 (66.0)	
Amphetamine and related substances	581 (19.4)	574 (22.1)	7 (1.9)	
Opioids	566 (18.9)	394 (15.2)	172 (45.7)	
Clinical features				
Hypotension (systolic blood pressure < 80 mmHg)	110 (3.9)	86 (3.5)	23 (7.1)	2.35; 1.42-3.89
Bradypnoea (respiratory rate < 12/minute)	80 (3.8)	58 (3.2)	22 (7.8)	1.81; 1.03-3.16
Hypertension (systolic blood pressure > 180 mmHg)	44 (1.7)	32 (1.4)	12 (3.8)	2.59; 1.28-5.25
Anxiety	868 (32.2)	809 (32.4)	57 (17.6)	0.51; 0.38-0.70
Chest pain	500 (17.6)	467 (18.7)	30 (9.3)	0.47; 0.31-0.70
Palpitations	476 (16.7)	445 (17.8)	31 (9.6)	0.57; 0.38-0.84
Vomiting	261 (9.7)	244 (9.8)	17 (5.3)	0.54; 0.32-0.90
Tachycardia (heart rate > 100 bpm)	1 107 (40.9)	1 015 (42.9)	87 (27.59)	0.51; 0.39-0.67

Sedative drugs were given in 29.3 % of presentations involving cocaine. The median length of hospital stay was 4 hours and 2 minutes; 22.1 % of patients were admitted to hospital from the emergency department; and 0.4 % (*n* = 12) died (all of whom had powder cocaine-related toxicity).

GHB/GBL

GHB/GBL are among the most frequently reported drugs in the Euro-DEN Plus dataset, involved in 13.1 % of presentations, although most cases were from just two or three centres. An analysis of the differences in the clinical manifestations produced by intoxication with GHB/GBL alone and in combination with other substances, based on the data from the first year of the project (October 2013 to September 2014) (Miró et al., 2017), found that in the 710 GHB/GBL presentations reported the most frequently co-ingested substances were alcohol (50 % of presentations), amphetamines (36 %), cocaine (12 %) and cannabis (8 %). The three most frequently identified clinical features were altered behaviour (39 %), reduced consciousness (34 %) and anxiety (14 %). The severity ranged from mild cases requiring no treatment (43.4 %) to severe cases requiring admission to intensive care (14.6 %) and mechanical ventilation (6.9 %). No deaths were reported. In comparison with presentations involving GHB/GBL alone, the GHB/GBL presentations involving other substances (alcohol or drugs) were more likely to involve vomiting (15 % versus 3 %, $p < 0.001$) and 'other cardiovascular features' (e.g. palpitations, chest pain, arrhythmias) (5.3 % versus 1.5 %, $p < 0.05$), a greater need for treatment (59.8 % versus 48.3 %, $p < 0.01$) and a longer length of hospital stay (hospital of stay of > 12 hours, 11.3 % versus 3.6 %, $p < 0.01$).

The clinical impact of the co-ingestion of alcohol in those with acute GHB/GBL toxicity was also studied using Euro-DEN Plus data for the period October 2013 to December 2016 (Galicia et al., 2019). Of the 17 371 Euro-DEN Plus presentations in this period, 2 349 involved GHB/GBL. Whether or not alcohol was involved was known for 1 882 presentations of these presentations. While 1 273 of these involved GHB/GBL and other drugs, the remaining 609 presentations involved no drug other than GHB/GBL. Of these, 183 involved GHB/GBL alone and 426 involved GHB/GBL with alcohol. Presentations involving co-ingestion with alcohol generally related to younger patients than those involving GHB/GBL alone, and these patients were more likely to arrive at the emergency department by ambulance (86.6 % versus 68.3 %; $p < 0.001$) and less likely to have bradycardia (15.7 % versus 23.5 %; $p = 0\ 027$) and/or a reduced level of consciousness (Glasgow Coma Score < 13 points, 58.9 % versus 49.1 %; $p = 0.031$). Those presenting with alcohol co-ingestion were also more likely to receive treatment (60.4 % versus 49.2 %; $p = 0.011$) — specifically sedatives (20.1 % versus 12.8 %; $p = 0.034$) — be admitted to critical care (55.3 % versus 22.4 %; $p < 0.001$) and have a hospital stay lasting longer than 6 hours (28.4 % versus 16.9 %; $p = 0.003$).

Geographical variation and city profiles

There is geographical variation in the proportions of presentations involving the main drug groups across the Euro-DEN Plus centres (Figure 11 and Appendix 2). The geographical patterns found in presentations related to stimulants reflect those found in other indicators such as the prevalence of use of stimulants reported in general population surveys and other indicators (e.g. web surveys and wastewater analysis), as reported in the *European Drug Report 2019* (EMCDDA, 2019). Amphetamines are most common in the north and east of Europe, whereas presentations related to cocaine are predominant in the south and west of Europe (EMCDDA, 2019).

In addition to this geographical variation seen across countries, there are also differences between Euro-DEN Plus centres that may reflect variations in hospital catchment areas and local patterns of use, for example the NPS trends discussed on page 15.

Beyond age and gender, the profiles of those presenting with drug acute toxicity vary, as illustrated by the data from the centres with the largest numbers of cases: Oslo, Oslo Accident and Emergency Outpatient Clinic (OAEOC); Dublin; London, St Thomas' Hospital (STH); and Antwerp. In Oslo and Dublin, heroin is the drug primarily involved. In both centres, a stimulant was the second most frequently reported drug, but the drug involved differed: amphetamine in Oslo and cocaine in Dublin. Both sites had medicines as the third most frequently involved drug: clonazepam in Oslo and zopiclone in Dublin. Other depressant drugs (methadone, other prescription opioids and benzodiazepines) and other medicines were also frequently reported in both centres. In contrast, London STH and Antwerp reported primarily stimulant and recreational drugs. GHB/GBL, cocaine and synthetic cannabinoids were predominant in London STH, while cocaine, cannabis and amphetamines were the most common drugs in Antwerp (Figure 12).

FIGURE 11

Frequencies of cocaine, amphetamine and methamphetamine presentations (percentage of presentations), aggregated by country, 2017

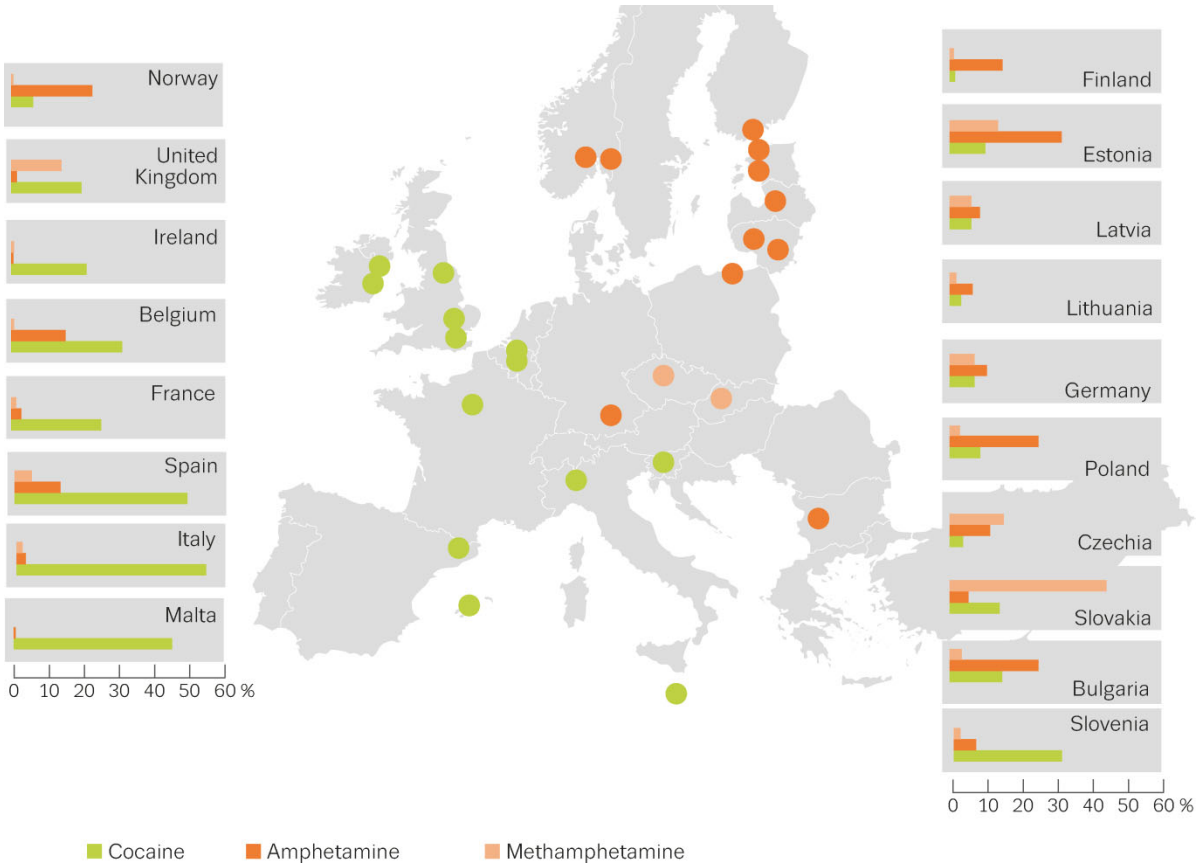
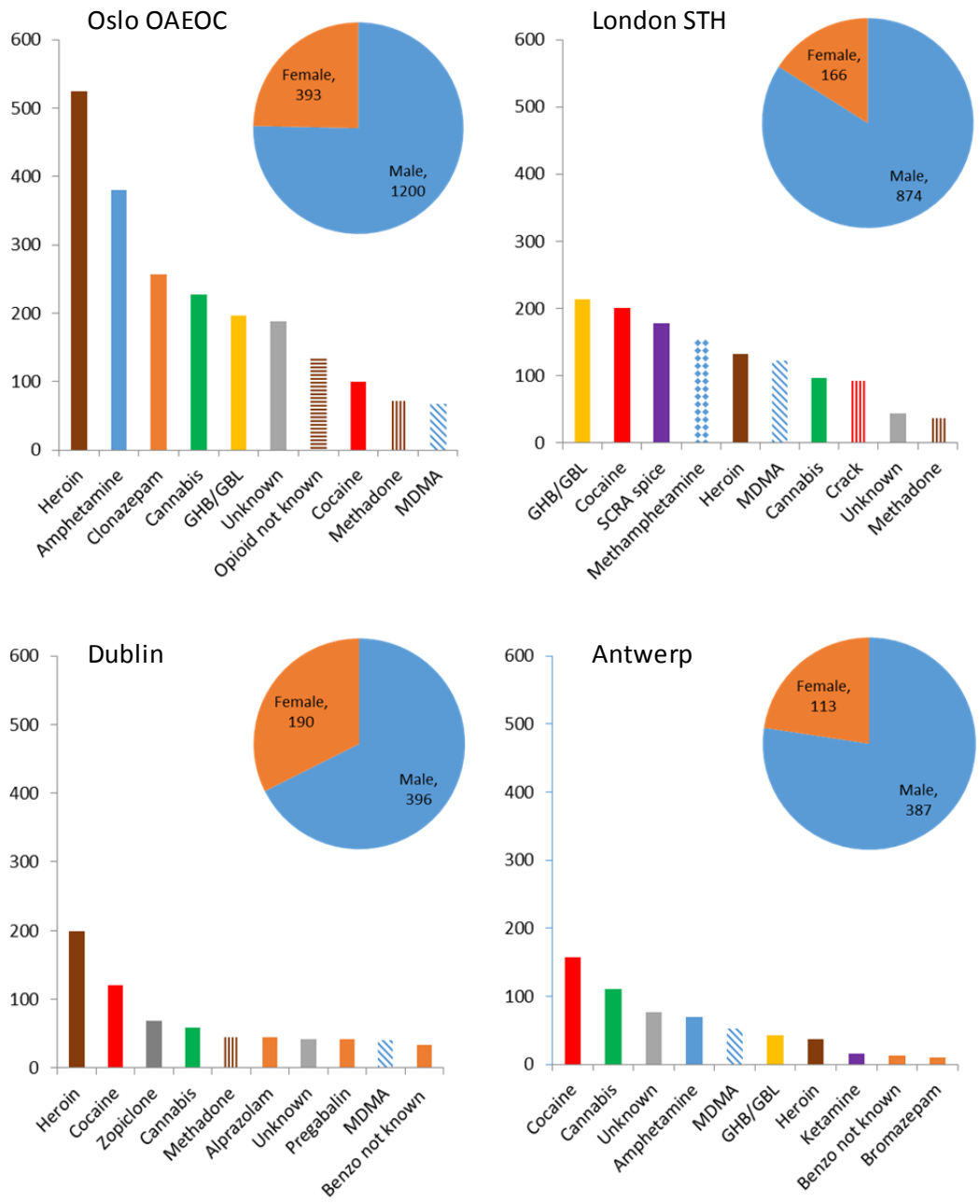


FIGURE 12
Age, gender and main drugs involved in the presentations in selected centres, Euro-DEN Plus, 2017

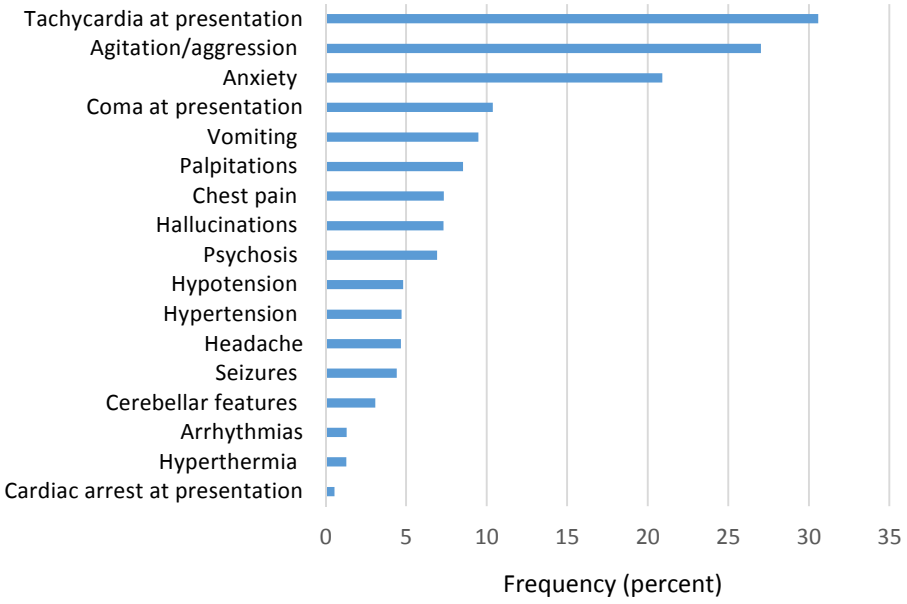


Oslo OAEOC — median age 33 years (IQR 27-42 years); Dublin — median age 31 years (IQR 25-38 years); London STH — median age 32 years (IQR 26-40 years); Antwerp — median age 32 years (IQR 25-39 years).

Clinical features

Data are collected for all Euro-DEN Plus presentations on whether or not the patients develop pre-defined clinical features during their hospital stay (Wood et al., 2014a). Figure 13 shows the proportion of patients who developed certain symptoms and/or had these or other abnormal physiological symptoms on presentation. As several features may be reported for one presentation, the totals are greater than the total number of presentations. While the clinical features are drug-dependent, as could be seen above with regard to powder cocaine, crack cocaine and GHB, the most commonly reported features overall were tachycardia (heart rate > 100 bpm) on presentation, agitation and anxiety, all

FIGURE 13
Clinical effects reported in presentations to Euro-DEN Plus centres, 2014-17



associated with stimulant toxicity; these were each recorded in over 20 % of presentations. Severe clinical features including coma, psychosis, seizures and arrhythmias were less frequent, seen in 5-10 % of presentations; however, these are important, as they have implications for service organisation and resourcing. Agitation and psychosis can be particularly problematic in patients with acute drug toxicity, requiring the involvement of several members of staff.

Most of those presenting (54.6 %) received some active treatment over and above observation; data are collected on five types of treatment (sedation, intubation, naloxone (antidote to opioids), flumazenil (antidote to benzodiazepines) and 'other antidotes'). Of these, the most common were sedation (39.5 % of those treated) and naloxone (29.3 %); of those receiving naloxone, two thirds received it in the pre-hospital setting. Smaller proportions were intubated (6.1 % of those treated) or received flumazenil (3.9 %).

Synthetic cannabinoids versus cannabis: a comparison

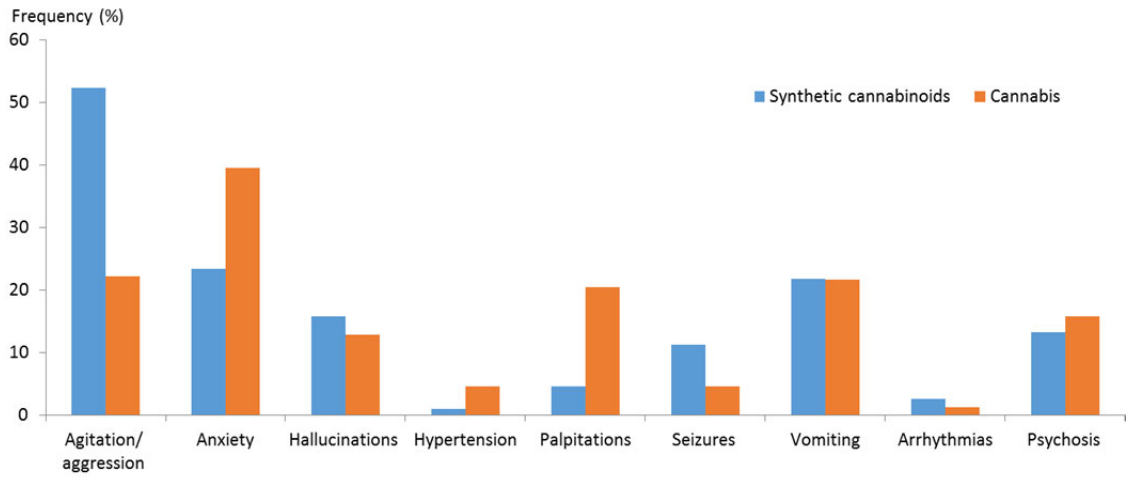
Synthetic cannabinoids are the largest group of NPS reported to the EMCDDA European Early Warning System (EMCDDA and Europol, 2019), and numerous recent case reports and small case series have confirmed the potential for severe toxicity, including fatalities, associated with the use of second and particularly third generation synthetic cannabinoids. As shown above (see page 15), synthetic cannabinoid reports increased within the Euro-DEN Plus dataset, and they became the NPS most commonly involved in Euro-DEN Plus presentations in 2016 and 2017. Only one previous study has compared acute synthetic cannabinoid and acute cannabis toxicity presentations; this study was limited by its small size (17 presentations involving a synthetic cannabinoid) and the presence of co-ingestants (Zaurova et al., 2016).

The demographic and clinical characteristics of Euro-DEN Plus presentations involving synthetic cannabinoids and cannabis were compared. Cannabis was involved in presentations to all 31 Euro-DEN Plus centres, with 4 153 presentations (17.3 % of all presentations) during the 4-year period between 1 January 2014 and 31 December 2017. In comparison, synthetic cannabinoids were involved in 737 presentations (3.1 % of all presentations) to only 13 centres (42 % of all centres) over the 4-year period. The majority of the presentations involving a synthetic cannabinoid were seen in the Euro-DEN Plus centres in the United Kingdom and Malta; these presentations accounted for over 80 % of all Euro-DEN Plus synthetic cannabinoid presentations (Figure 14).

The most commonly co-used substance for both cannabis and synthetic cannabinoids was cocaine, which was associated with 63 % of synthetic cannabinoid receptor agonist (SCRA) cases and with 34 % of cannabis cases. Amphetamine was associated with 21 % of SCRA cases and 20 % of cannabis cases. In contrast to cocaine, heroin was more likely to be involved in polydrug cannabis presentations (15 % of cases) than in polydrug synthetic cannabinoid presentations (5 %). Excluding alcohol, cannabis was reported as the only substance in 49 % of cannabis presentations, whereas synthetic cannabinoids, when reported, were more commonly the only drug involved (82 % of the 737 presentations involving a synthetic cannabinoid involved only a synthetic cannabinoid). Cannabis and synthetic cannabinoids were reported together in only 54 presentations over the 4-year period.

Preliminary findings demonstrate different demographics and clinical characteristics for cannabis-only and synthetic cannabinoid-only presentations. Among the cannabis presentations, 76 % involved males, compared with 88 % of the SCRA presentations, while the mean age was 28.8 years (SD ± 10.6 years) for cannabis and 32.0 years (SD ± 10.8 years) for synthetic cannabinoids. Clinical characteristics were different too. The most frequently observed clinical features among the synthetic cannabinoid only presentations were agitation (52 %), anxiety (23 %), vomiting (21 %) and hallucinations (15 %). For cannabis-only presentations, anxiety (39 %), agitation (22 %), vomiting (22 %) and palpitations (20 %) were the most common clinical features (Figure 14). These findings on cannabis-only presentations over 4 years were consistent with the findings of an earlier analysis of the Euro-DEN cases, which showed that agitation, aggression and anxiety were prominent clinical features (Dines et al., 2015b). Those presenting with synthetic cannabinoid toxicity were more likely to arrive by ambulance, to present with seizures and to require intubation. Furthermore, presentations involving synthetic cannabinoids more frequently resulted in admission to hospital or self-discharge from the emergency department than presentations involving only cannabis.

FIGURE 14
Most frequently observed clinical features among Euro-DEN Plus presentations involving only synthetic cannabinoids and Euro-DEN Plus presentations involving only cannabis, 2014-17



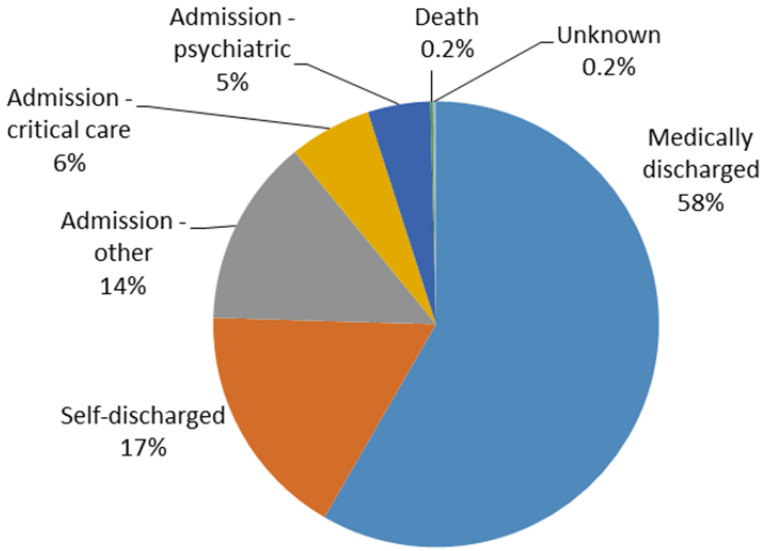
Outcomes

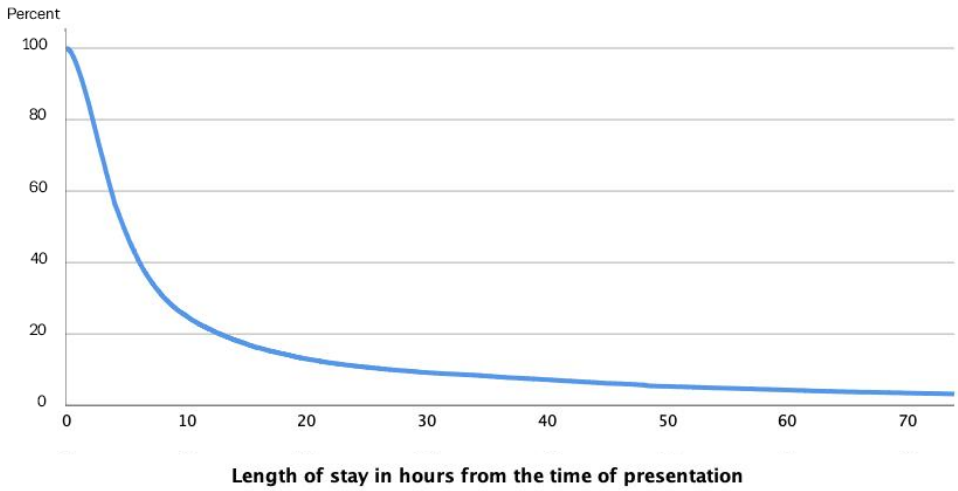
Discharge from the emergency department

Three quarters (76 %) of patients were discharged directly from the emergency department; the majority were medically discharged and 17.1 % were self-discharged (Figure 15 and the box 'Self-discharge in the Euro-DEN Plus dataset'). Of the 5 778 patients admitted, 24.8 % went to critical care because of severe clinical features and 4.5 % went to a psychiatric ward.

The length of hospital stay is defined as the time from presentation to the emergency department to discharge from the hospital. As shown in Figure 15, 88.9 % of presentations were discharged within 24 hours. Overall, the median length of stay was 4 hours 45 minutes (IQR 2 hours 34 minutes to 9 hours 59 minutes), and the range was 2 minutes to 206 days.

FIGURE 15:
Outcome of presentation (top) and length of hospital stay (bottom), Euro-DEN Plus presentations, 2014-17





Self-discharge in the Euro-DEN Plus dataset

Self-discharging patients leave the medical facility against medical advice or before seeing a doctor. This has significant clinical implications, as some of these patients are likely to need longer observation or specific treatment. It also entails missed opportunities to offer brief interventions or identify patients for possible referral to community services. In the 4-year dataset, 4 098 (17.1 %) of the 23 947 presentations self-discharged from the emergency department. There were large variations in self-discharge rates between the centres, with the highest reported by the Munich centre (66.4 %), Prague, Dublin, Gdańsk and Kaunas, where more than one quarter of presentations were self-discharged. There were no self-discharging patients at the centres in Sofia and Tbilisi, and less than 1 in 10 patients discharged themselves from the centres in Tallinn, Barcelona, Oslo (Oslo University Hospital), Riga, Lugano, Pärnu, Mallorca, Bern, Antwerp, Ghent, Bratislava, London (King's College Hospital) and Basel (Vallersnes et al., 2020).

Deaths

There were 101 deaths reported (deaths were recorded if they occurred after presentation to the emergency department and before discharge from hospital), giving an overall fatality rate of 0.4 %. Of these deaths, 47 occurred within the emergency department and 54 after admission to hospital; 32 of the deaths occurred 24 hours or more after hospital presentation.

The majority of patients who died — 68 of 101 patients (67.3 %) — arrived in the emergency department in cardiac arrest. Most (74, or 73.3 %) of the deaths were in males, which is consistent with the sex profile of the presentations, and the median age at death was 36 years (IQR 30.0-41.5 years, range 18-63 years); those who died were slightly older than the cohort as a whole (median age 31 years, IQR 25-39 years). This could be because of the predominance of opioids and heroin in presentations that result in death.

The drugs most commonly involved in deaths were opioids (53 deaths; including 25 with heroin and 15 with methadone) and stimulants (31 deaths; most commonly involving cocaine, amphetamine or MDMA). NPS were involved in 10 deaths, and the most common NPS was mephedrone, which was involved in 5 deaths. A synthetic cannabinoid was reported in only one death (in combination with methadone).

Seizures: drugs responsible and clinical importance

Seizures are a recognised and potentially serious complication of recreational drug use. An analysis was conducted that compared Euro-DEN Plus presentations with and without seizures and estimated seizure incidence for different drugs involved in presentations in which no other drug was involved (regardless of whether alcohol was present or not) (Wolfe, 2019) (Table 2).

In the 23 947 presentations between January 2014 and December 2017, there were 1 013 reported seizures (4.2 %). The demographics were similar for those with and those without seizures. With respect to other clinical features and outcomes, coma (odds ratio, OR, 3.34, 95 % confidence interval, CI, 2.82-3.96, $p < 0.01$), cardiac arrest (OR 2.16, 95 % CI 1.16-4.02, $p = 0.001$), arrhythmias (OR 2.38, 95 % CI 1.56-3.56, p <0.001), intubation (OR 5.56, 95 % CI 4.56-6.77, $p < 0.001$), critical care admission (OR 4.22, 95 % CI 3.58-4.99, $p < 0.001$) and death (OR 2.27, 95 % CI 1.24-4.53, $p = 0.002$) were more common in the seizure group. There were significant associations between several drugs and seizure incidence, most notably fentanyl and synthetic cannabinoids; other drugs were associated with a lower seizure incidence, including heroin, clonazepam and cannabis.

Validity of Euro-DEN Plus data and complementarity with key indicator datasets

Self-report versus analytical confirmation (immunoassay and confirmatory screening)

The drugs involved in Euro-DEN Plus presentations are identified based on the patient's self-report and information recorded in the patient's notes by the treating physician. Only a minority (around 15-20 %) of presentations involve analytical toxicology tests being undertaken; this reflects routine clinical practice. When analytical toxicology is undertaken, this may involve immunoassay (bedside or laboratory) or confirmatory mass-spectrometry analyses, depending on hospital routines, resources and available equipment.

The use of analytical testing was examined to explore the extent of agreement between test results and self-reporting. The findings of immunoassays compared with those of the less available but more specific confirmatory mass-spectrometry analyses, using Euro-DEN Plus data for the period from October 2013 to September 2015 (Liakoni et al., 2018). During this period, 1 674 (15.3 %) of the 10 956 presentations resulted in a 'drugs of abuse' test being performed. In 213 (12.7 %), both an immunoassay and a mass-spectrometry test were performed. Generally, there was a high degree of agreement between the self-reported drugs used and the analytical toxicology results; this was particularly the case for commonly used illicit drugs, such as heroin and cocaine (Liakoni et al., 2018).

NPS could be detected only with mass spectrometry. For amphetamine-type substances, including classic amphetamines, mass spectrometry is more sensitive than immunoassay. In contrast, immunoassay performed well for cannabis (THC), cocaine and methadone.

An additional analysis was performed looking at the toxicological analyses undertaken in 2 688 (18.8 %) of the 14 330 Euro-DEN Plus presentations between October 2015 and December 2017 (Liakoni et al., 2018). Mass spectrometry was available in addition to immunoassay in 11 centres, while 6 centres used only immunoassay. Again, the analytical findings largely confirmed the self-reported drugs. This was the case in 95 % of cases involving a drug declared to be cocaine, 91 % for heroin, 89 % for cannabis, 78 % for sedatives and 60 % for amphetamines. Amphetamines and NPS (cathinones and synthetic cannabinoids) were detected relatively more frequently in centres where mass spectrometry was available than in centres that had immunoassay only. Cannabis (THC), cocaine and opioids (heroin) were detected reliably with immunoassay alone.

These analyses confirm that patient self-reporting of the drugs used in acute toxicity presentations to the emergency department is reliable, particularly for established illicit drugs; further work is required to determine the value of self-reporting in NPS-related cases.

Euro-DEN Plus coding and ICD-10 projects

Previous studies have shown that there is limited systematic collection of data on acute drug-related harm in Europe (Heyerdahl et al., 2014). Information at national level on healthcare resource utilisation related to acute illicit drug toxicity generally relies on collated hospital admissions data. Typically, these data are classified using the *International Classification of Diseases* version 10 (ICD-10) coding system, and previous studies have shown that this approach has serious limitations for acute drug toxicity presentations and significantly underestimates presentations (Wood et al., 2019). To better understand the scale of the underestimation and to explore the possibilities of using available healthcare data, a mapping exercise was conducted across 29 of the Euro-DEN Plus centres in November 2018, to describe the coding of presentations related to acute drug toxicity. The majority of centres (22) used ICD-10 for coding, with smaller numbers using ICD-9, the 4th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV), DSM-V, SNOMED or other coding systems. Among the centres studied, 19 coded all presentations, whereas 10 coded only cases that resulted in admission to hospital; 83 % identify both primary and subsequent codes for each presentation, with 17 % identifying only the primary diagnostic code. Typically, coding was done within a week of a presentation in 75 % of centres, and a variety of sources were used to find information to enable coding to be undertaken (medical and nursing notes in 28 centres, discharge summaries in 19 centres and investigations in 14 centres).

Previous work to identify deficiencies in the coding of acute toxicity (Wood et al., 2011, 2019) reviewed the coding of 619 presentations to three Euro-DEN Plus centres that use ICD-10 for their primary coding. Only 34 % (213 presentations) were coded, with variability in the proportion that received a primary ICD-10 code that related to drug toxicity (100 %, 18.9 % and 9.6 %). Overall, when a presentation was coded, the recording of the use of a drug was very good, with 90 % receiving a primary or secondary ICD-10 code that related to drug toxicity, with coding better for more frequently used drugs.

Previous studies in the United Kingdom (Wood et al., 2011; Shah et al., 2011) and qualitative feedback from the Euro-DEN Plus mapping exercise have demonstrated that ICD-10 coding poorly captures the true healthcare resource utilisation related to the use of illicit drugs and NPS. This is due to a number of factors, including (i) a lack of ICD-10 codes for a range of established drugs (e.g. MDMA); (ii) the fact that the majority of NPS have emerged many years after the ICD-10 codes were finalised; (iii) the fact that presentations are coded based on clinical features rather than the drug involved (e.g. cocaine-induced chest pain is coded as chest pain rather than cocaine use); (iv) the fact that, in some countries, only those presentations that result in admission to hospital are coded, with cases in which the patient is discharged directly from the emergency department not coded; and (v) the fact that in some countries only the primary codes applied are recorded, and not subsequent codes that may indicate drug use.

Future work is planned by Euro-DEN Plus to further understand the deficiencies in the current (i.e. ICD-10) and proposed (e.g. ICD-11) coding systems. A revision (ICD-11) of the current *International Classification of Diseases* coding system has been proposed, which is currently in draft form and awaiting final approval from the World Health Organization, prior to its wider roll-out and implementation. This revised ICD-11 coding system has an increased number of drugs and drug classes mentioned by name, as well as including a range of NPS.

The ultimate aim of this work is to inform the development of a tiered acute harm data collection model, with high-level resolution and detailed data from the Euro-DEN Plus sentinel centres, complemented by lower level background data from routine hospital coding across all or at least a much larger number of hospitals.

Complementarity with national level data

The participating national focal points from France, the Netherlands, Spain and Sweden presented the different models of national acute drug intoxication monitoring that are in place in their countries, and discussed their strengths and weaknesses in terms of routine monitoring and early warning systems on drug-related harm.

There are notable differences in the nature and design of the monitoring systems in place across these countries. Most systems record only the number of acute drug toxicity presentations to hospital emergency departments, and sometimes only cases in which the patient is admitted (EMCDDA, 2014; Heyerdahl, 2014). However, other models exist, in particular the Dutch system (Monitor Drugsincidenten) and the Spanish system (Indicator of the Spanish Observatory on Drugs and Addiction), which are ‘based on multiple indicators, allowing broad coverage of different catchment areas, settings (emergency departments, ambulance services, forensic services, first aid stations at dance parties) and types of drug use. These systems contribute to monitoring new trends, in particular in high-risk drug use, and to validating data from other indicators (including on treatment, deaths, drug checking and drug consumption rooms).

In the Netherlands, the national system is also instrumental in the initiation of drug-related ‘red alert’ procedures. Similarly, in France, real-time data from hospital surveillance, collection of which began in 2003, are valuable to the national early warning system on drugs. In addition to revealing long-term trends and providing good coverage (capturing 9 out of 10 emergency department visits in France), the system is also relatively cheap and simple, based on automated extraction of data from patients’ electronic medical records. However, a weakness of the system is a lack of sensitivity due to coding

limitations (see Wood et al., 2011, 2019). Another weakness of the French system and other systems for routine national data collection compared with the collection of data from sentinel emergency departments is a lack of precision regarding the substances involved (especially for opioids) and a lack of clinical and outcome information. Furthermore, in many countries the systems are based on retrospective data extraction and thus not suitable for informing early warning systems.

In several countries, such as Sweden, there is not yet any systematic collection of data from hospitals, poison centres or other emergency settings, but discussions on implementing relevant systems are under way.

Synergies with Euro-DEN Plus could be explored, in particular where local (hospital, city or regional level) routinely collected data could be cross-checked against local Euro-DEN Plus figures. This could validate the routine data or contribute to estimating the extent of the invisible fraction of cases flagged by Euro-DEN Plus but missed in routine statistics. Other exploratory work could look at the possible complementarity of data from other sources, such as poison centres (Wood et al., 2014b).

Conclusions

Every year in Europe, thousands of individuals suffer drug-related acute toxicity that requires hospital attendance. These drug-related hospital emergency presentations are most likely to occur in young adults and to involve heroin, cocaine and cannabis. Findings from Euro-DEN Plus also highlight the potentially considerable burden on health services. Over three quarters of cases are brought to the emergency department by ambulance and, while most cases are discharged quickly, a small but significant minority (6 %) involve severe acute toxicity requiring critical care admission, and some deaths are reported among this cohort. It is also important to note that clinical features associated with significant medical and nursing staff input, such as agitation/psychosis, are commonly seen in these patients. This has clear implications from a resource and staffing perspective, particularly as these presentations are most common at weekends and in the late evening to early hours of the morning.

Data on hospital emergency department presentations provide a unique insight into acute health harms related to drug use, complementing data from the EMCDDA key indicators and broadening the scope of monitoring of the health consequences of drug use. This is particularly important in the light of the limited systematic data reported on acute drug toxicity in Europe. Findings from the Euro-DEN Plus project help to increase understanding of the drugs responsible for acute toxicity in Europe, whether they are illicit substances, misused prescription medicines or NPS. This dataset also enables analysis of geographical and time trends, patterns of acute toxicity and the potential implications of these presentations. While the data do not necessarily provide a nationally representative picture, as only selected sites in participating countries are included, using a number of sentinel sites in significant locations provides useful data on the drugs resulting in presentations to emergency departments in Europe and the trends in these drugs and these locations over time, and the increasing size and geographical reach of Euro-DEN Plus helps to minimise this limitation.

Continuation and further development of work in this area will be important to enable a greater understanding of the acute harm associated with drug use in Europe. The next steps in the development of the Euro-DEN Plus project — in addition to continuing to recruit centres to increase the representativeness of the data — is to further consider triangulation of the Euro-DEN Plus dataset with key indicator and other complementary and developing drug datasets in Europe. This will help to inform delivery of appropriate healthcare and prevention activities and provide a more complete picture to legislative and public health bodies of the overall implications of drug use in Europe for the European population.

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Alison Dines, London, United Kingdom, 'Pregabalin in Euro-DEN Plus heroin presentations'.

Miguel Galicia, Barcelona, Spain, 'GHB in Euro-DEN Plus presentations'.

Isabelle Giraudon, EMCDDA, 'Cocaine EMCDDA trendspotter summary'.

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Kerry Layne, London, United Kingdom, 'Prescription medicine misuse in Euro-DEN Plus presentations'.

Matthias Liechti, Basel, Switzerland, 'Self-report versus analytical confirmation (immunoassay and confirmatory screening)'.

Òscar Miró, Barcelona, Spain, 'Euro-DEN Plus: powder cocaine and crack cocaine'.

Roberta Noseda and Alessandro Ceschi, Lugano, Switzerland, 'Euro-DEN Plus: MDMA presentations'.

Odd Martin Vallersnes, Norway, 'Self-discharge in the Euro-DEN Plus dataset'.

Stephen Waring, York, United Kingdom, 'Euro-DEN Plus presentations in younger and older patients'.

David Wood, London, United Kingdom, 'Euro-DEN Plus coding and ICD-10 projects'.

Caitlin Wolfe, London, United Kingdom, 'Seizures: drugs responsible and clinical importance in Euro-DEN Plus presentations'.

Chris Yates, Mallorca, Spain, 'Synthetic cannabinoids versus cannabis: a comparison'.

Some researchers conducted original analysis of the dataset for presentation and discussion with the research group and that some of the analysis have been published since or are under review for publication.

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Appendices

Appendix 1: Number of presentations by centre and by year, Euro-DEN Plus, 2014-17

Country	City	2014	2015	2016	2017	Total
Denmark	Copenhagen	155				155
	Roskilde		89	66		155
Estonia	Pärnu	13	31	28	25	97
	Tallinn	115	91	97	113	416
France	Paris	377	261	243	273	1 154
Germany	Munich	213	152	115	113	593
Ireland	Drogheda	29	11	24	20	84
	Dublin	524	543	436	586	2 089
Norway	Oslo OAEOC	1 529	1 576	1 303	1 593	6 001
	Oslo OUH	192	180	194	196	762
Poland	Gdańsk	158	236	125	103	622
Spain	Barcelona	182	108	147	224	661
	Mallorca	190	237	249	350	1 026
United Kingdom	London STH	934	921	960	1 040	3 855
	London KCH	405	439	379	434	1 657
	York	204	180	124	76	584
Switzerland	Basel	224	210	244	275	953
	Bern			206	259	465
	Lugano				105 (from July)	105
Bulgaria	Sofia			49 (from May)	87	136
Czechia	Prague			26	26	52
Malta	Msida			218	369	587
Slovakia	Bratislava			91	56	147
Belgium	Antwerp				500	500
	Ghent				113	113
Finland	Helsinki				253	253
Georgia	Tbilisi				8 (from May)	8
Italy	Monza				113	113
Latvia	Riga				81	81
Lithuania	Kaunus				164	164
	Vilnius				203	203
Slovenia	Ljubljana				156	156
Total		**5 444**	**5 265**	**5 324**	**7 914**	**23 947**

NB: Ordered by year when participation began and country.

Appendix 2: Number of presentations related to selected drugs, by centre, Euro-DEN Plus, 2017

Country	City	Heroin	Cocaine	Cannabis	Amphet-amine	MDMA	Methadone	GHB/GBL	Metham-phetamine	NPS	Number of presenta-tions
Belgium	Antwerp	37	157	111	69	53	8	42	1	4	500
	Ghent	5	37	43	26	15	8	16	4	1	113
Bulgaria	Sofia	9	13	45	22	2	8	0	3	0	87
Czechia	Prague	1	1	5	3	6	0	1	4	1	26
Denmark	Roskilde										
Estonia	Pärnu	0	1	8	9	8	0	4	9	0	25
	Tallinn	1	13	19	35	11	5	39	10	0	113
Finland	Helsinki	2	4	17	38	6	4	110	3	8	253
France	Paris	13	70	82	8	51	23	15	4	9	273
Georgia	Tbilisi	0	0	2	0	0	0	0	0	2	8
Germany	Munich	7	8	12	12	3	9	2	8	20	113
Ireland	Drogheda	0	10	6	0	7	0	0	1	0	20
	Dublin	199	120	58	4	41	45	9	4	9	586
Italy	Monza	11	61	56	3	0	3	0	2	0	113
Latvia	Riga	9	5	13	7	1	8	2	5	3	81
Lithuania	Kaunus	12	3	13	5	5	6	0	1	6	164
	Vilnius	98	9	31	19	1	8	3	6	16	203
Malta	Msida	93	166	103	2	17	1	1	0	92	369
Norway	Oslo OAEOC	524	99	227	380	67	71	196	11	1	1 593
	Oslo OUH	27	13	13	33	9	2	104	1	0	196
Poland	Gdańsk	1	9	19	26	4	1	2	3	54	103
Slovakia	Bratislava	0	8	27	3	9	0	0	25	2	56
Slovenia	Ljubljana	21	48	28	10	11	25	15	3	6	156
Spain	Barcelona	2	102	52	49	12	1	56	25	4	224
	Mallorca	47	180	139	26	23	2	1	3	3	350
Switzerland	Basel	27	112	117	12	12	16	8	2	1	275
	Bern	51	101	81	35	9	7	9	1	2	259
	Lugano	8	39	47	2	0	3	0	0	0	105
United Kingdom	London STH	132	200	97	11	122	37	214	154	205	1 040
	London KCH	62	90	60	12	58	5	106	68	29	434
	York	18	21	19	3	19	6	1	0	4	76
Total		1 417	1 700	1 550	864	582	312	956	361	482	7 914

NB: ordered by country and by centre, 2017. A presentation may involve more than one drug and therefore the number of presentations by drug do not add up to the total number of presentations in the far left column.

Appendix 3: Euro-DEN Plus centres and contributors, 2014-19

Country	Institution and contributors
Belgium	ZNA Stuivenberg, Antwerp, Belgium — Kurt Anseeuw, Johan Gillebeert
Belgium	Ghent University Hospital, Ghent, Belgium — Cathelijne Lyphout, Ibolya Toth, Laurence Daveloose
Bulgaria	University Hospital for Emergency Medicine N. I. Pirogov, Sofia, Bulgaria — Julia Radenkova-Saeva
Czechia	Czech Toxicological Information Centre, Prague, Czechia — Sergej Zacharov, Jan Rulisek, Zuzana Kolpach
Denmark	Clinical Pharmacology Unit, Zealand University Hospital, Roskilde, Denmark — Gesche Jurgens, Bue Fogh Juvik, Kenneth Skov
Estonia	Emergency Department, Pärnu Hospital, Pärnu, Estonia — Raido Paasma
Estonia	Emergency Medicine Department, North Estonia Medical Centre, Tallinn, Estonia — Kristiina Põld
Finland	Malmi Hospital, Helsinki, Finland — Jutta Konstari
France	Emergency Department, Lariboisière Hospital, Paris-Diderot University, Paris, France — Bruno Megarbane, Lucie Chevillard, Karim Jaffal
Georgia	Archangel St Michael Multiprofile Clinical Hospital, Tbilisi, Georgia — Soso Kutubidze, Ketevan Gorozia
Germany	Department of Clinical Toxicology, Technical University of Munich, Munich, Germany — Florian Eyer, Stefanie Geith, Christian Rabe, Tobias Zellner
Ireland	Emergency Department, Our Lady of Lourdes Hospital, Drogheda, Ireland — Niall O' Connor, Gerard Markey, Sarah-Jane Yeung, Radhika Sopirala, Paddy Hillery
Ireland	Emergency Department, Mater Misericordiae University Hospital, Dublin, Ireland — Adrian Moughty, Sinead Kilgarrif, Iarlaith Kennedy
Italy	San Gerardo Hospital (UOS Pronto Soccorso), ASST Monza, Italy — Federico Vigorita
Latvia	Riga East Clinical University Hospital, Riga, Latvia — Roberts Stašinskis, Viesturs Liguts
Lithuania	The Hospital of Lithuanian University of Health Sciences, Kauno Klinikos, Kaunus, Lithuania — Jonas Surkus, Marius Perminas
Lithuania	Republic Vilnius University Hospital, Vilnius, Lithuania — Gabija Laubner, Robertas Badaras
Malta	Clinical Toxicology Lead Mater Dei Hospital, Valletta, Malta — Jeffrey Bonnici
Netherlands	Onze Lieve Vrouwe Gasthuis, Amsterdam, the Netherlands — Femke Gresnigt
Netherlands	Dutch Poisons Information Centre, University Medical Centre Utrecht, the Netherlands — Laura Hondebrink, Irma van den Hengel-Koot
Norway	Department of Acute Medicine, Oslo University Hospital, Oslo, Norway — Knut Erik Hovda, Fridtjof Heyerdahl, Per Sverre Persett
Norway	Oslo Accident and Emergency Outpatient Clinic, City of Oslo Health Agency, Norway — Odd Martin Vallersnes

Poland	Pomeranian Centre of Clinical Toxicology, Medical University of Gdańsk, Gdańsk, Poland — Jacek Anand, Piotr Kabata, Wojciech Waldman
Romania	Children's Hospital Grigore Alexandrescu, Bucharest, Romania — Viorela Nitescu
Slovakia	National Toxicological Information Centre, University Hospital Bratislava, Slovakia — Blazena Caganova
Slovenia	Centre for Clinical Toxicology & Pharmacology, University Medical Centre Ljubljana, Slovenia — Miran Brvar, Damjan Grenc
Spain	Emergency Area, Clinical Toxicology Unit, Hospital Clinic, Barcelona, Spain — Òscar Miró, Miguel Galicia
Spain	Emergency Department and Clinical Toxicology Unit, Hospital Universitari Son Espases, Mallorca, Spain — Chris Yates, Jordi Puiguriguer, Catalina Homar, Juan Ortega Perez
Switzerland	Division of Clinical Pharmacology and Toxicology, University Hospital Basel, Basel, Switzerland — Matthias Liechti, Yasmin Schmid
Switzerland	Clinical Pharmacology and Toxicology, University Hospital Bern, Switzerland — Evangelia Liakoni, Irene Scholz
Switzerland	Institute of Pharmacological Sciences of Southern Switzerland, Ente Ospedaliero Cantonale, Lugano, Switzerland — Alessandro Ceschi, Laura Müller, Roberta Noseda
United Kingdom	Clinical Toxicology and Emergency Department, St Thomas' Hospital, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners, London, United Kingdom — Paul Dargan, David Wood, Alison Dines, John Archer, Takahiro Yamamoto, Luke de la Rue, Kerry Layne, Craig Leaper, Caitlin Wolfe, Grainne Cullen
United Kingdom	Emergency Department, Kings College Hospital, King's College Hospital NHS Foundation Trust and King's Health Partners, London, United Kingdom — Paul Dargan, David Wood, Alison Dines, Melvin Lipi
United Kingdom	Emergency Department, York Hospital, York Teaching Hospital NHS Foundation Trust, York, United Kingdom — Stephen Waring