



European Monitoring Centre
for Drugs and Drug Addiction

RAPID COMMUNICATION

Hospital emergency presentations and acute drug toxicity in Europe

Update from the Euro-DEN Plus research group
and the EMCDDA

August 2016



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Aim of this report

This rapid communication provides an update on drug-related hospital emergency presentations in Europe with a specific focus on the latest results for acute drug toxicity presentations to the European Drug Emergencies Network (Euro-DEN). The Euro-DEN network was established in 2013 as a European Commission DG Justice funded project with the aim of improving knowledge at a European level on acute established illicit/recreational drug and new psychoactive substance (NPS) toxicity. The project has continued as the Euro-DEN Plus project since the European Commission funding for the original Euro-DEN project ended in April 2015.

This report is primarily based on presentations and discussions at a two-day meeting of the Euro-DEN Plus network in Lisbon on 7 and 8 April 2016. The meeting provided a platform for the presentation of new analyses from the Euro-DEN dataset, and further development and

analyses of the Euro-DEN project were also discussed. Data presented here relate to analysis of acute drug toxicity presentations to the 16 original sentinel centres in the Euro-DEN network for the first two years of data collection (October 2013 to September 2015). This review also includes highlights from the new findings discussed during the meeting and consideration of the further development of the work of the Euro-DEN network and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in this field. It should be noted that as this publication is, in part, based on the presentations to the meeting, some of the information outlined here is necessarily preliminary.

While the data do not necessarily provide a nationally representative picture, as only selected sites are included from participating countries, using a number of sentinel sites in significant locations provides useful information on the types of drug involved in presentations to emergency services in Europe, and the trends at these sites.

At a glance: a summary of key points

Hospital emergency data can provide a unique insight into acute health harms related to drug use, although at present there is limited systematic data collected on acute drug toxicity in Europe.

Euro-DEN Plus is a sentinel monitoring system of hospital emergency services that currently provides data on acute drug toxicity from 20 sentinel sites in 14 countries.

There were a total of **10 956 presentations** to the 16 original sentinel Euro-DEN Plus centres over the two-year period October 2013 to September 2015.

Opioids and heroin were the drugs most frequently associated with acute drug toxicity presentations at emergency departments. Over the two-year period heroin was the most common drug and was involved in 2 604 (24 %) of the presentations.

Cocaine and cannabis were also prominent with, respectively, 1 806 (16 %) and 1 741 (16 %) presentations where these drugs were involved.

New psychoactive substances (NPS) were, comparatively, much less commonly reported, seen in

11 % of presentations over the two-year period.

The most frequently seen NPS were cathinones, in particular mephedrone.

Alcohol and prescription medicines were frequently observed in acute drug toxicity presentations — the most common prescription medicines implicated were benzodiazepines and opioids.

Polydrug use (defined as two or more drugs other than alcohol involved in the presentation) was reported in 38 % of presentations; overall, the mean number of drugs per presentation was 1.6.

Three-quarters (76 %) of the presentations were in **males**, and presentations were most common among those **aged 20–39**.

Most patients (76 %) were **discharged** directly from the emergency department, and almost half (45 %) were discharged within four hours.

Cases with acute drug toxicity can constitute a **burden on emergency health services**. Agitation and aggression are common features, and presentations are more common at weekends, late evenings or night.

Background

Despite the potential for the use of illicit drugs and NPS to cause significant morbidity and mortality, there is currently limited systematic data on acute drug-related harm available in Europe (Heyerdahl et al., 2014) beyond data on drug-related infectious diseases, drug-related deaths (overdoses) and treatment.

However, a unique insight into acute health harms related to drug use is provided by hospital emergency data, which broaden the scope and potential impact of monitoring the health consequences of drug use, as detailed in a previous EMCDDA review (EMCDDA, 1999). Emergency data can serve a number of purposes along two main axes: both as a routine drug-trend monitoring tool, and as an early warning/signalling tool.

With regard to this epidemiological monitoring function, emergency data may act as an indicator of high-risk drug use trends (namely numbers, age and gender of cases with acute drug toxicity related to the most frequent drugs — heroin, cocaine, cannabis and amphetamine — and also the misuse of prescription medicines). This is also a source of information on harms among certain sub-populations of drug users (e.g. crack cocaine users, NPS users). Emergency data can also provide information on the serious consequences of drug use (e.g. fatal and near-fatal toxicity, drug-related psychosis), and on specific substances (e.g. case series of acute cannabis toxicity (Dines et al., 2015)). Finally, data from emergency settings can be used as a source for capture-recapture studies aiming to estimate prevalence (Domingo-Salvany et al., 1998; Espelt et al., 2015). The potential of this data to complement other, more established indicators on the drug situation has been explored in several reports and papers (EMCDDA, 2014; Heyerdahl et al., 2014; Mena et al., 2013; Wood et al., 2014) ⁽¹⁾.

In terms of providing an early warning function, hospital emergency data are useful for detecting and monitoring new patterns of use or misuse of substances (such as NPS), as a source on new trends related to established drugs, for example new epidemics in heroin toxicity. Data from emergency settings may also contribute to early warning systems, as they often capture signals earlier than other monitoring systems based on mortality or treatment data.

⁽¹⁾ See more information, expert presentations, other outputs such as videos, and publications on cocaine and benzodiazepines at <http://www.emcdda.europa.eu/topics/pods/cocaine-related-emergencies> and <http://www.emcdda.europa.eu/topics/pods/benzodiazepines>. Guidelines in several languages are also available from <http://www.emcdda.europa.eu/activities/emergencies>

A review of the monitoring of drug-related acute emergencies, including an analysis of cocaine-related emergencies in 30 European countries, was published in 2014 (EMCDDA, 2014). This Europe-wide review revealed that while many countries can report some basic, routine surveillance data from hospital emergencies and/or hospitalisation, these tend to be limited to the main drugs (heroin, cocaine, cannabis) and few countries have set up enhanced monitoring systems. The review notes that the Drug Abuse Warning Network (DAWN) in the United States, which ran for many years until its closure in 2011 ⁽²⁾, provided a model for hospital emergency surveillance systems in some European countries.

While routine monitoring of drug-related emergencies exists in some countries, it has a number of limitations, in particular a significant underestimation of cases, due mainly to problems with the coding systems used at a hospital level for acute drug toxicity presentations (Shah et al., 2011; Wood et al., 2011).

With a view to addressing the paucity of available data on acute drug toxicity, the Euro-DEN group designed and implemented a 'sentinel' centre model to collect data on acute drug and NPS toxicity presentations to emergency departments in Europe in a systematic way.

From a European monitoring perspective, the sentinel network allows cross-checking of local emergency data with other indicators, such as prevalence of use, mortality, treatment demand, and market data including seizures and purity of the drugs. It can also contribute to the rapid information function of the EMCDDA (through contributions to 'Trendspotter' surveys and to the EU Early Warning System), with its capacity to provide reports of acute toxicity involving NPS.

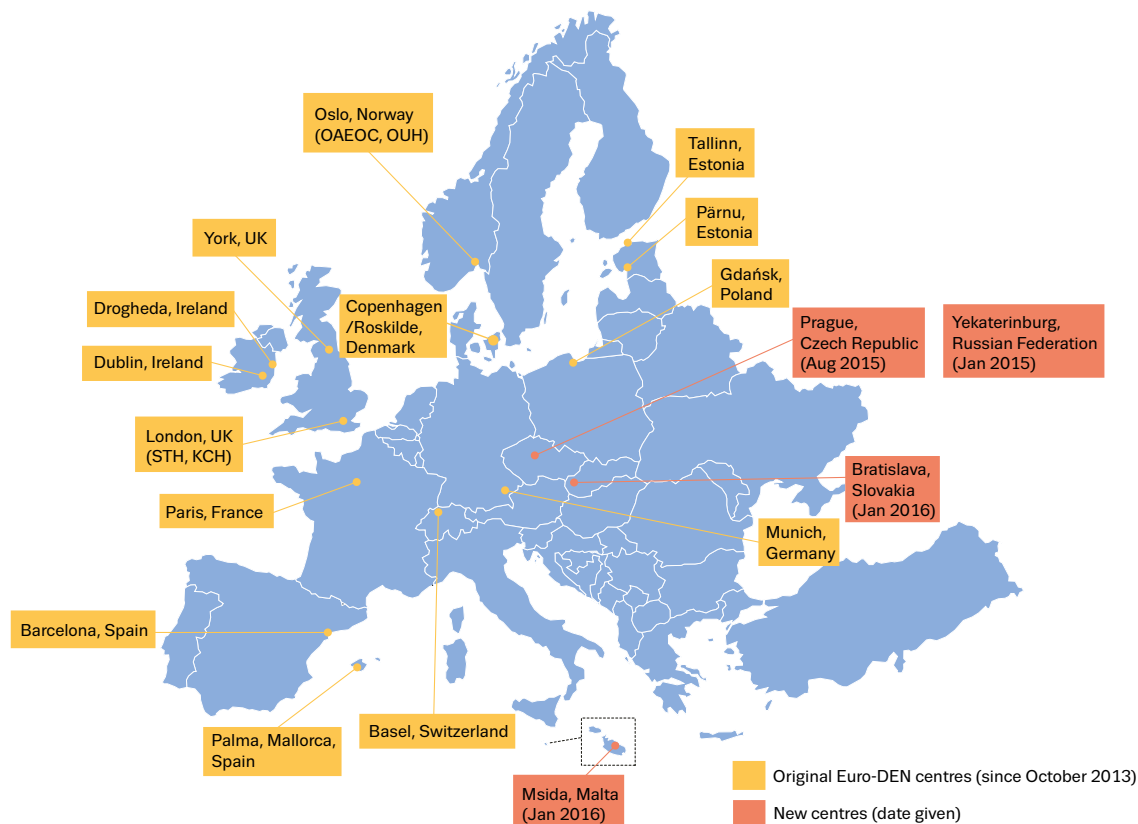
More information on EMCDDA activities in the drug-related hospital emergencies area is available from <http://www.emcdda.europa.eu/activities/emergencies>.

Euro-DEN methods of data collection

The Euro-DEN group developed a minimum dataset to capture the key demographic, clinical and outcome variables in presentations with acute drug and NPS toxicity to emergency departments. A network of sentinel centres with a specialist clinical and research interest in acute drug toxicity was developed (Figure 1) and these centres collect data using the Euro-DEN minimum dataset on all

⁽²⁾ <http://www.samhsa.gov/data/emergency-department-data-dawn/about>

FIGURE 1
Geographical location of the Euro-DEN Plus centres



acute drug toxicity presentations to their emergency department (Wood et al., 2014).

A Microsoft Excel spreadsheet was created using pre-formatted variables and drop-down menus where possible to ensure consistency in the collection of the minimum dataset. In the first year of data collection 58 variables were collected; this was refined for year 2, with the number of data variables cut to 43 — this represents the final Euro-DEN Plus minimum dataset. Data variables no longer collected include those in which there is often limited information available (for example, the dose and route of drug administration) and those that were particularly time-consuming to collect and were felt to be less important to the overall picture of drug-related harm (for example, electrocardiogram and biochemical parameters).

Each centre obtained appropriate local ethical approval from their institution for the collection of the data. The recording of the drug(s) involved in the presentations is based on the patient’s self-report and/or the clinical interpretation of the drugs used by the clinicians managing the patient and collecting the Euro-DEN data in each centre. If drug screening is undertaken as part of routine clinical care the results of the screening are collected, but

analysis is not specifically undertaken for the project. This is representative of international best practice in the management of acute drug toxicity where patients are treated on the basis of the clinical pattern of toxicity and the self-reported drugs used, rather than on the basis of analytical confirmation of the drug(s) detected.

Case definition

Inclusion criteria: Presentations are included if they have a history of use or clinical features consistent with acute established illicit/recreational drug or NPS toxicity, or if they relate to misuse of a prescription/over-the-counter medicine.

Exclusion criteria: Presentations are excluded if they are not directly related to acute recreational drug toxicity (for example, trauma, infection or drug withdrawal) or are the result of self-harm. Cases of lone alcohol intoxication are also excluded, but data on whether or not alcohol is co-used with a drug/NPS is collected.

Each centre collects the data from information recorded in the medical records and returns the Euro-DEN data collection sheets to the lead centre at Guy's and St Thomas' NHS Foundation Trust in London for collation and further analysis.

Euro-DEN Plus two-year dataset: overview of the current situation

Description of the presentations

There were 10 956 presentations to the 16 original sentinel Euro-DEN centres over the two-year period between October 2013 and September 2015, with 5 529 of these presentations between October 2013 and September 2014 and 5 427 between October 2014 and September 2015. As shown in Figures 2 and 3, there were variations in the number of presentations per centre, with the greatest number to the Oslo Accident and Emergency Outpatient Clinic (OAEOC) and London St Thomas' Hospital (STH)

centres (Figure 2). A total of 70.2 % of the Euro-DEN Plus presentations were to five of the 16 centres (Oslo OAEOC, London STH, Dublin, London King's College Hospital (KCH) and Paris) and 60.7 % were in two of the 10 countries (Norway and the United Kingdom) (Figure 3). For the 11 centres for which data were available for both years, Euro-DEN Plus presentations were a median of 0.5 % (IQR 0.2–1.1 %, range 0.1–2.8 %) of all emergency department presentations over the two-year period.

Overall, there were a similar number of presentations to the Euro-DEN Plus centres in year 1 (5 529) and year 2 (5 427). Although the number of Euro-DEN Plus presentations remained relatively stable over the two-year collection period in six centres, five centres had an increase of more than 10 % in the number of presentations between year 1 and year 2 and five had a decrease of more than 10 % (Figure 2).

Overall, 68.5 % of presentations arrived at the emergency department by ambulance, indicating significant utilisation of pre-hospital emergency services and associated resources.

FIGURE 2
Number of Euro-DEN presentations per centre for year 1 and year 2

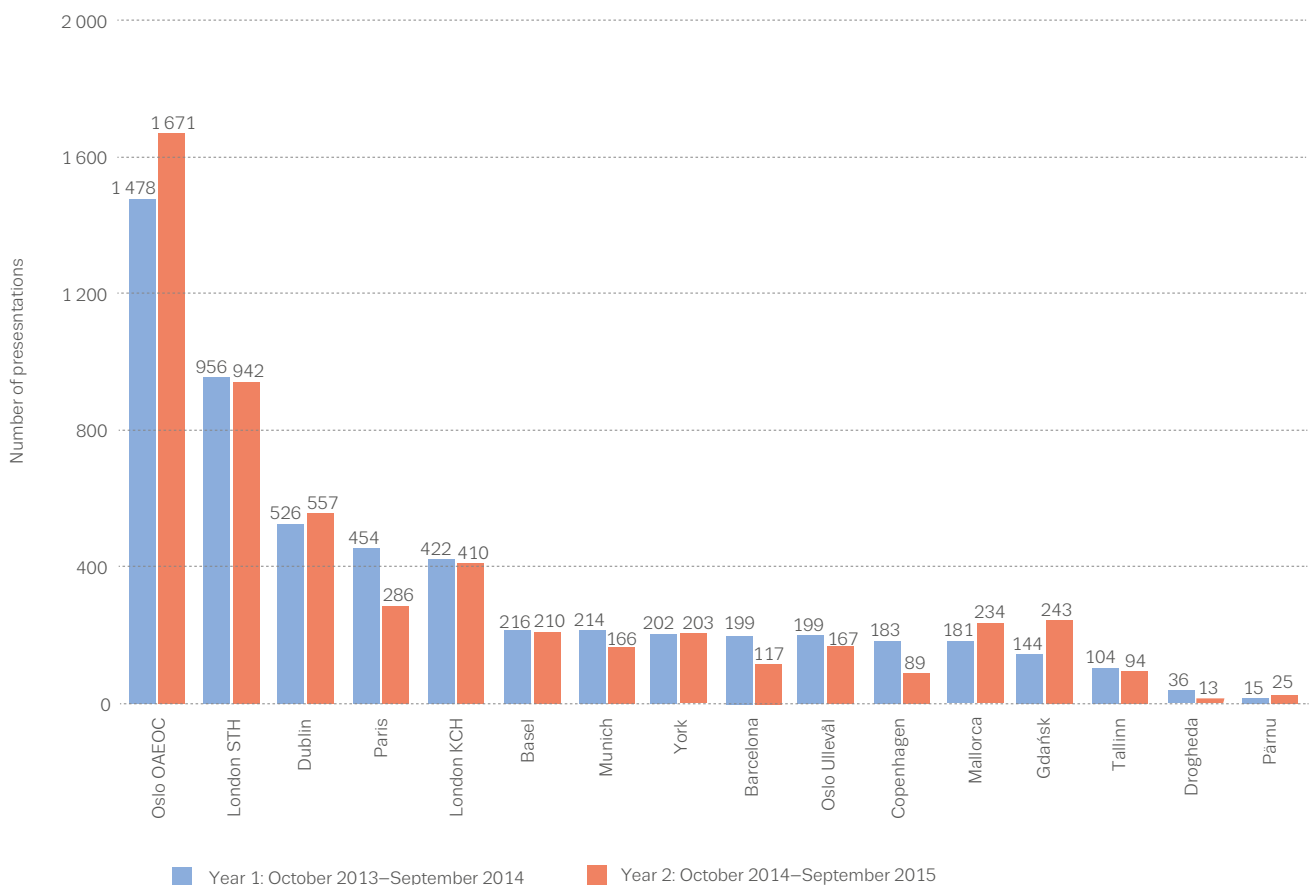
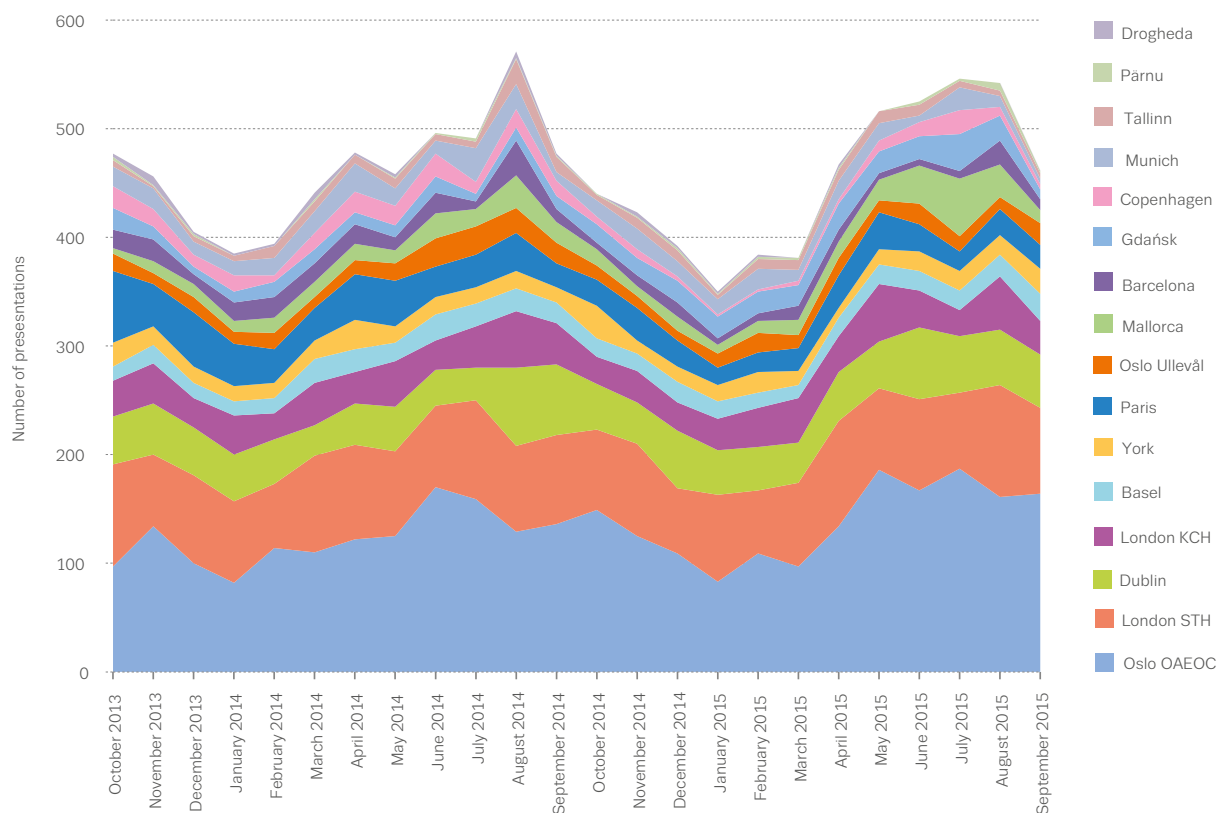


FIGURE 3

Trends in number of Euro-DEN presentations per centre for year 1 and year 2, from October 2013 to September 2015



Demographics

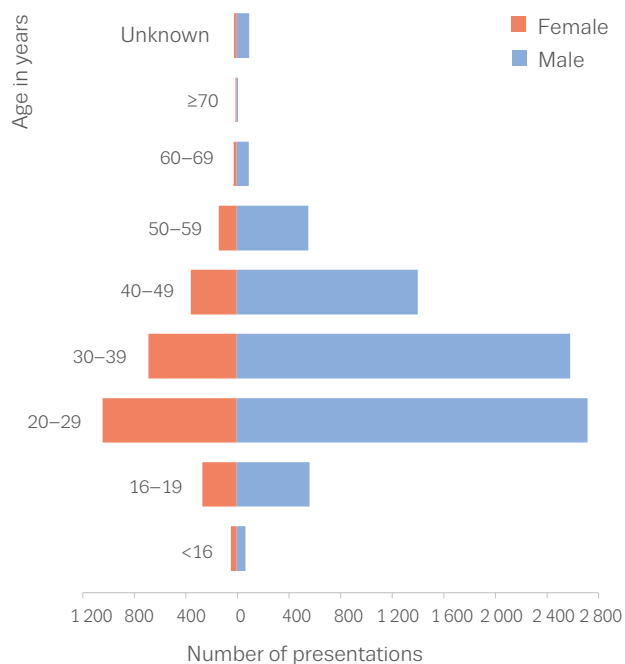
There was a predominance of males amongst the presentations at all ages, and 76.0 % of all Euro-DEN Plus presentations over the two-year period were in males (Figure 4). Presentations were most common among those aged 20–39 (65.8 % of presentations); the median (inter-quartile range (IQR)) age was 31 (24–39) years, with a range from 11 to 90 years old.

Place of residence

Data on the place of residence for each presentation were collected during the first year of the project (October 2013 to September 2014). Across all of the centres, 73.9 % of individuals were resident in the city at which they presented, 19.5 % were resident in another city in that country and 3.6 % were from another country (place of residence was unknown or not recorded in 2.8 % of presentations). There was some variation between the centres in relation to the proportion of presentations that were classified as ‘local residents’ of the city in which they presented, from more than 90 % in Paris, Pärnu and York to less than 70 % in Barcelona, Gdańsk, Munich, Oslo OAEOC and Oslo Ullevål.

FIGURE 4

Age and gender profile of the presentations to the Euro-DEN centres from October 2013 to September 2015 (n=10 953 cases with information)



Time patterns in the presentations

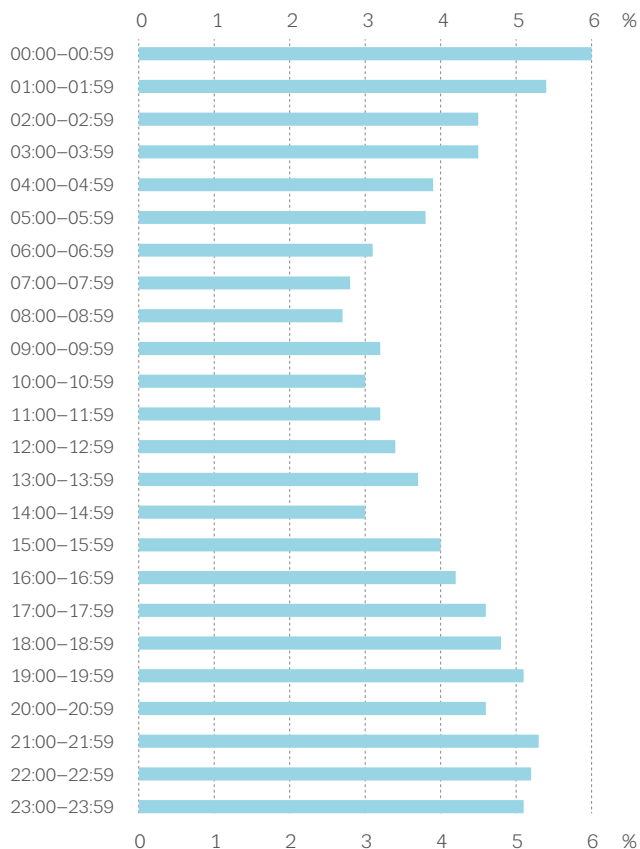
There appears to be a seasonal variation in presentations, with fewer presentations in the winter months (December, January and February) compared to the summer months (June, July and August) (Figure 3). Analysis of the 5 529 presentations over the first year between October 2013 and September 2014 showed that there was a greater proportion of presentations per day at the weekend (18.4 % and 17.4 % of presentations occurred on a Saturday and Sunday respectively) compared to other days of the week (12.1 % to 13.4 % occurred per day from Monday to Friday). Presentations were also more common in the evening and early hours of the morning than during 'core' working hours — more than 4.5 % of presentations per hour from 17:00 to 04:00 and fewer than 4.0 % from 04:00 to 15:00 (Figure 5).

Drugs involved in the presentations

A total of 16 986 drugs (excluding alcohol) were involved in the 10 956 presentations, which is a mean \pm SD of 1.55 \pm 0.73 drugs per presentation. The majority of presentations involved one (61.9 %) or two (26.0 %) drugs and only 3.5 %

FIGURE 5

Percentage of presentations to the Euro-DEN centres, by time of day (year 1, October 2013 to September 2014)



involved four or more drugs. Whether or not alcohol was involved in the presentation was not recorded in 3.8 % of presentations; where it was recorded, alcohol was used in 61.7 % of presentations and not used in 38.3 % of presentations.

Drug categories

The drugs involved in the presentations were predominantly established illicit drugs (64.3 % of drugs) or prescription/over-the-counter (OTC) medicines (25.5 % of drugs) (Figure 6).

Over the two-year period, 7.0 % of drugs involved in the presentations were NPS. There was an increase in presentations involving an NPS, from 5.6 % of reported drugs in year 1 (October 2013 to September 2014) to 8.5 % in year 2 (October 2014 to September 2015).

Analysis of biological samples for detection of the drug(s) used was undertaken as part of routine clinical care in 15.6 % of presentations, and predominately this was by immunoassay without confirmatory high-pressure liquid chromatography (HPLC), gas chromatography–mass spectrometry (GC-MS) or liquid chromatography–tandem mass spectrometry (LC-MSMS).

FIGURE 6

Drug categories reported by the Euro-DEN centres in year 1 and year 2

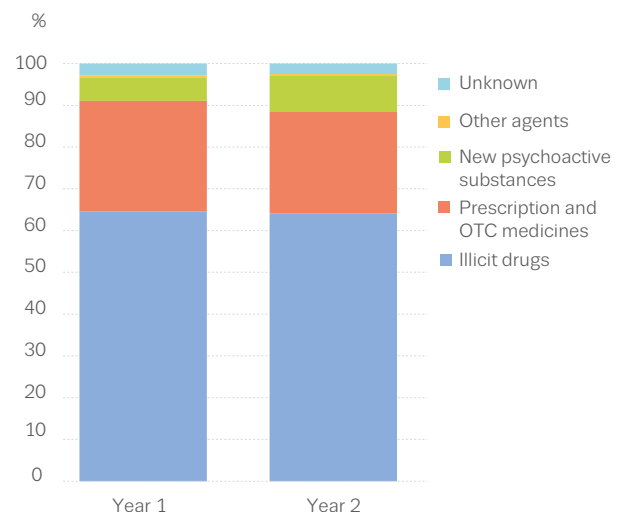
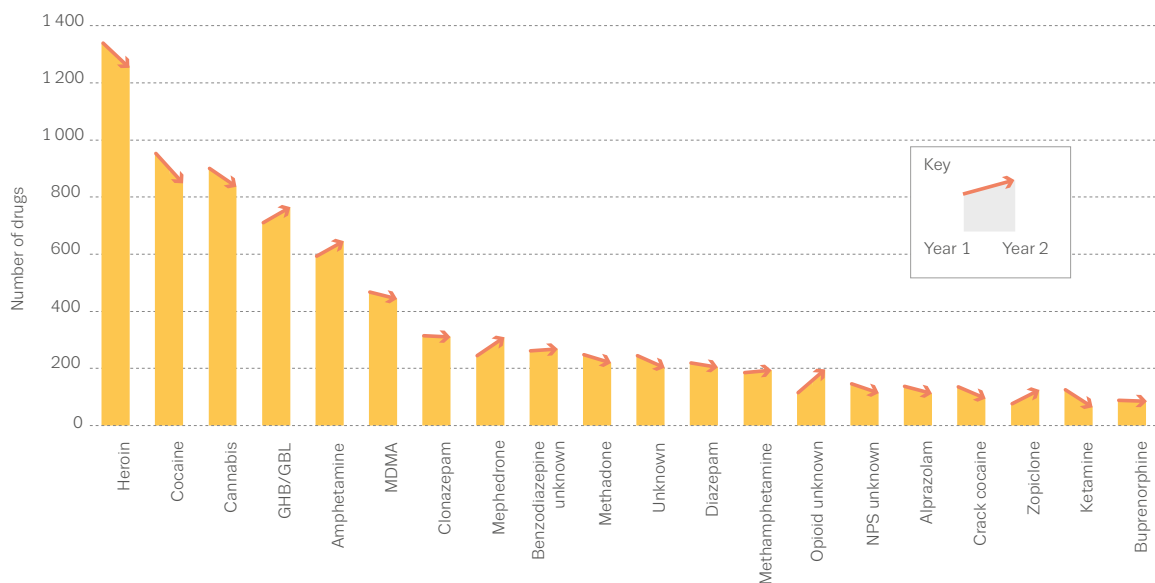


FIGURE 7

Top 20 drugs (16 986 drugs in 10 956 presentations) reported by the Euro-DEN centres from October 2013 to September 2015



Top 20 drugs

The top 20 most commonly reported drugs and the relative change between the two years are shown in Figure 7. Nineteen drugs were in the top 20 in both years; methedrone was number 19 in year 1 but had dropped to number 23 in year 2, and zopiclone was number 21 in year 1 and had risen to number 15 in year 2. The most commonly reported illicit drug, NPS and prescription medicine were: heroin (number 1), mephedrone (number 8) and clonazepam (number 7).

There is geographical variation in the drugs involved in the Euro-DEN presentations — one example of this is GHB/GBL, which was involved in more than 20 % of presentations in four centres (the two London centres, Oslo Ullevål and Barcelona) but in contrast was involved in less than 2 % of presentations in six centres (Gdańsk, Basel, Dublin, Mallorca, Drogheda and York). The geographical variation reflects the diversity of the populations served, the availability of drugs/NPS in each country and the local pattern/prevalence of use of these drugs/NPS in the areas covered by the sentinel centres.

Clinical features

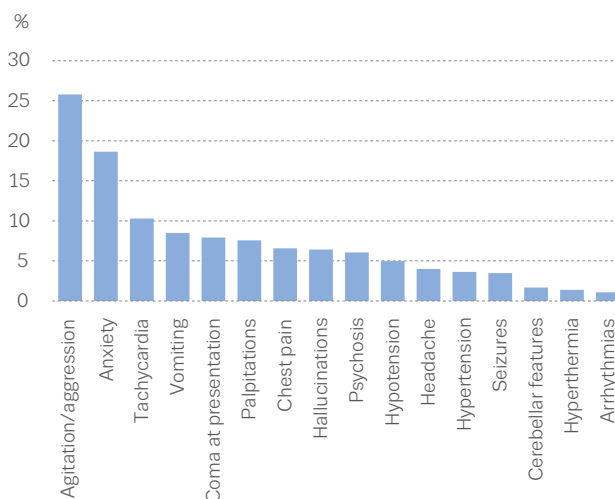
Data are collected for all Euro-DEN Plus presentations on whether or not individuals develop 14 predetermined clinical features during their hospital stay (Wood et al., 2014). The proportion of presentations that developed

these features and the proportion that had tachycardia and coma at presentation are shown in Figure 8.

Overall, 38.1 % did not develop any of these clinical features. The most commonly reported clinical feature was agitation/aggression, which was recorded in 25.8 % of the presentations. A clinically significant minority also had other severe clinical features, including chest pain (6.6 % of presentations), psychosis (6.1 %), seizures (3.5 %) and hyperthermia (temperature ≥ 39 °C, 1.4 %). Furthermore,

FIGURE 8

Clinical features in the acute drug toxicity presentations reported by the Euro-DEN centres from October 2013 to September 2015



58 (0.5 %) patients arrived in the emergency department in cardiorespiratory arrest; of these 26 (45 %) survived to hospital discharge.

Outcomes

Discharge from the emergency department

Over three-quarters of patients (75.7 %) were discharged directly from the emergency department, either medically discharged (58.5 %) or self-discharged (17.2 %) (Figure 9). Only a minority were admitted to hospital, with 5.7 % requiring admission to a critical care area and 4.2 % to a psychiatric ward.

Length of hospital stay

The length of hospital stay is defined as from the time of presentation to the emergency department, to the time of discharge from the hospital. As shown in Figure 10, almost half (44.7 %) of the presentations were discharged from hospital within four hours of their presentation to the emergency department and only 10.6 % of presentations had a hospital stay of more than 24 hours. The overall median (IQR) length of stay from time of presentation to the emergency department to final hospital discharge was 4 hours 36 minutes (2 hours 28 minutes to 9 hours 34 minutes).

Deaths

There were 49 deaths (deaths were recorded if they occurred after attendance at the emergency department and before discharge from hospital), giving an overall fatality rate of 0.4 %. Thirty-two (65 %) of the patients who died arrived in the emergency department in cardiorespiratory arrest. The majority (41; 84 %) of the

FIGURE 10
Length of stay of the presentations to the Euro-DEN network from October 2013 to September 2015

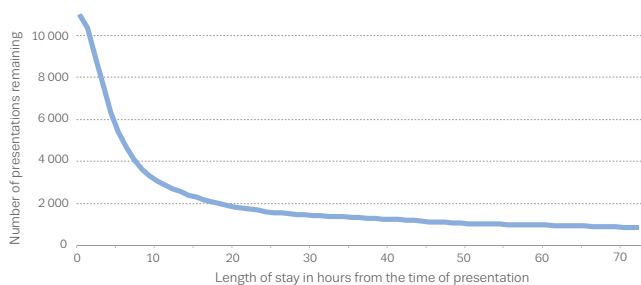
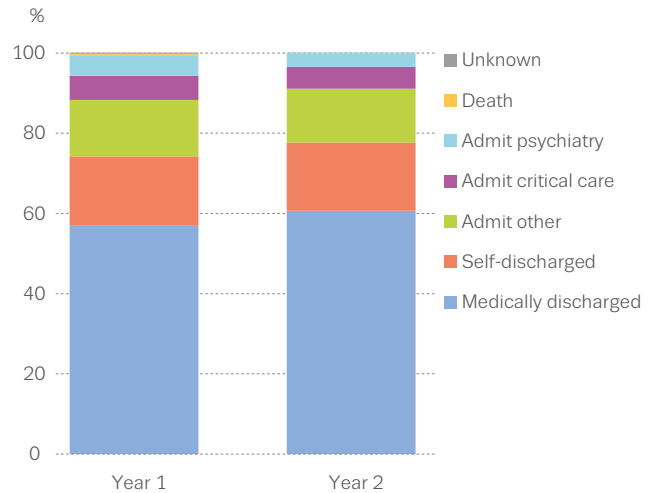


FIGURE 9

Destination following discharge from the emergency department for the Euro-DEN presentations from October 2013 to September 2015



deaths were males and the median age was 29 (IQR 29–39, range 18–53 years). Twenty-three of the deaths occurred within the emergency department and 26 deaths occurred after admission to hospital; 22 of these deaths occurred 24 hours or more after hospital presentation.

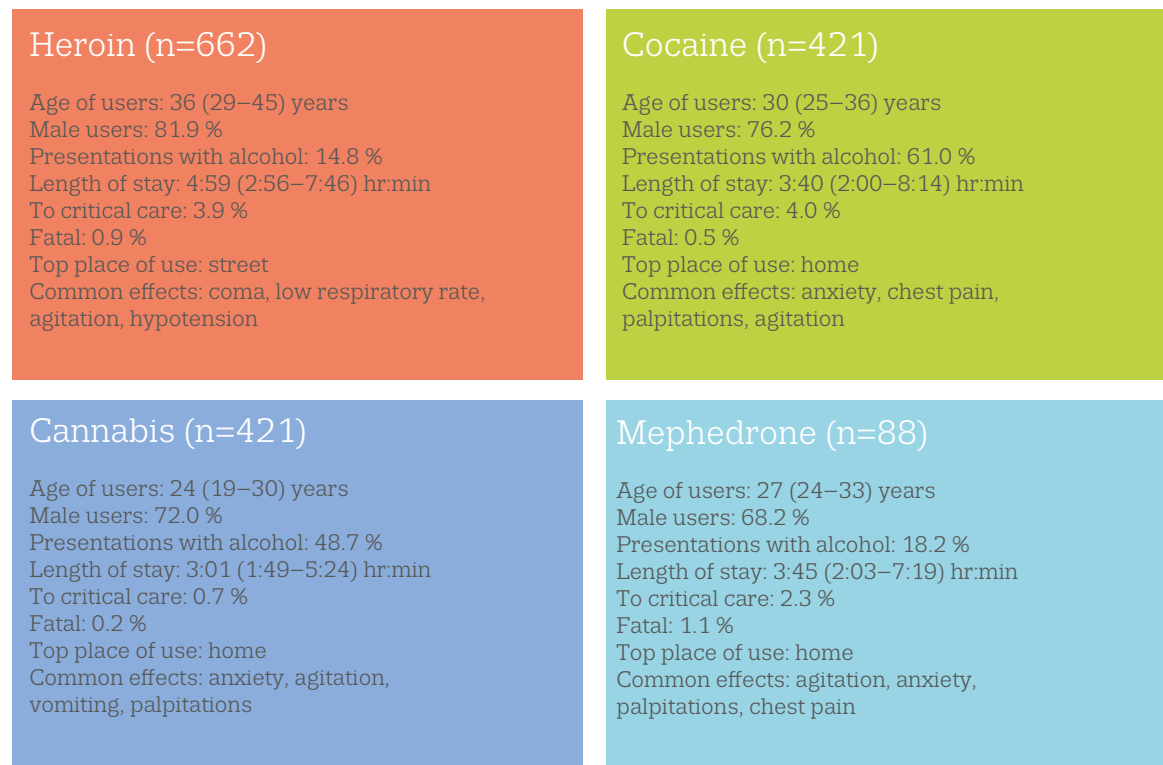
The most common drugs involved in the deaths were opioids (23 deaths: 12 heroin and 11 other opioids) and/or stimulants (15 deaths; most commonly involving cocaine, amphetamine, mephedrone and MDMA). NPS were involved in nine deaths and the most common NPS involved was mephedrone, which was involved in four deaths.

Drug profiles

The overall characteristics of those presenting during year 1 of the Euro-DEN project with problems related to the use of the top three established illicit drugs (heroin, cocaine, cannabis) and the most common NPS mephedrone, where no other drug was reported to have been used, are profiled in more detail in Figure 11. This summarises the demographics of users, most commonly reported place of use of the drug, clinical features and outcomes.

FIGURE 11

Drug profiles for the Euro-DEN presentations involving heroin, cocaine, cannabis and mephedrone, when reported as the only drug (year 1: October 2013 to September 2014)



Limitations of the Euro-DEN sentinel network data

There are limitations in the representativeness of the available Euro-DEN data, as sentinel centres have limited coverage locally (at a city level), and do not represent national data. They are not necessarily representative of other settings and reflect the catchment area and its problem drug use patterns. Only a minority of the cases have a laboratory toxicology confirmation so most of the data comes from the patient's self-reports and the clinician's judgement. However, this is in line with current international recommendations and practice in the management of presentations to emergency departments of individuals with acute drug toxicity. Nevertheless, these limitations are balanced by the systematic data collation for all presentations with acute drug toxicity to the sentinel centres. This is more sensitive and provides more comprehensive data compared to those automatically extracted from hospital databases (Shah et al., 2011; Wood et al., 2011) and provides a unique insight into acute drug toxicity presentations in Europe, in the context of the current limited systematic collection of data in this area (Heyerdahl et al., 2014).

Further development of the network

The data presented in this report are from the original Euro-DEN network of 16 sentinel emergency departments in 10 European countries. However, the Euro-DEN group recognises that, to enhance the European relevance of this dataset, further sentinel centres should be recruited — increasing both the number of countries involved and the number of centres per country. In light of this, the Euro-DEN Plus group has continued to recruit new sentinel centres to increase both the geographical coverage across Europe (now 14 countries) and the number of specialist sentinel centres (now 20 centres; see Figure 1). The other recent change to the network is that the centre in Denmark moved from Copenhagen to Roskilde in January 2016.

Discussions are currently taking place to recruit new sentinel centres in three other countries. The group plans to focus on increasing the recruitment of new sentinel centres in the Baltic regions and Eastern Europe over the next two to three years.

Snapshots

In addition to the expansion of the sentinel centre network, the Euro-DEN group has been exploring other potential avenues to collect representative data on emergency department presentations with acute drug toxicity. One potential strategy is the use of 'snapshots' to identify and collect data on emergency department acute drug/NPS toxicity presentations over shorter periods of time in multiple centres. This would extend the coverage to countries and regions that are currently unrepresented. It is also possible that the data could be used in some cities to cross-check other local data sources, including wastewater monitoring ⁽³⁾.

The Euro-DEN Plus group has undertaken some modelling looking at cases in year 1 of the project to determine whether it would be possible to identify the optimum time period for snapshot sampling that was representative of the whole year data collection period. Initial review suggests that several of these snapshot periods and/or frequencies may provide reasonably representative data for demographics (age and gender), length of stay and discharge from the emergency department; critical care admissions were only representative when whole data was collected, reflecting the infrequent rate of admission to critical care. Using snapshots to identify the drugs involved in presentations was more dependent on the volume (number) of presentations to each centre and on the frequency of the individual drugs in that centre.

In conclusion, the snapshots appeared to provide fairly reliable data across all centres for 'high frequency' drugs (the top four to six in each centre, typically heroin, cannabis, cocaine, GHB, amphetamines), but with decreasing volume of presentations the representativeness decreased as the time period for the snapshot decreased. In relation to NPS, the snapshots might only provide reliable data for the most frequently reported NPS, mephedrone.

Highlights of the Euro-DEN Plus analysis

The Euro-DEN Plus research group has started to undertake a number of specific analyses of the Euro-DEN and/or Euro-DEN Plus datasets to look in more detail at geographical, demographic, clinical and outcome parameters with a view to produce further evidence on the current state and trends in acute drug toxicity in Europe. This section summarises the main findings from some presentations at the meeting on

prescription medicines, benzodiazepines and Z drugs ⁽⁴⁾, the impact of the co-use of benzodiazepines on acute heroin toxicity, NPS and MDMA.

Prescription medicine presentations

Of the 10 956 presentations in the Euro-DEN Plus dataset, approximately 29 % involved at least one prescription/OTC medicine, and of these 45 % involved only prescription medicines, with no illicit drugs or NPS. There was considerable variation between centres in the proportion of cases related only to prescription medicines, with less than 10 % of cases at seven centres, and more than 20 % at five centres.

The two drug groups most commonly involved in the prescription medicine presentations were benzodiazepines/Z-drugs and opioids. The results for benzodiazepines and Z-drugs are discussed in more detail in the next section. The most common named opioids involved were methadone and buprenorphine. The pattern of opioids involved in the presentations is significantly different from the pattern of opioids misused in the USA — there were no reports of hydrocodone or hydromorphone in Euro-DEN Plus presentations, and oxycodone was involved in only 14 (1.1 %) presentations involving a prescription opioid (of these 14 presentations involving oxycodone, five involved only oxycodone with no illicit drug or NPS). (Source: A. Dines, *presentation at the Euro-DEN Plus research group meeting*.)

Benzodiazepines and Z-drugs: geographical variations across Europe

An analysis of the 20 % of Euro-DEN presentations that involved the use of a benzodiazepine showed that the cohort who presented after use of a benzodiazepine was older (median (IQR) age 35 (28–44)) than the overall Euro-DEN Plus group (median age 31 (24–39)). The most commonly named benzodiazepines were clonazepam, diazepam and alprazolam; and the most common Z-drug was zopiclone. There was geographical variation in the most commonly reported benzodiazepine: clonazepam was common in Norway and Ireland; diazepam in the UK and Switzerland; alprazolam in Spain and Poland; and zopiclone in Denmark. The Euro-DEN Plus group is currently looking at whether comparison with other indicators such as prescribing or population level drug utilisation data, or drug user surveys, could be used to understand whether these patterns reflect differences in prescribing (and therefore availability), or user preferences in benzodiazepines that lead to those who are

⁽³⁾ See the EMCDDA's Perspectives on drugs, *Wastewater analysis and drugs — a European multi-city study*, available from <http://www.emcdda.europa.eu/topics/pods/waste-water-analysis>

⁽⁴⁾ Z-drugs are a group of non-benzodiazepine drugs with effects similar to benzodiazepines, which are used in the treatment of insomnia and most of whose names start with the letter 'Z' (e.g. zaleplon, zolpidem and zopiclone).

using benzodiazepines seeking different drug(s) from alternative routes of supply. (Source: C. Yates, presentation at the Euro-DEN Plus research group meeting.)

The impact of co-use of benzodiazepines with heroin: a common choice for polydrug use

Previous work on benzodiazepines at the EMCDDA, summarised in the 2015 Perspectives on drugs ⁽⁵⁾, has suggested that heroin users who co-used benzodiazepines have greater utilisation of emergency and non-emergency healthcare services and are at greater risk of heroin toxicity with poorer outcome following an overdose than those who had not co-used benzodiazepines. An analysis was carried out of the first year of the Euro-DEN dataset on the clinical features and outcomes in presentations associated with lone heroin use (662 presentations) compared to presentations in which there was reported combined use of heroin with benzodiazepines (163 presentations). Clinically significant features and outcomes (proportion with coma, requiring intubation for respiratory support and/or requiring critical care admission; and overall length of hospital stay) were no different between the lone heroin and heroin/benzodiazepine groups. This suggests that co-use of benzodiazepines with heroin, in this cohort, was not associated with poorer clinical outcomes. Further work is required to understand whether this may be related to other factors, such as lower dose heroin use in those co-using a benzodiazepine. (Source: D. M. Wood and T. Yamamoto, presentation at the Euro-DEN Plus research group meeting.)

NPS: mainly cathinones but synthetic cannabinoid receptor agonists (SCRAs) are increasing

Over the last decade there has been increasing detection of NPS, with 98 new compounds detected in Europe in 2015 and a total of 560 NPS currently being monitored by the European Early Warning System at the EMCDDA (EMCDDA, 2016a; EMCDDA and Europol, 2016). One of the challenges in the risk assessment of NPS is the limited availability of data on the epidemiology of use and harms associated with the use of NPS in Europe. Euro-DEN Plus provides a valuable insight into acute NPS presentations in a large European cohort with acute drug toxicity. Approximately 7 % of cases in the two-year Euro-DEN Plus dataset involved the use of an NPS. There was a distinct geographical distribution of cases, with more than 10 % of cases involving an NPS seen in the UK (London STH, London KCH and York), Germany (Munich), Ireland (Dublin) and Poland (Gdańsk)

The largest class of NPS seen were the cathinones, in almost two-thirds of cases involving an NPS. There was a significant increase in the number of cases involving synthetic cannabinoid receptor agonists (SCRAs) and 'branded' products between year 1 (October 2013 to September 2014) and year 2 (October 2014 to September 2015). The most frequently reported single NPS was the cathinone mephedrone (554 cases, representing almost three-quarters of the cathinone presentations). The clinical features seen in the Euro-DEN Plus mephedrone cases were similar to those reported in other published datasets of acute mephedrone toxicity (EMCDDA, 2011). This suggests that the information being collected from self-reported use of NPS in the Euro-DEN Plus dataset is comparable to other datasets, including those with analytical confirmation, and provides validity for the Euro-DEN Plus method of collection of data on acute NPS toxicity. Future analysis of the Euro-DEN Plus NPS cohort will concentrate on the geographical pattern of presentations, and as the Euro-DEN Plus dataset grows it will enable description of the patterns of acute toxicity associated with individual NPS and NPS classes. (Source: D.M. Wood, presentation at the Euro-DEN Plus research group meeting.)

Focus on MDMA presentations

In October 2015 the EMCDDA held an expert meeting as a component in a study that explored changes in the availability and purity of MDMA ('ecstasy') together with reports of increasing use, harm and deaths associated with ecstasy around Europe (EMCDDA, 2016b). Euro-DEN provided input into the study with an analysis of Euro-DEN Plus cases involving MDMA over the 15-month period between October 2013 and December 2014. Over this time period there were 549 Euro-DEN Plus presentations involving MDMA — this represented 8 % of all Euro-DEN presentations; there were no reported cases involving PMA (para-methoxyamphetamine) or PMMA (para-methoxy-N-methylamphetamine). There was geographical variation in the proportion of cases in which MDMA was involved — from over 10 % in five centres (Basel, Copenhagen, Drogheda, London STH, London KCH) to less than 5 % in seven centres (Barcelona, Gdańsk, Munich, Oslo OAECC, Oslo Ullevål, Pärnu and Tallinn). There was no difference in the proportion of cases involving MDMA from October to December 2013 (9.1 %) and from October to December 2014 (7.2 %). Clinical features were consistent with acute stimulant/sympathomimetic toxicity (common features included agitation/aggression in 32 %, tachycardia at presentation (≥ 120 bpm) in 23 %, palpitations in 13 %, chest pain in 10 % and seizures in 7 %). Hyperpyrexia (temperature $\geq 39^\circ\text{C}$) was seen in only 3 % of presentations

⁽⁵⁾ See the EMCDDA's Perspectives on drugs, *The misuse of benzodiazepines among high-risk opioid users in Europe*, available from <http://www.emcdda.europa.eu/topics/pods/benzodiazepines>

but when present, this was associated with poorer clinical outcomes (longer length of stay, admission to critical care) and both of the deaths were in individuals who developed hyperpyrexia. (Source: *P. I. Dargan, C. Lyphout, J. Mounteney and I. Giraudon, presentation at the Euro-DEN Plus research group meeting.*)

Brief interventions

The recent EMCDDA review on the effectiveness of brief interventions ⁽⁶⁾ in patients presenting to emergency departments with substance-related problems showed that by 2015 there had been five systematic reviews and 14 randomised controlled trials of brief interventions in these settings (EMCDDA, 2016c). The majority related to alcohol, and only four randomised controlled trials focused on illicit drugs (three focused on drug use and one included individuals with substance use in general). A variety of brief interventions were used in these four studies, delivered by a range of healthcare professionals, with differing outcome measures. The studies reported that the emergency department provided a unique setting for delivering brief interventions for both illicit drugs and alcohol. Although there were potential benefits from brief interventions in terms of behavioural changes, the heterogeneity of the studies means the results are not more widely generalisable. It is also important to recognise the balance, in busy emergency departments, between providing acute medical care for patients within the department and secondary outputs such as brief interventions. The Euro-DEN Plus steering group will be investigating the expansion of its work projects to include an evaluation of brief interventions in emergency department settings, in particular the feasibility of training general emergency department clinicians to deliver them. (Source: *M. Ferri, presentation at the Euro-DEN Plus research group meeting.*)

Conclusions

Data show that every year in Europe thousands of individuals suffer drug-related acute toxicity that requires some medical assistance. These drug-related hospital emergency presentations are most likely to occur in young adults, and, in the Euro-DEN sample at least, to involve heroin, cocaine and cannabis. Findings from the Euro-DEN Plus network also highlight the potentially considerable burden on health services and related costs. While most cases are discharged quickly, a small but significant proportion develops severe acute toxicity requiring critical care admission and there are some deaths amongst this cohort.

Data from hospital emergency department presentations provide a unique insight into acute health harms related to drug use, complementing other key indicator data and broadening the scope and potential impact of monitoring the health consequences of drug use. 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 are included from participating countries, using a number of sentinel sites in significant locations provides useful information on the kinds of drugs impacting on presentations to emergency services in Europe and the trends in these sites.

Continuation and further development of work in this area is important to enable a greater understanding of the acute harm associated with the use of a range of substances in Europe. This will help to inform delivery of appropriate healthcare and prevention activities, enable a better understanding of the patterns of toxicity associated with drug use, ensure that policy is informed by evidence of the harms these drugs cause and provide input into risk assessment of NPS.

⁽⁶⁾ Brief interventions are psychosocial techniques designed to help recipients recognise harmful patterns of substance use, and to motivate and support them to address that use.

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Resources

- EMCDDA activities in the area of hospital emergency data: <http://www.emcdda.europa.eu/activities/emergencies>
- Other related EMCDDA activities:
 - Early warning system — <http://www.emcdda.europa.eu/themes/new-drugs/early-warning>
 - Wastewater analysis — <http://www.emcdda.europa.eu/activities/wastewater-analysis>
 - Assessing illicit drugs in wastewater: advances in wastewater-based drug epidemiology — <http://www.emcdda.europa.eu/publications/insights/assessing-drugs-in-wastewater>
 - Best practice portal — <http://www.emcdda.europa.eu/best-practice>
- European Union Drugs Strategy (2013–20): available at <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A52012XG1229%2801%29>

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