Final Report of the European Drug Emergencies Network (Euro-DEN)  
March 2015

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European Commission DG Justice: JUST/2012/DPIP/AG/3591
Executive summary

The European Drug Emergencies Network (Euro-DEN) is a two year European Commission DG Justice DPfP funded project. It was led by the Clinical Toxicology Service at Guy’s and St Thomas’ NHS Foundation Trust and King’s Health Partners, London, UK together with Steering Group members from Oslo University Hospital, Oslo, Norway; Hospital Universitari Son Espases, Palma de Mallorca, Spain; and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Lisbon, Portugal.

The EMCDDA collects data on a number of key indicators related to drug and new psychoactive substance (NPS) use in Europe, these contribute to our understanding of the scale and impact of the use of drugs in Europe. However, despite the potential for drugs/NPS to cause significant morbidity and mortality, there is no standardised routine collection of data on acute drug/NPS toxicity or hospital presentations at a national level in Europe. This is a significant data gap in the understanding of the public health impact of these substances. The EU Drugs Strategy 2005-12 stated that new approaches to improve the knowledge of drug-related adverse consequences and assess the risks associated with drugs in general, and NPS in particular, were required. One of the components of the EU Drug Strategy 2013-20 is to ensure a reduction in health harms caused by drugs in Europe. The Euro-DEN project provides a system to inform the first of these EU Drug Strategy objectives and to enable monitoring to inform the second objective.

The overarching objectives of the Euro-DEN project were to develop a network of sentinel centres across Europe with a specialist clinical and research interest in the acute toxicity (harm) of recreational drugs and new psychoactive substances (NPS) and through this network to i) increase European knowledge on the acute toxicity of drugs and NPS and ii) improve the health and wellbeing of European citizens through improved acute toxicity management by training of staff working in recreational settings.

The first activity completed within the project was a study to determine the quality and completeness of current European national data on hospital presentations related to acute drug toxicity. This involved a literature review together with a survey of the EMCDDA National REITOX Focal Points. The study confirmed that, whilst there are some examples of good practice with data collection at a local and regional level, overall there is limited systematic data being collected and reported at a national level on acute drug harms in Europe. Where this is occurring, the systems used are diverse in nature with limited opportunity for comparison.

Alongside this, the Euro-DEN Steering Group developed a minimum dataset to enable capture of the key demographic, clinical and outcome variables in presentations with acute recreational drug and NPS toxicity to the Emergency Department. A Microsoft Excel® spreadsheet was created using pre-formatted variables and drop-down menus where possible to ensure consistency. A network of 16 sentinel centres in 10 European countries (Denmark, Estonia, France, Germany, Ireland, Norway, Poland, Spain, Switzerland and the UK) with a specialist clinical and research interest in acute recreational drug toxicity collected data using the Euro-DEN minimum dataset on all acute drug toxicity presentations to their ER over the 12 month period (October 2013 - September 2014). Presentations were included if they had clinical features consistent with acute recreational drug / NPS toxicity (presentations related to lone alcohol toxicity, those not directly related to acute recreational drug toxicity (e.g. trauma, withdrawal) and those with self-harm were excluded). Each centre obtained appropriate local ethical approval to collect the data from their institution. The drugs involved in the presentations were based on the patient’s self-report and clinical interpretation of the drugs used. If drug screening was undertaken as part of routine clinical care the results of the screen were collected, but analysis was not specifically undertaken for the project. This is representative of international best practice in the management of
recreational 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.

Data were collected on a total of 5529 presentations over the 12 month period. There were over 200 presentations in 8 centres, 200-500 presentations in 5 centres and over 500 presentations in 3 centres. Presentations were most common at weekends and peaked from 1900-0200. Recreational drug presentations represented a median (IQR) of 0.3 (0.2-0.7)% of all ED presentations at the Euro-DEN centres. The median (IQR, range) age was 31 (24-39, 11-90) years and 75.4% presentations were in males. Most (73.9%) individuals were resident in the city of the Euro-DEN centre at which they presented; a significant minority were resident in another city (19.5%) or in another country (3.6%); this has implications for discharge planning and follow up care. There were 8709 drugs involved in the 5529 presentations (mean ± SD 1.6 ± 0.97 drugs per presentation). Classical recreational drugs were the most common category of drugs (64.6%) followed by prescription drugs (26.5%); NPS were only involved in 5.6% of presentations. The ‘top six’ drugs recorded were heroin (1345), cocaine (957), cannabis (904), GHB/GBL (711), amphetamine (593) and MDMA (467). The commonest prescriptions drugs were clonazepam (315), unknown benzodiazepines (259), methadone (248), diazepam (219), alprazolam (140) and zopiclone (77). There were 484 reports of NPS use, cathinones (378) were the most common (mephedrone (245), methedrone (92) and MDPV (22) were the most common cathinones); after the cathinones the most common NPS were ‘branded NPS’ (48), synthetic cannabinoid receptor agonists (26) and phenylethylamines (17). There was significant geographical variation in NPS presentations with three centres reporting no presentations involving NPS, in contrast two centres had NPS reported in more than a fifth of presentations.

Serious or potentially life threatening clinical features were not seen in the majority of presentations. However, over a quarter of presentations were associated with agitation/aggression, over 10% with coma and 6% with psychosis. Almost 70% of presentations were brought to hospital by ambulance. Overall, more than 50% of presentations received some form of treatment (including over 20% requiring sedation) and 6% required critical care admission. There were 35 cases who presented in cardiac arrest of whom 19 died, in addition there were a further 8 in-hospital fatalities. Opioids were the most commonly implicated group of drugs in fatal cases (involved in 13 of the 27 deaths); NPS were reported in three of the fatal cases. The median length of stay in hospital was 4 hours 38 minutes, 78% were discharged within 12 hours and 89% within 24 hours. The most common time of presentation was overnight and at weekends when staffing numbers may be lower and less experienced staff may be on duty. Therefore although acute drug / NPS toxicity presentations represent a small proportion of total ER presentations, they represent a substantial and disproportionate clinical workload with associated resource implications for both pre-hospital and hospital acute medical services.

From a public health perspective, data on patterns of harms associated with drug/NPS use and where it occurs, along with demographic data such as age, gender and home location is useful for deciding where to provide specialist treatment and target interventions. Although there is often media interest in NPS, data from the Euro-DEN project suggests that ‘classical’ recreational drugs are most commonly associated with ER presentations and severe toxicity including deaths. Over a quarter of the drugs associated with presentations were prescription/OTC medicines and further work is required to understand patterns of recreational misuse of these drugs in Europe to inform prevention work to prescribers, the public and other key stakeholders in this area.

The Euro-DEN dataset is a rich dataset which provides a unique insight into the drugs involved in, and the clinical patterns and outcomes of, acute recreational drug and NPS toxicity presentations to ERs in Europe. Further, more detailed analyses will be undertaken by the Euro-DEN group and papers
submitted for publication. In particular topics that will be subject to further analysis include specific user groups (such as extremes of age); specific aspects of acute drug toxicity management (such as use of sedation); and specific groups of drugs, their geographical distribution, place of use, clinical features and outcome of toxicity including resource implications.

With regards to second component of the project, previous studies have shown that staff in recreational settings such as nightclubs and bars can be poor at identifying acute drug toxicity and this can result in delays in appropriate assessment and management of individuals with acute drug toxicity resulting in the potential for increased morbidity and mortality. The final workstream of the Euro-DEN project involved the development of a training package for staff in recreational settings on acute drug toxicity and on the use of guidelines on when to call the emergency services for an individual with acute drug toxicity. The training was run in the summer of 2014 in nightclubs in London, Oslo, Tallinn and Pärnu; 147 individuals attended the training sessions. The training was well received and participants felt more confident in the assessment of individuals with acute drug toxicity after the training. The guidelines produced by the Euro-DEN project: “When to call the emergency services for unwell recreational drug users” have been published on the EMCDDA Best Practice Portal and been submitted for publication in the peer-reviewed literature to further increase their dissemination and use in the field.

The Euro-DEN project has been presented at international conferences in Europe, the USA and Asia in both invited keynote lectures and original scientific presentations. There have also been three peer-reviewed papers published to date, one paper submitted for publication and the Steering Group will continue to oversee the submission of papers relating to the Euro-DEN dataset after the completion of the grant.

The Euro-DEN project has demonstrated the value of data collection from sentinel centres across Europe in documenting the acute toxicity associated with recreational drugs and NPS. Following the completion of Workstream 1 Activity 3 data collection in October 2014, all of the Euro-DEN sentinel centres have agreed to continue collecting data. In addition, two further centres have joined the project – these are in Ekaterinburg, Russia and Roskilde, Denmark. This ongoing data collection network will be referred to as the “Euro-DEN Plus” project. Currently this is unfunded but the centres are all happy to continue as they feel that there is significant value in continuation of the project. The EMCDDA will continue to provide support to the project and the lead Euro-DEN centre in London will continue to collate, analyse, and facilitate dissemination and reporting of the data.

The Euro-DEN project has successfully delivered all of the stated objectives in the grant. The project has developed and delivered training for staff in recreational settings and developed a minimum dataset that was been used to demonstrate that data can be successfully collected and analysed from sentinel centres across Europe to provide a unique insight into the acute harms associated with recreational drugs and NPS in Europe. The Euro-DEN sentinel network has created a benchmark from which future trends and patterns of acute drug/NPS toxicity can be followed. Continuation and further development of this work is important to enable a greater understanding on the acute harm of recreational drugs and NPS in Europe to inform delivery of appropriate healthcare and prevention activities, enable a better understanding of the patterns of toxicity associated with drugs and NPS, ensure that policy is informed by evidence of the actual drugs causing harms and inform more robust risk assessment of NPS.
Introduction
The European Drug Emergencies Network (Euro-DEN) is a European Commission DG Justice funded project (JUST/2012/DPIP/AG/3591; April 2013-March 2015), to improve the knowledge and management of acute recreational drug and new psychoactive substance toxicity.

The EU Drugs Strategy 2005-2012 (Council of the European Union 2004) stated that new approaches to improve the knowledge of drug-related adverse consequences and assess the risks associated with drugs, in general, and new psychoactive substances (NPS) in particular, were required. The Euro-DEN project was conceived to address and deliver on these themes through two integrally inter-linked pieces of work (known as workstreams). The Euro-DEN project also delivers a solution for monitoring one of the components of the EU Drug Strategy 2013-2020, which is to ensure a reduction in health harms caused by drugs in Europe (Council of the European Union 2012).

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) collects data on a number of key indicators related to drug and new psychoactive substance (NPS) use in Europe, which contribute to our understanding of the scale and impact of use of drugs in Europe (EMCDDA 2014 a, UNODC 2013). However, despite the potential for drugs and NPS to cause significant morbidity and mortality resulting in attendances to hospital Emergency Rooms (ERs), little data is routinely collected on acute drug/NPS toxicity or hospital presentations at a national level in Europe. This is a significant data gap in the understanding of the public health impact of these substances at a European level. By developing a network of sentinel centres with toxicological expertise across Europe, the Euro-DEN project has created a model for such data collection. This report will describe the development of this network and the data obtained from a full 12-month period of data collection.

In addition to data collection, the Euro-DEN project has also developed a training package for staff in recreational settings in the night-time economy, such as nightclubs and bars, on the features of acute toxicity of drugs/NPS and how to help individuals who develop these problems. Previous studies (Wood, Greene et al. 2008) have shown that staff in these settings can be poor at identifying acute drug toxicity and this can result in delays in appropriate assessment and management of unwell individuals, with the potential for increased morbidity and mortality.

The Euro-DEN project was divided into three Workstreams (WS). Workstream 0 related to overall project management, Workstream 1 to Emergency Room (ER) data on drug related emergencies and Workstream 2 to the training package for staff in recreational settings; workstreams 1 and 2 were divided into discrete work packages known as activities. Workstream 0 was run by the lead centre at Guy’s and St Thomas’ NHS Foundation Trust, London, UK supported by Steering Group members from Oslo University Hospital, Oslo, Norway; Hospital Universitari Son Espases, Mallorca, Spain; and the EMCDDA (Roumen Sedefov, Head of Unit, Supply Reduction and New Trends Unit and Isabelle Giraudon, Scientific Analyst, Health Consequences).

The first activity in Workstream 1 (WS1A1) was, as a baseline for the project, a survey to determine what systematic data was being collected and reported nationally in Europe on ER presentations with acute toxicity related to classical recreational drugs and NPS. The second activity (WS1A2), was to develop a representative minimum dataset which included the parameters needed to capture the most clinically important aspects of acute drug/NPS toxicity, with basic demographic information, data on the drugs/NPS used and clinical features. The third activity (WS1A3) was a 12-month prospective study by the Euro-DEN network, using the minimum dataset designed in WS1A1, to establish the drugs/NPS responsible for Emergency Room admissions across Europe, the clinical patterns of acute toxicity seen and the outcome in these presentations.
The first activity in Workstream 2 (WS2A1) was the development of a training package for staff in recreational setting on the patterns of acute toxicity of drugs/NPS and the development and finalization of guidelines to identify individuals with significant acute drug toxicity requiring urgent clinical assessment. The second activity (WS2A2), was a feasibility study on the delivery of this training package for training staff in recreational settings across Europe.

**Workstream 1 Activity 1 (WS1A1)**

A peer-reviewed paper describing the methods and results of this activity has been published (Heyerdahl, Hovda et al. 2014) and so we only provide a brief summary here.

**Objective**

The objective of this activity was to determine the quality and completeness of current European national data on Emergency Room admissions with drug-related adverse consequences (acute toxicity).

**Methods**

Three approaches were taken to identify systematic collection of data on drug/NPS toxicity in Europe.

i. A literature search was undertaken in PubMed using the following search strategy: *(street drugs or drugs of abuse or recreational drugs or designer drugs or psychotropic drugs or psychoactive drugs or hallucinogens) and (epidemiology or prevalence) and (Emergency room or emergency department or Emergency Service, Hospital or overdose or poisoning).* This was limited to the last 10 years and to languages spoken by the authors (Bulgarian, Danish, English, French, Norwegian, Portuguese, Spanish and Swedish) and excluded single cases or case series, papers not describing clinical data per se and/or not describing systematic collection of clinical data.

ii. A Survey Monkey® questionnaire was distributed by e-mail in July 2013 to the nominated experts for the 30 European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) national reporting Focal Points. The survey collected information on whether there was any systematic data collection on ER presentations with acute toxicity related to classical recreational drugs and/or NPS at a national or regional level, what kind of data was collected and how the data was collected.

iii. Euro-DEN, EMCDDA and additional personal networks of the Euro-DEN Steering Group were used as a supplemental method for identifying current examples of the best practice in classical drug and NPS acute toxicity data collection.

**Results**

21 papers were identified that were appropriate for assessment and only one of these (Wood, Greene et al. 2013) described a structured collection of data from ER presentations which related to acute drug and NPS toxicity.

There were 35 complete responses from 27 (90%) of the 30 countries sent the SurveyMonkey® questionnaire. In the eight countries from which two surveys were received, the most complete set of data was used. Fourteen countries (52%) did not report any national systematic data collection on toxicity in EDs for either classical recreational drugs or NPS. Fifteen countries (56%) had no collection at all at a regional level.

Several examples of good practice of systematic collection of data on drug toxicity (but which did not necessarily include NPS toxicity) were identified in the Netherlands, Spain and the Czech Republic. The Dutch system, MDI (Monitor Drugs Incidenten), has collected data on drug-related emergencies from ambulance services, ERs and others since 2009 whilst the Emergencies Indicator from the Spanish Drug Observatory has collected data since 1987 by reviewing cases from the ER of sentinel hospitals. Similar sentinel hospital based surveillance takes place in the Czech Republic and the characteristics of these systems were described in an EMCDDA review (EMCDDA 2014 b).
Overall, we found that limited systematic data was being collected and that there were diverse systems in place collating information from a wide range of sources such as ER, poisons centres and pre-hospital emergency services. These systems relied on self-reported drug use and/or extraction from databases based on clinical data used as part of routine patient care so there was the potential for NPS-related effects to be unrecognised as they were not being systematically looked for. The systems identified were useful at following trends in drug use, particularly of classical recreational drugs, but it was difficult to compare information from different countries and it was very likely that they underestimated drug use and harms relating to it.

**Workstream 1 Activity 2 (WS1A2)**

**Objective**

The objective of this activity was to develop a representative minimum dataset to be able to identify, monitor and respond to new trends and patterns of adverse consequences related to the use of drugs and NPS.

**Methods**

A previous EMCDDA funded pilot study [EMCDDA CT.08.EPI.042.1.0] carried out in 2008 by the London and Mallorca centres of the Euro-DEN project (Dargan and Wood 2009), provided the initial basis for the wider scope and the minimum dataset used for the Euro-DEN project. Patterns of drug use in Europe were obtained from the EMCDDA annual reports from 2009 to 2013. Information on available NPS came from the EU Early Warning System (EWS) via a search of the European Database on New Drugs (EDND). This data was used to predict the clinical features likely to be seen in NPS toxicity and further define the minimum dataset.

**Results**

From a clinical standpoint, collecting data on features that related to the expected toxicity of established drugs and the larger groups of new drugs would be expected to identify the stimulant, hallucinogenic or sedative effects of most individual substances. Specific fields for cerebellar toxicity and neuropsychiatric symptoms were included in the minimum dataset to address recognised additional toxicity from NPS. Fields for vital signs, presenting symptoms, laboratory parameters and ECG findings were added to enable capture of the most clinically important toxic events. In order to facilitate data entry and analysis, a drop-down list for nominal (i.e. the clinical signs) and dichotomous (i.e. route of use) variables and free text fields for quantitative variables (i.e. blood pressure) were created. Additional fields for open responses allowed for the identification of unexpected or isolated clinical phenomena. It was felt that outcome and treatment fields would allow an evaluation of the severity of presentations as well as their impact on resources. A specific part of the data collection was dedicated to sedation used for recreational drug/NPS induced agitation/aggression to provide a European perspective on this controversial area.

Given the vast list of potential substances, the lack of a current universal coding system, along with awareness of the uncertain nature of responses from individuals presenting with acute toxicity, it was agreed that the minimum dataset would use a free text answer to record the substance(s) responsible for each presentation. A copy of the Excel® spreadsheet with the minimum dataset used to collect the data from each Euro-DEN centre is shown in Appendix 3.
Workstream 1 Activity 3 (WS1A3)

Objective
The objective of this activity was to establish a network of sentinel centres and use the minimum dataset to collect systematic data on adverse consequences (acute toxicity/harm) related to recreational drugs and NPS.

Methods
Case definition
For the purpose of data collection for the Euro-DEN project, the following case definition was used: “An individual who presents to participating acute care facilities with symptoms and/or signs consistent with acute recreational drug toxicity and/or directly related to recreational drug use. Patients with a primary diagnosis of isolated ethanol intoxication will be excluded (although those who co-ingest ethanol and present with recreational drug toxicity will be included)”.

Definition of a recreational drug
A recreational drug was defined as “a psychoactive compound that was taken for the purpose of recreational activities rather than for medical or work purposes or as part of (deliberate) self-harm”. The types of drugs, agents or activities included were:
- Established scheduled recreational drugs (classical recreational drugs)
- New (novel) psychoactive substances (NPS)
- Plants, fungi or herbal/alternative medicines
- Use of prescription and over the counter (OTC) medicines for recreational purposes
- Use of industrial and/or domestic products (i.e. solvents, propellants etc.) for recreational purposes

The identification of the recreational drug(s) associated with the presentation was based on one or a combination of the following:
- the patient’s self-reported use;
- information retrieved from witnesses;
- the opinion of the physician assessing the patient; and/or
- the toxicologist reviewing data entry/case records.

In addition some centres routinely analyse blood and/or urine samples when drug use is suspected and, if available as part of routine clinical care, the results were recorded in the dataset.

Case inclusion criteria
Any case in which a patient had symptoms and/or signs consistent with acute recreational drug toxicity and/or directly related to acute recreational drug use was included in the data collection. This included patients who presented to the ER because of concerns about an acute episode of drug use or who had been unwell prior to attendance to the ER (e.g. seizures in a nightclub) even if they had no clinical signs at the time of examination. The clinical symptoms the patients described or that they were witnessed to have experienced were recorded.

Case exclusion criteria
A patient who attended the ER with any of the following presentations was excluded from the data collection:
- Lone alcohol ingestion or intoxication, including cases involving ‘spiked drinks’ (i.e. drinks to which it is alleged a substance has been maliciously added) where patients had no symptoms of acute recreational drug toxicity
■ Symptoms and signs consistent with an alternate medical diagnosis and not related to acute recreational drug toxicity
■ Injury related to trauma, unless the trauma was directly related to drug use e.g. as a result of hallucinations
■ Drug or ethanol withdrawal
■ Secondary complications of chronic drug use (e.g. infected injection sites, viral infection (HIV/HBV/HCV), endocarditis) and no evidence of acute recreational drug toxicity
■ Secondary complications of previous acute drug use complications (e.g. previous stroke secondary to hypertensive intracranial haemorrhage, presentation with aspiration pneumonia)
■ An individual transferred through the ER for care to other areas of the participating centres (e.g. intensive care, surgery etc.) and not for a primary emergency evaluation

Data collection
The lead Euro-DEN centre at Guy’s and St Thomas’ NHS Foundation Trust in London, UK co-ordinated the data collection from the 16 sentinel centres participating in the Euro-DEN project which were (a brief description of each centre is given in Appendix 1 and the centres are shown on the map in Figure 1):

■ Emergency Area, Clinical Toxicology Unit, Hospital Clinic, Barcelona, Spain
■ Division of Clinical Pharmacology and Toxicology, University Hospital Basel, Basel, Switzerland
■ Emergency Department, Bispebjerg Hospital, Copenhagen, Denmark
■ Emergency Department, Our Lady of Lourdes Hospital, Drogheda, Ireland
■ Emergency Department, Mater Misericordiae University Hospital, Dublin, Ireland
■ Pomeranian Centre of Clinical Toxicology (PCT), Medical University of Gdansk, Gdansk, Poland
■ Clinical Toxicology and Emergency Department, St Thomas’ Hospital, Guy’s and St Thomas’ NHS Foundation Trust and King’s Health Partners, London, UK (London STH)
■ Emergency Department, Kings College Hospital, King’s College Hospital NHS Foundation Trust and King’s Health Partners, London, UK (London KCH)
■ Emergency Department and Clinical Toxicology Unit, Hospital Universitari Son Espases, Mallorca, Spain
■ Department of Clinical Toxicology, Technical University of Munich, Munich, Germany
■ Oslo Accident and Emergency Outpatient Clinic, Department of Emergency General Practice, City of Oslo Health Agency, Oslo, Norway (Oslo OAEOC)
■ Department of Acute Medicine, Oslo University Hospital, Oslo, Norway
■ Emergency Department, Lariboisière Hospital, Paris-Diderot University, Paris, France
■ Emergency Department, Pärnu Hospital, Pärnu, Estonia
■ Emergency Department, York Hospital, York Teaching Hospital NHS Foundation Trust, York, UK
■ Emergency Medicine Department, North Estonia Medical Centre, Tallinn, Estonia
The sentinel centres collected the minimum dataset developed in WS1A1 on each case presenting to them over the 12 months from 1st October 2013 to 31st September 2014 which met the criteria given above. Pre-formatted Excel® spreadsheets were circulated bi-monthly by the lead centre in London; the completed spreadsheets were then collated by the lead centre. Every case was given a unique Euro-DEN number and the centres held separate spreadsheets to match this number to patient identifiers, ensuring no sensitive or identifiable information was collected in the dataset but allowing the case to be traced if necessary. Each centre obtained appropriate ethical approval to collect the data from their institution; this was facilitated by the fact that no data other than that collected as part of the routine clinical examination was being used for the project.

Each spreadsheet with the minimum dataset (Appendix 3) contained six worksheets and was used to collect data for a calendar month at each Euro-DEN centre. On the first worksheet demographic and outcome details were recorded e.g. date and time of presentation and discharge, age, sex, home location, where the patient was discharged to from ER and if they died in hospital. On the second worksheet details of the exposure were recorded e.g. drug used, where and when the drug was used; the initial observations on arrival at the hospital were recorded on the third worksheet. The clinical features were recorded on the fourth worksheet. The treatments received before and/or in hospital, and what sedation the patient had received, if any, were recorded on the fifth and sixth worksheets respectively. To ensure consistency most cells had a dropdown menu from which specific answers were
selected. Free text entry was used for the agent name, the initial observations, age and the laboratory analysis; there was also a free text field for any additional comments about the case. A standard operating procedure (SOP) was written to assist the data collection process. In addition to the inclusion/exclusion criteria each data field and the pre-determined responses were defined in the SOP.

**Results**

**Number of presentations reported**

In total, 5529 presentations were reported during the 12 month data collection period (Figure 2). Tables 1 to 3 show the numbers of cases reported by each centre per month together with the proportion of attendances relating to acute recreational drug/NPS toxicity at each centre. The median was 0.3% (IQR 0.2-0.7%) with a range of 0 to 2.8%. As the centre in Gdansk is not within an institution with an ER, and the figures given relate to toxicology presentations only, they have not been included in this analysis.

The large variation in the number of presentations reported by the centres reflects the size and mix of the urban and semi-rural populations they serve and the function of the centres. The Oslo Accident and Emergency Outpatient Clinic (OAEOC) is a primary care emergency unit with limited treatment options and is therefore different from the other centres which are all Emergency Departments and/or specialist clinical toxicology units with full treatment options. This variation gives strength to the network providing data with an appropriate European dimension and balance. However, the large number of presentations to a few of the centres does influence the overall data and therefore some results are shown by centre.
Figure 2: Total number of acute drug/NPS toxicity presentations reported per month per centre, together with the annual total per centre.
Table 1. Presentations to Euro-DEN centres from October 2013 – January 2014 and total number of emergency presentations (all causes)

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*Total monthly ER figures not available
Table 2. Presentations to Euro-DEN centres from February 2014 – May 2014 and total number of emergency presentations (all causes)

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*Total monthly ER figures not available
Table 3. Presentations to Euro-DEN centres from June 2014 to September 2014 and total number of emergency presentations (all causes)

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<th>% Euro-DEN</th>
<th>Number of Euro-DEN cases</th>
<th>Total in ER/unit</th>
<th>% Euro-DEN</th>
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<td>571</td>
<td></td>
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<td>477</td>
<td></td>
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*Total monthly ER figures not available
Demographics

The age and gender breakdown of the presentations is shown in Figure 3. The median (IQR, range) age was 31 (24-39, 11-90) years and 75.4% presentations were in males. There were 46 (0.8%) cases in which the age was either unknown or not recorded. The median age of males was 31 (IQR 25-39) years and of females was 28 (IQR 22-37) years. Some centres did not treat paediatric patients which may have influenced the number of presentations reported in the under 16-18 year age group. The age and gender profile of each centre is given in the centre snapshot profiles.

Figure 3. Age range and gender of patients

Most individuals (4091, 73.9%) were resident in the city of the Euro-DEN centre at which they presented, with 1079 (19.5%) resident in another city and 201 (3.6%) from another country. The place of residence was unknown or not recorded in 158 (2.8%) presentations. It is important to note that almost a fifth of individuals were not resident in the city in which they attended hospital as this can have significant implications for discharge planning and follow-up care. The variation in whether the individuals lived locally (in the city of the Euro-DEN centre) or not (all other locations, including unknown/not recorded) between the centres was large, as shown in Figure 4. This was probably influenced by the size of the catchment area of the centre, and other factors such as proximity to a city centre where individuals from other areas visit bars or nightclubs. There was limited variation over the 12 months of data collection -the least presentations involving local individuals were in July (68.0% of those attending that month) and most in August (77.2% of those attending that month).
Figure 4. Percentage of presentations involving local residents at each centre

Time and date of presentations
The proportion of presentations per month and the day of presentation across all centres are shown in Figures 5 and 6. Most presentations were seen in August (571, 10.3%) and fewest in January (385, 7.0%) with Saturday being the most common day of presentation (1020, 18.4%) and Tuesday the least common (667, 12.1%).

Figure 5. Percentage of presentations per month
The times of presentation are shown in Figure 7, the peak time of presentation was between midnight and 0100 hours (332, 6.0%) with fewest between 0800 and 0859 hours (147, 2.7%). These figures indicate that many presentations occur outside normal working hours when more experienced staff may not be readily available to assist in the management of complex cases. The definition of ‘normal’ working hours will vary between centres, especially as ERs are 24-hour services, but between 2000 and 0759 there were 2996 (54.2%) presentations.
Drugs reported

Overall there were 8709 drugs reported to have been used in the 5529 presentations, the mean ± standard deviation number of drugs used per presentation was 1.6 ± 0.97. Excluding ethanol, 3349 (60.6%) presentations involved a single agent, 1492 (27.0%) involved two agents, 471 (8.5%) involved three agents, 148 (2.7%) involved four agents, 43 (0.8%) involved five agents and 26 (0.5%) involved six agents. As a result of the polysubstance use the total occurrences, or counts, of drugs (8709 in the full dataset) in the following graphs are greater than the number of presentations.

In 2145 (38.8%) presentations ethanol was co-ingested and in 1128 (20.4%) presentations it was not; whether or not ethanol was co-ingested was not recorded in 2256 (40.8%) presentations.

The proportions of the different types of drug reported to be used are shown in Figure 8 with the ‘top 20’ shown in Figure 9. The most commonly reported classical recreational drugs in the presentations were heroin, cocaine and cannabis and the most commonly reported NPS were the cathinones mephedrone and methedrone. The most commonly used prescription/over the counter (OTC) drugs were clonazepam and methadone. The ‘other’ category included agents such as butane, caffeine and ‘unknown psychotropic agent’ and any unidentified agent was classed as ‘unknown’; this did not include any agent that was partly identified such as ‘unknown benzodiazepine’ or ‘unknown opioid’.

Figure 8. Types of drugs reported (N=8709)
Figure 9. ‘Top 20’ most commonly reported drugs with NPS highlighted (n=8709 in 5529 presentations)
The large range in the number of presentations reported by the centres (from 1478 to Oslo OAEOC to 15 in Pärnu) influenced the data. For example 701 (52.1%) of the 1345 presentations involving heroin were from Oslo OAEOC; 293 (41.2%) of the 711 presentations involving GHB/GBL were from London STH and 280 (88.9%) of the 315 presentations involving clonazepam were from Oslo OAEOC. In order to illustrate this variation Table 4 lists the number of presentations for each centre with the four most common drugs and the most common NPS.

Table 4. Number of presentations per centre for the four most common drugs and the most common NPS mephedrone by Euro-DEN centre

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New Psychoactive Substances (NPS)
There were 470 presentations involving use of at least one NPS. As shown in Figure 10, the geographical spread of the NPS presentations varied considerably from no presentations in three centres to more than 20% of the total presentations to the centres in Gdansk (predominantly NPS ‘branded’) and London STH (predominantly mephedrone and methedrone).
Figure 10. Percentage of total presentations at each centre associated with use of one or more NPS

The total number of NPS used in the 470 NPS presentations was 484. Cathinones were the most commonly reported (n=378) of which mephedrone was the most frequent (n=245) as shown in Figure 11.

Figure 11: Most commonly reported cathinones

\[ MDPV = 3,4\text{-}methylenedioxyppyrovalerone \]
\[ 3\text{-}MMC = 3\text{-}methylmethcathinone \]
\[ Alpha-PVP = \text{alpha-pyrrolidinovalerophenone} \]
\[ Cathinone nk = cathinone \text{ not known} \]

The other 106 NPS reported in the presentations are shown in Table 5. NPS ‘branded’ included named compounds such as ‘bath salts’ and ‘Blue Ghost’ or ‘unknown NPS’.
### Table 5: Number of reports of NPS use – excluding cathinones

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<td>2</td>
</tr>
<tr>
<td>• 4-ethylamphetamine (4-EA)</td>
<td>2</td>
</tr>
<tr>
<td>• 1-(4-ethoxy-3,5-dimethoxyphenyl)propan-2-amine (3C-E)</td>
<td>1</td>
</tr>
<tr>
<td>• 2,5-dimethoxy-4-iodophenethylamine (2C-I)</td>
<td>1</td>
</tr>
<tr>
<td>• 2,5-dimethoxy-4-chloroamphetamine (DOC)</td>
<td>1</td>
</tr>
<tr>
<td>• 2-fluoroamphetamine (2-FA)</td>
<td>1</td>
</tr>
<tr>
<td>• 4-fluoromethamphetamine (4-FMA)</td>
<td>1</td>
</tr>
<tr>
<td>• 4-methylthioamphetamine (4-MTA)</td>
<td>1</td>
</tr>
<tr>
<td>• 4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine (25I-NBOME)</td>
<td>1</td>
</tr>
<tr>
<td>• 2-(4-bromo-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl) ethanamine (25B-NBOME)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Tryptamines</strong></td>
<td>7</td>
</tr>
<tr>
<td>• 5-methoxy-N-methyl-N-isopropyltryptamine (5-MeO-MiPT)</td>
<td>1</td>
</tr>
<tr>
<td>• alpha-methyltryptamine (AMT)</td>
<td>1</td>
</tr>
<tr>
<td>• N,N-dimethyltryptamine (DMT)</td>
<td>5</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>8</td>
</tr>
<tr>
<td>• Ethylphenidate (Ethyl 2-phenyl-2-(piperidin-2-yl)acetate)</td>
<td>4</td>
</tr>
<tr>
<td>• Methoxetamine (MXE)</td>
<td>3</td>
</tr>
<tr>
<td>• Methoxphenidine (MXP)</td>
<td>1</td>
</tr>
</tbody>
</table>

**Opioids, Benzodiazepines and ‘Z Drugs’**

Heroin was the most commonly reported opioid and Figure 12 shows the occurrence of all the opioids reported, including compound analgesics such as co-codamol. Of the 47 fentanyl cases, 24 were from the Tallinn centre and 21 were from the Munich centre. Of the 87 buprenorphine cases, 29 were from the Munich centre, 27 from the Oslo OAEOC centre and 21 were from the Paris centre.
The most commonly reported group of prescription medicines was the benzodiazepines, they were also the second most common group of drugs reported in the overall Euro-DEN data set (opioids 1962, benzodiazepines 1099, cocaine/crack cocaine 1093). The breakdown of the benzodiazepines is shown in Figure 13 with the ‘z drugs’ zopiclone and zolpidem included (there were no reports of the use of zaleplon). As shown in Table 6, there was widespread use of these drugs across all centres. However, some were only reported in a small number of centres and even for those reported by the majority of centres, a small number of centres accounted for a large proportion of the presentations.
Table 6: Reports of use of selected benzodiazepines and ‘z drugs’ by centre

<table>
<thead>
<tr>
<th>Centre</th>
<th>Number of presentations</th>
<th>Clonazepam</th>
<th>Diazepam</th>
<th>Alprazolam</th>
<th>Zopiclone</th>
<th>Oxazepam</th>
<th>Bromazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barcelona</td>
<td>199</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Basel</td>
<td>216</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Copenhagen</td>
<td>183</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Drogheda</td>
<td>36</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dublin</td>
<td>526</td>
<td>0</td>
<td>21</td>
<td>7</td>
<td>23</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gdansk</td>
<td>144</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>London STH</td>
<td>956</td>
<td>4</td>
<td>18</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>London KCH</td>
<td>422</td>
<td>5</td>
<td>17</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mallorca</td>
<td>181</td>
<td>1</td>
<td>4</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Munich</td>
<td>214</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Oslo OAEOC</td>
<td>1478</td>
<td>280</td>
<td>83</td>
<td>67</td>
<td>13</td>
<td>43</td>
<td>0</td>
</tr>
<tr>
<td>Oslo Ullevaal</td>
<td>199</td>
<td>17</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Paris</td>
<td>454</td>
<td>4</td>
<td>40</td>
<td>26</td>
<td>25</td>
<td>13</td>
<td>31</td>
</tr>
<tr>
<td>Pärnu</td>
<td>15</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>York</td>
<td>202</td>
<td>0</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tallinn</td>
<td>104</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Number of centres reporting this drug</strong></td>
<td><strong>10</strong></td>
<td><strong>15</strong></td>
<td><strong>13</strong></td>
<td><strong>8</strong></td>
<td><strong>5</strong></td>
<td><strong>3</strong></td>
<td></td>
</tr>
</tbody>
</table>

Other prescription medicines
Another prescription medicine that was commonly reported was pregabalin (80); there were fewer reports of presentations reporting use of other GABA-ergic drugs such as gabapentin (8) and baclofen (11). Pregabalin was reported in eight centres, although the majority of presentations (54, 67.5%) were in the Munich centre.

Euro-DEN Centre Profiles
Figures 14-29 show the ‘top five’ most commonly reported drugs from each centre as the count of how many times the drug was reported and as a percentage of the number of presentations. The latter is more than 100% because of the number of polydrug presentations; the number of agents taken in each presentation and if ethanol was co-ingested is shown at the side of these figures. The number of presentations involving unidentified, ‘unknown’, agents varied between centres and counts of these are also given; these counts do not include any agent that was partly identified such as ‘opioid unknown’, ‘benzodiazepine unknown’. Demographic data is also included.
Hospital Clinic is an inner city hospital with a high number of bars and nightclubs in its locality, especially those popular with the MSM (men who have sex with men) community. Patients under 14 years are not usually treated by the ER.

The hospital is located in central Basel, one of the larger cities in Switzerland but still rather provincial compared to Zurich. The hospital serves a population with mixed socioeconomic characteristics. There is a heroin/methadone substitution program running in a nearby specialised clinic. The ER treats patients over the age of 16 years.
The hospital is located in a socially deprived area of Copenhagen with a high proportion of low income and education and high unemployment rates compared to other areas of the city. The relatively high proportion of presentations due to methadone reflects the use of methadone for opioid substitution treatment. The ER treats both adult and paediatric cases but if the latter require admission they are transferred to another hospital.

Drogheda is an hour from Dublin, heroin users tend to migrate to Dublin and therefore heroin toxicity presentations are rare, otherwise, the pattern of recreational drug abuse is similar to Dublin. The ER treats both adult and paediatric patients.
The area the hospital serves includes some of the most socially deprived areas in Ireland with a significant intravenous drug problem in the locality. Children above the age of 16 years are treated in the ER.

The hospital is located in the centre of Gdansk, an urban, industrial area with a mixed population but it also serves the cities of Sopot, a widely recognised tourist and clubbing destination, popular with young people, and Gdynia, a modern affluent city with a large port. Additionally the hospital is surrounded by rural areas and this variety of communities is reflected in the drug use reported. Children from the age of 12 years are treated at the centre.
The hospital is situated in central London, close to Vauxhall, an area with one of the highest concentration of nightclubs in Europe, many of which are popular with the MSM (men who have sex with men) community. This is reflected in the high number of presentations involving GHB/GBL, MDMA and mephedrone which are used in this club scene. The ER treats adult and paediatric patients.

The hospital serves a similar population to STH but without the high number of nightclubs. It is located in inner city, south east London. It is an ethnically diverse area with significant social deprivation. The ER treats adult and paediatric patients.
Son Espases serves the city of Palma and other areas of the island including tourist destinations frequented by foreign tourists, especially British. There is a small population of heroin users, who tend to use multiple substances especially cocaine and benzodiazepines. The ER treats patients aged 15 years and over.

The university hospital is located fairly close to a night-clubbing area. There are a high proportion of patients who are under regular opioid substitution. Patients from 12 years old may be treated at the centre, although usually they are over 18 years old.
The Oslo Accident and Emergency Outpatient Clinic (OAEOC) is a primary care emergency institution, serving the entire city. Nearly all poisoned patients are assessed at the OAEOC unless triaged directly to hospital treatment by the ambulance service. Heroin use is widespread in Oslo, and most heroin overdoses are managed at the OAEOC or by the ambulance service. Amphetamine is the main stimulant drug used in Norway. The OAEOC treats both adult and paediatric patients.

Oslo University hospital is one of four hospitals serving the different areas of the city and is a tertiary centre for the most severely poisoned patients. Paediatric patients (under 16 years until September 2014 and now under 18 years) are treated at a separate part of the hospital with a separate ER, not included in this study.
Figure 26: Most commonly reported drugs – Paris

The hospital is in central Paris close to the Gare du Nord and Gare De L’Est, with a mix of affluent, socially deprived and an ethnically diverse population. The hospital has a specialist toxicology intensive care unit and the ER does not treat paediatric patients (under 15 years and 3 months in France).

Figure 27: Most commonly reported drugs – Pärnu

The hospital is in central Pärnu, a popular summer seaside resort, and has relatively few presentations of recreational drug use. In Estonia opioid overdoses are usually treated in the pre-hospital environment and patients only very rarely attend the ER. The ER treats both paediatric and adult patients.
The hospital is one of three with ERs in Tallinn and, as is not located in the town centre, patients with recreational drug use may be taken to one of the other hospitals. In Estonia opioid overdoses are usually treated in the prehospital environment and no cases of heroin use where admitted to the hospital during the study period. The ER does not treat paediatric patients.

York serves a semi-rural region with a mix of affluent and deprived areas, and the population is somewhat mobile as a result of the local universities and comparatively large volume of tourists during the summer. The number of attendances related to heroin is positively skewed by recurrent attendances by a small number of patients. The ER serves both paediatric and adult patients.
**Toxicological Screening**

The drugs reported to be used in the Euro-DEN presentations are based on patient self-report and clinical interpretation of the drugs used. Laboratory toxicological analysis was carried out in 864 (15.6%) presentations. This reflects current international best practice in which patients with acute recreational drug toxicity are managed on the basis of the clinical pattern of toxicity rather than on the basis of analytical confirmation which can often be delayed and rarely influences individual patient management (although clearly it can be extremely beneficial from an academic, epidemiological and wider perspective).

There was considerable variation in the breadth and extent of analysis as shown in Table 7. Analysis using an immunoassay detects some classical recreational drugs and is subject to a high false positive and false negative rate requiring further confirmatory analysis. NPS are only likely to be identified using mass spectrometry (MS) or liquid chromatography (LC) techniques which are only available in specialist laboratories and are expensive /complex to undertake. Most centres used an immunoassay and further analysis was not routinely undertaken; when it was, the samples often had to be transferred to another institute. The exceptions were Basel where approximately 50% of the samples were analysed using LC-MS/MS and Munich where 40% were analysed by HPLC.

In 49 (5.6%) of the 864 presentations in which laboratory analysis was performed no drugs were detected and in 33 (3.8%) only ethanol was detected; in 100 (11.6%) the drug(s) detected were not specified.

**Table 7: Summary of laboratory analysis (excludes presentations when only ethanol was tested for)**

<table>
<thead>
<tr>
<th>Centre</th>
<th>Number of presentations with analysis (% of presentations to centre)</th>
<th>Sample most frequently used</th>
<th>Analysis most frequently used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barcelona</td>
<td>123, 61.8%</td>
<td>Urine</td>
<td>Immunoassay (MS available)</td>
</tr>
<tr>
<td>Basel</td>
<td>178, 82.4%</td>
<td>Blood</td>
<td>Immunoassay then approximately 50% LC-MS/MS</td>
</tr>
<tr>
<td>Copenhagen</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Drogheda</td>
<td>28, 77.8%</td>
<td>Urine</td>
<td>Immunoassay</td>
</tr>
<tr>
<td>Dublin</td>
<td>42, 7.9%</td>
<td>Urine</td>
<td>Immunoassay</td>
</tr>
<tr>
<td>Gdansk</td>
<td>37, 25.7%</td>
<td>Urine</td>
<td>Immunoassay</td>
</tr>
<tr>
<td>London STH</td>
<td>10, 1.0%</td>
<td>Blood +urine</td>
<td>LC-MS/MS</td>
</tr>
<tr>
<td>London KCH</td>
<td>7, 1.7%</td>
<td>Urine</td>
<td>Immunoassay</td>
</tr>
<tr>
<td>Mallorca</td>
<td>32, 17.7%</td>
<td>Urine</td>
<td>Immunoassay (GC/MS available)</td>
</tr>
<tr>
<td>Munich</td>
<td>204, 95.3%</td>
<td>Urine</td>
<td>Immunoassay then approximately 40% HPLC</td>
</tr>
<tr>
<td>Oslo OAEOC</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Oslo Ulleval</td>
<td>60, 30.1%</td>
<td>Urine</td>
<td>Immunoassay (GC/MS available)</td>
</tr>
<tr>
<td>Paris</td>
<td>31, 6.8%</td>
<td>Urine</td>
<td>Immunoassay</td>
</tr>
<tr>
<td>Pärnu</td>
<td>3, 20.0%</td>
<td>Urine</td>
<td>Immunoassay (MS available)</td>
</tr>
<tr>
<td>York</td>
<td>7, 3.5%</td>
<td>Urine</td>
<td>Immunoassay (HPLC available)</td>
</tr>
<tr>
<td>Tallinn</td>
<td>78, 75.0%</td>
<td>Urine</td>
<td>Immunoassay (MS available)</td>
</tr>
</tbody>
</table>

**Location of drug use prior to presentation**

In the majority of presentations the location of the drug use was not recorded or unknown (3188, 57.7%). Figure 30 shows the location of use in the 2341 (42.3%) presentations in which it was recorded;
most commonly this was at home (751, 32.1%), on the street (612, 26.1%) or in a bar/nightclub (376, 16.1%).

**Figure 30. Location of drug use (in the 42.3% of presentations when it was known)**

The five drugs most often used in the different locations are shown in Figures 31-36. The drug most commonly used at home was cannabis (169 reports), in the street it was heroin (173 reports) and in bars/nightclubs it was MDMA/ecstasy (99 reports).
Most patients came to the ER by ambulance (3844, 69.5%) but in 133 cases (2.4%) this was not recorded. In the majority of presentations the time between using the drugs and presenting to the ER was unknown (2939, 53.2%). Of the remaining cases, the most common time to attend the ER was within 1-4 hours of use (1239, 47.8%) as shown in Figure 37.
Clinical features
The observations recorded on presentation are summarised in Table 8, with the peak creatine kinase and creatinine results.

Table 8. Presentation observations and other clinical data

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Number of presentation recorded (%)</th>
<th>Number of presentations when high (%) of total</th>
<th>Number of presentations when low (%) of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of consciousness at presentation</td>
<td>5363 (97.0)</td>
<td>Not applicable</td>
<td>GCS&lt;8/’coma’ 583 (10.5)</td>
</tr>
<tr>
<td>Heart rate at presentation</td>
<td>5268 (95.3)</td>
<td>&gt;120 bpm 577 (10.4)</td>
<td>&lt;60 bpm 338 (6.1)</td>
</tr>
<tr>
<td>Blood pressure at presentation</td>
<td>4920 (89.0)</td>
<td>systolic ≥180 mmHg 65 (1.2)</td>
<td>systolic ≤90 mmHg 167 (3.0)</td>
</tr>
<tr>
<td>Respiration rate at presentation</td>
<td>4381 (79.2)</td>
<td>Not applicable</td>
<td>&lt;12 per min 527 (9.5)</td>
</tr>
<tr>
<td>Temperature at presentation</td>
<td>4558 (82.4)</td>
<td>≥39°C 32 (0.6)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Peak creatine kinase</td>
<td>1016 (18.4)</td>
<td>&gt;200 IU/L 441 (8.0)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Peak creatinine</td>
<td>2172 (39.8)</td>
<td>&gt;100 mcmol/L or 1.13 mg/dL 289 (5.2)</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

The presence of 15 pre-defined clinical features (occurring at any stage before/during the hospital stay) was recorded; in 2097 (37.9%) presentations none of these clinical features were seen. As shown in Figure 38, the most commonly reported clinical features were agitation/aggression (1467, 26.5% presentations) and anxiety (1040, 18.8%). As several features could be reported in one presentation the counts are greater than the total number of presentations.

Figure 38. Percentage of presentations with each clinical feature at any time
Treatment
In 2634 (47.6%) presentations the patients received no treatment and in two cases the treatment was not recorded. As shown in Figure 39, sedation was the most commonly used treatment (in 1204, 21.8% presentations) followed by the opioid antagonist naloxone (859, 15.5%). The most commonly used drugs for sedation were benzodiazepines, used in 1067 (19.3%) presentations: 171 (16.0%) pre-hospital, 825 (77.3%) in hospital and 71 (6.6%) in both pre-hospital and in hospital. The other common agents used for sedation were propofol (126 (2.3%) presentations) and hydroxyzine (109 (2.0%) presentations, all of this was in the Gdansk centre).

Other antidotes were less commonly used: methylthioninium chloride in 12 (0.2%) presentations for methaemoglobinaemia, acetylcysteine in 11 (0.2%) for paracetamol and biperiden (7, 0.1%) for dystonia.

Figure 39. Number of presentations receiving different treatments

Outcome
The majority of patients (3148, 56.9%) were medically discharged from the ER as shown in figure 40.
The median length of stay in hospital was 4 hours 38 minutes (IQR 2h 29m - 9h 51m) and the range was two minutes to 69.5 days. As shown in Figure 41, the majority of patients stayed in hospital less than 12 hours (4311, 78.0%). In 24 (0.4%) presentations the length of stay was not available.

**Figure 41. Length of stay in hospital**

Cardiac Arrests
35 (0.6%) patients were in cardiac arrest on arrival at the ER and 19 (54.3%) of these patients died in hospital. The key characteristics of the non-fatal cardiac arrests are shown in Table 9.

**Table 9. Summary of the 16 non-fatal cardiac arrests**

<table>
<thead>
<tr>
<th>Ages (years), gender</th>
<th>Drug(s)</th>
<th>Ethanol Y=yes, N=no, NR=not recorded</th>
<th>Place of use</th>
<th>Time from use to presentation (hours)</th>
<th>Time in hospital (hrs: mins)</th>
<th>Qualitative analytical results (sample: drugs) B = blood, U = urine, NS = not specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>17, F</td>
<td>Amphetamine, cannabis, cocaine</td>
<td>Y</td>
<td>Unknown</td>
<td>Unknown</td>
<td>0:32</td>
<td></td>
</tr>
<tr>
<td>20, M</td>
<td>LSD</td>
<td>NR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>5:43</td>
<td></td>
</tr>
<tr>
<td>22, F</td>
<td>Alprazolam, clonazepam, heroin</td>
<td>Y</td>
<td>Street</td>
<td>1-4</td>
<td>14:09</td>
<td></td>
</tr>
<tr>
<td>28, M</td>
<td>Heroin</td>
<td>NR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>476:35</td>
<td></td>
</tr>
<tr>
<td>29, M</td>
<td>Cannabis</td>
<td>Y</td>
<td>Street</td>
<td>Unknown</td>
<td>10:25</td>
<td>B: negative</td>
</tr>
<tr>
<td>34, M</td>
<td>Diazepam, heroin</td>
<td>Y</td>
<td>Home</td>
<td>Unknown</td>
<td>4:37</td>
<td></td>
</tr>
<tr>
<td>38, M</td>
<td>Heroin</td>
<td>N</td>
<td>Home</td>
<td>1-4</td>
<td>34:28</td>
<td></td>
</tr>
<tr>
<td>38, M</td>
<td>Cocaine, heroin</td>
<td>NR</td>
<td>Home</td>
<td>Unknown</td>
<td>442:13</td>
<td>NS: Heroin</td>
</tr>
<tr>
<td>39, M</td>
<td>Heroin, pregabalin</td>
<td>N</td>
<td>Home</td>
<td>&lt;1</td>
<td>28:40</td>
<td>U: Opiates, pregabalin</td>
</tr>
<tr>
<td>40, F</td>
<td>Amphetamine</td>
<td>Y</td>
<td>Bar/night club</td>
<td>1-4</td>
<td>2:24</td>
<td>U: Amphetamine</td>
</tr>
<tr>
<td>41, M</td>
<td>Amphetamine, benzodiazepine nk, cocaine, heroin</td>
<td>N</td>
<td>Other private location</td>
<td>Unknown</td>
<td>46:55</td>
<td>NS: Cannabinoides, ecstasy, cocaine, opiates</td>
</tr>
<tr>
<td>44, M</td>
<td>Bromazepam,</td>
<td>N</td>
<td>Home</td>
<td>1-4</td>
<td>308:30</td>
<td></td>
</tr>
</tbody>
</table>
### Table 10. Summary of the 27 fatal cases

<table>
<thead>
<tr>
<th>Ages (years), gender</th>
<th>Drug(s)</th>
<th>Ethanol Y= yes, N= no, NR= not recorded</th>
<th>Place of use</th>
<th>Time from use to presentation (hours)</th>
<th>Time in hospital prior to death (hrs:mins)</th>
<th>Qualitative analytical results (sample: drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18, M</td>
<td>Cannabis</td>
<td>N</td>
<td>Bar/nightclub</td>
<td>&lt;1 hour</td>
<td>1:32</td>
<td>U: Cannabis</td>
</tr>
<tr>
<td>20, M</td>
<td>Benzodiazepine nk, cannabis, methadone</td>
<td>NR</td>
<td>Home</td>
<td>Unknown</td>
<td>98:32</td>
<td>U: Benzodiazepines, cannabis, methadone</td>
</tr>
<tr>
<td>25, M</td>
<td>Fentanyl</td>
<td>Y</td>
<td>Home</td>
<td>1-4 hours</td>
<td>96:16</td>
<td>U: not specified</td>
</tr>
<tr>
<td>25, M</td>
<td>Amphetamine, MDPV, paracetamol</td>
<td>NR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>88:30</td>
<td>B: MDPV</td>
</tr>
<tr>
<td>27, M</td>
<td>Heroin</td>
<td>NR</td>
<td>Street</td>
<td>&lt;1 hour</td>
<td>42:33</td>
<td></td>
</tr>
<tr>
<td>29, M</td>
<td>Baclofen, oxazepam, zolpidem</td>
<td>Y</td>
<td>Home</td>
<td>Unknown</td>
<td>3:05</td>
<td></td>
</tr>
<tr>
<td>30, M</td>
<td>Benzodiazepine nk</td>
<td>NR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>80:11</td>
<td></td>
</tr>
<tr>
<td>30, M</td>
<td>Methadone</td>
<td>N</td>
<td>Home</td>
<td>Unknown</td>
<td>1:08</td>
<td></td>
</tr>
<tr>
<td>31, F</td>
<td>Cocaine</td>
<td>N</td>
<td>Home</td>
<td>Unknown</td>
<td>26:05</td>
<td></td>
</tr>
<tr>
<td>Ages (years), gender</td>
<td>Drug(s)</td>
<td>Ethanol Y= yes N=no NR=not recorded</td>
<td>Place of use</td>
<td>Time from use to presentation (hours)</td>
<td>Time in hospital prior to death (hrs:mins)</td>
<td>Qualitative analytical results (sample: drugs). B = blood, U = urine, NS = not specified</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------</td>
<td>-------------------------------------</td>
<td>-------------</td>
<td>--------------------------------------</td>
<td>---------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>31, M</td>
<td>Unknown</td>
<td>N</td>
<td>Police/prison</td>
<td>Unknown</td>
<td>3:24</td>
<td></td>
</tr>
<tr>
<td>33, M</td>
<td>Opioid nk</td>
<td>Y</td>
<td>Unknown</td>
<td>Unknown</td>
<td>0:15</td>
<td>B: Codeine, ethanol, morphine</td>
</tr>
<tr>
<td>34, F</td>
<td>3-MMC, buprenorphine</td>
<td>N</td>
<td>Home</td>
<td>&lt;1 hour</td>
<td>175:03</td>
<td>U: 3-MMC, buprenorphine</td>
</tr>
<tr>
<td>34, F</td>
<td>Heroin</td>
<td>NR</td>
<td>Other</td>
<td>&lt;1 hour</td>
<td>2:44</td>
<td></td>
</tr>
<tr>
<td>34, M</td>
<td>Unknown</td>
<td>NR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>nk</td>
<td></td>
</tr>
<tr>
<td>35, M</td>
<td>Methadone</td>
<td>NR</td>
<td>Home</td>
<td>Unknown</td>
<td>1:52</td>
<td></td>
</tr>
<tr>
<td>36, M</td>
<td>Heroin</td>
<td>NR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>6:11</td>
<td></td>
</tr>
<tr>
<td>36, M</td>
<td>Heroin</td>
<td>N</td>
<td>Other private location</td>
<td>1-4 hours</td>
<td>56:43</td>
<td>NS: Amphetamine, cocaine, methamphetamine, morphine</td>
</tr>
<tr>
<td>36, M</td>
<td>Unknown</td>
<td>NR</td>
<td>Other</td>
<td>Unknown</td>
<td>0:31</td>
<td></td>
</tr>
<tr>
<td>37, F</td>
<td>Unknown</td>
<td>NR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>0:24</td>
<td></td>
</tr>
<tr>
<td>38, M</td>
<td>Methadone</td>
<td>Y</td>
<td>Unknown</td>
<td>Unknown</td>
<td>2:19</td>
<td>B: Ethanol, methadone</td>
</tr>
<tr>
<td>41, M</td>
<td>Amphetamine, cocaine,</td>
<td>NR</td>
<td>Home</td>
<td>&gt;24 hours</td>
<td>0:17</td>
<td></td>
</tr>
<tr>
<td>41, M</td>
<td>Cocaine, MDMA</td>
<td>Y</td>
<td>Other private location</td>
<td>1-4 hours</td>
<td>1:14</td>
<td>U: Cocaine, MDMA</td>
</tr>
<tr>
<td>41, M</td>
<td>Mephedrone</td>
<td>NR</td>
<td>Home</td>
<td>13-23 hours</td>
<td>0:18</td>
<td></td>
</tr>
<tr>
<td>43, M</td>
<td>Heroin</td>
<td>NR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>240:13</td>
<td></td>
</tr>
<tr>
<td>46, M</td>
<td>Cocaine</td>
<td>Y</td>
<td>Unknown</td>
<td>Unknown</td>
<td>468:39</td>
<td></td>
</tr>
<tr>
<td>48, M</td>
<td>Heroin</td>
<td>NR</td>
<td>Home</td>
<td>Unknown</td>
<td>17:28</td>
<td></td>
</tr>
</tbody>
</table>

**Snapshot Summaries for the Most Common Recreational Drugs / NPS**

To give an overall picture of the characteristics of the most common classical recreational drugs and the most common NPS reported, ‘snapshots’ were compiled from those presentations when the drug was used with no other recreational drug, see figure 42. The median (IQR) of the age and length of hospital stay are shown, with the percentage of the presentations that were transferred to critical care and the overall number of fatal cases.
Figure 42. Snapshots of the most commonly reported classical recreational drugs and NPS when reported as the only drug

<table>
<thead>
<tr>
<th>Drug</th>
<th>n</th>
<th>Age of users (years)</th>
<th>% male users</th>
<th>Top place of use</th>
<th>% presentations with ethanol</th>
<th>Common effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HEROIN (n=662)</strong></td>
<td></td>
<td>36 (29-45)</td>
<td>81.9%</td>
<td>street</td>
<td>14.8%</td>
<td>coma, low RR, agitation, hypotension</td>
</tr>
<tr>
<td><strong>COCAINE (n=421)</strong></td>
<td></td>
<td>30 (25-36)</td>
<td>76.2%</td>
<td>home</td>
<td>61.0%</td>
<td>anxiety, chest pain, palpitations, agitation</td>
</tr>
<tr>
<td><strong>CANNABIS (n=421)</strong></td>
<td></td>
<td>24 (19-30)</td>
<td>72.0%</td>
<td>home</td>
<td>48.7%</td>
<td>anxiety, agitation, vomiting, palpitations</td>
</tr>
<tr>
<td><strong>Mephedrone (n=88)</strong></td>
<td></td>
<td>27 (24-33)</td>
<td>68.2%</td>
<td>home</td>
<td>18.2%</td>
<td>agitation, anxiety, chest pain</td>
</tr>
</tbody>
</table>

**Length of stay (hr:min):**
- **HEROIN:** 4:59 (2:56-7:46)
- **COCAINE:** 3:40 (2:00-8:14)
- **CANNABIS:** 3:01 (1:49-5:24)
- **Mephedrone:** 3:45 (2:03-7:19)

**% to critical care:**
- **HEROIN:** 3.9%
- **COCAINE:** 4.0%
- **CANNABIS:** 0.7%
- **Mephedrone:** 2.3%

**% fatal:**
- **HEROIN:** 0.9%
- **COCAINE:** 0.5%
- **CANNABIS:** 0.2%
- **Mephedrone:** 1.1%

Feedback on Data Collection Process
Prior to the Euro-DEN project most of the centres had not been routinely and systematically collecting this type of data. Half the centres used a keyword or code search of the ER admissions database as the main way of identifying the cases but a quarter manually searched the admissions logbook or patient records (in one centre 8500 ER records a month were manually checked to identify Euro-DEN cases). The other most common ways of identifying cases were being told about them by colleagues or through requests for toxicological opinions; two centres also cross referenced with the laboratory. The difficulties most often encountered were confirming what agent the patient had used, identifying the recreational drug cases, reading the handwriting in the patient record and obtaining an ambulance/emergency services summary. Almost half the centres felt that the allocated two days per month were not sufficient time for the data collection; despite this all of the centres returned the full Euro-DEN dataset in time for inclusion in the project.
An Excel® spreadsheet was used as it was considered the simplest means of collecting and manipulating the data. The size of some of the worksheets meant that columns could be hidden from view and therefore not completed, this occurred most commonly with the clinical features sheet. Using six separate worksheets prevented cross analysis of the information sets unless the worksheets were combined into one single sheet; this process was labour intensive. The data was collected from the clinical records made at the time of presentation and the minimum dataset could be completed from this source in most presentations. This meant the activity was similar to an audit of specific cases, the advantage of which was that patient consent was not required. However certain information was regularly not recorded, for example where the drug had been used (57.7%), how long ago it had been used (53.2%), the route of use (40.4%) and whether ethanol had been co-ingested (40.8%). It is possible that the relevant questions were asked during the clinical assessment but the answers were not recorded in the patient record. In the fatal cases, some centres found it difficult to obtain post mortem results as these had to be obtained from the pathologist or another department and there could be delays in releasing them because of the length of time before an inquest took place.

Workstream 2: Training and guidelines for staff in recreational settings to respond to drug related incidents

Workstream 2 Activity 1 (WS2 A1)

Objective
The objective of this activity was to develop a training package to deliver training for staff in recreational settings (nightclubs, bars etc.) to use guidelines to enable them to identify individuals with acute recreational drug toxicity requiring further clinical assessment.

Methods
The Steering Group reviewed the previously developed training package which the lead centre had used in training staff working in night-time economy venues in South East London in 2008. This package was revised, particularly to include information on NPS. The ambulance referral guidelines on when to call an ambulance for an individual with acute recreational drug toxicity, developed by the lead centre (Wood, Greene et al. 2008) and the revised version of these guidelines adapted to a European context through a desktop international expert panel review [ECMDDA Contract Code CC.11.SAT.020], were reviewed by the Steering Group. This review also incorporated information from Australian published guidelines for ambulance staff on managing individuals with acute recreational drug toxicity (Jenner, Spain et al. 2006).

Results
The finalised training package was a 14-slide PowerPoint® presentation which consisted of four components: i) background information on acute toxicity related to the use of classical recreational drug and novel psychoactive; ii) introduction to the ambulance referral guidelines (discussed in more detail in the WS2A2 below); iii) interactive case discussion based on simulated case scenarios covering three acute recreational drug/NPS toxicity related scenarios; and iv) practical session on use of the recovery position. Detailed notes were made on each PowerPoint® slide to ensure consistency in the content of the training in the different centres. The PowerPoint® slides and associated notes for trainers are in Appendix 4.

The revised guidelines (Appendix 5) that were produced were translated from English into Spanish, Norwegian and Estonian. The main changes from the previous versions of the guidelines were i) replacement of the AVPU assessment for the level of consciousness to a more simplified assessment method (still based on the AVPU scale); ii) rearrangement of the order in which the clinical features were
listed (e.g. putting agitation higher up in the assessment process); iii) simplifying the temperature parameters for situations where a thermometer is not be available; and iv) changing the word ‘ambulance’ to ‘emergency services’ followed by their usual telephone number (e.g. 999 in the UK). The guidelines were renamed “Guidelines on when to call the Emergency Services for unwell recreational drug users”. They were then translated into Spanish, Norwegian and Estonian and formatted with the assistance of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), see Appendix 5 for the English version.

**Workstream 2 Activity 2 (WS2 A2)**

**Objective**

The objective of this activity was to determine the feasibility of delivering training to staff in recreational settings (nightclubs, bars etc) to use guidelines to identify individuals with significant drug related adverse consequences requiring further clinical assessment and to use data obtained from this to refine the guidelines developed in WS2 A1 and the associated training.

**Methods**

In the grant application this activity was due to be led by the Brno centre, however the Brno centre withdrew from the project at the end of Year 1 and therefore the London centre took over the lead of this activity. In addition the centre in Pärnu, Estonia was recruited to participate in the feasibility study, this ensured appropriate and equivalent pan-European coverage.

The training was organised by the local leads in London, UK; Oslo, Norway; Palma, Spain; and Tallinn, Estonia. Training sessions were undertaken in local night-time economy venues. The staff working within those venues were invited by the management of the venues to attend the sessions. Participants in the training sessions were asked to complete a pre- and post-training questionnaire; the post-training questionnaire had questions which assessed the length, quality, content and format of the training sessions (each scored out of a maximum of 10), and rated the usefulness (out of 10) of the guidelines on knowing when to contact emergency services. In addition, participants were able to provide unstructured free-text feedback on the training session as a whole.

**Results**

Training was undertaken in local night-time economy venues (nightclubs) in London, UK (2 sessions), Oslo, Norway (2 sessions) and Pärnu and Tallinn, Estonia (1 session at each). It was not possible to organise training in Palma, Mallorca during the feasibility study; this was initially due to the inability of night-time economy staff during the summer season to attend the training when the feasibility study was undertaken (June-August 2014). It was not possible to arrange this later in the year (September-October 2014), as the majority of night-time economy staff are employed on a seasonal basis and therefore were no longer working there.

The total number of attendees was 147; 42 in London, 88 in Oslo and 17 in Pärnu and Tallinn. 135 (95.1%) participants felt the training session was the right length as designed; 6 (4.1%) felt it was too short, 4 (2.7%) felt it was too long and 2 (1.4%) did not answer the question. The mean ± SD overall rating (out of 10) of the training package was 8.2 ± 1.4; the recovery position was rated as 8.4 ± 2.3 and the interactive cases as delivered were rated as 7.6 ± 1.7. Thirty-seven participants provided additional free text comments on the training session. Qualitative review of the additional free text comments given by participants identified three main themes on how the training session could be improved: i) more interactive and/or practical training (21 participants); ii) changing the structure / format of the session (6 participants); and iii) increased information on different drugs (7 participants). In terms of those who provided comments about the structure / format of the session, the specific comments were: i) increase questions for participants (1 participant); reduce questions for participants (1 participant); iii)
increase breaks in session (1 participant); iv) not keen on using PowerPoint® as written (2 participants); v) session too medical (doctor) orientated (1 participant). Overall, these results indicated that the training sessions were well received and that the majority of participants felt that the training package was suitable.

The overall mean rating of the usefulness of the guidelines was as 8.7 ± 1.7; there were no free text comments regarding the content or the design of the one page guidelines from participants in the training session. Therefore, following the training sessions, it was decided that there would be no change in the guidelines on when to call an ambulance for someone who is unwell following the use of recreational drugs and NPS that had been trialled during the training sessions. As noted earlier the previous iterations of these guidelines had been published in the peer reviewed literature (Wood, Greene et al. 2008) and reviewed by an expert panel during an EMCDDA funded project [ECMDDA Contract Code CC.11.SAT.020].

There was additional interest in Oslo, Norway when the training of night-time economy workers was undertaken and the national television station included a segment on the training workshop and the reasons behind the work on its evening news programme.

Publications and Presentations from the Euro-DEN Project
The Euro-DEN project has been presented at international conference in Europe, the USA and Asia (13 invited keynote lectures and 8 abstracts (7 posters and 1 oral platform); these are detailed in Appendix 2. There have also been 3 peer-reviewed papers from the Euro-DEN project published to date, 1 further paper submitted for publication and the Steering Group plan to continue to oversee the submission of a number of papers relating to the Euro-DEN dataset after the completion of the grant which will enable further analysis of key information from the rich Euro-DEN data.

The guidelines on when to call the emergency services have been published on the EMCDDA Best Practice Portal (http://www.emcdda.europa.eu/news/2015/euro-den).

Discussion
The Euro-DEN project is a European Commission DPIP funded project that has delivered all of the stated objectives in the grant proposal and provided a unique insight into the acute harms associated with recreational drugs and NPS in Europe.

European Data on Acute Drug Toxicity
The survey undertaken in the initial stages of the project illustrated that there is currently little systematic data collection on attendances to hospital emergency rooms (ERs) related to the recreational use of drugs and new psychoactive substances (NPS) in Europe (Heyerdahl, Hovda et al. 2014). This represents a significant gap in the understanding of the Public Health impact of drug/NPS use in Europe.

By establishing a network of centres and using a relatively simple data collection tool, the Euro-DEN project has demonstrated that a comprehensive picture on the harms associated with drugs and NPS can be collated. This includes demographic information, data on the drugs/NPS responsible for toxicity, clinical pattern of toxicity, outcome (length of hospital stay, admission to critical care, mortality) and management of recreational drug/NPS presentations. The collaboration achieved by the project has resulted in data from over 5,500 presentations being available for analysis, showing the patterns of acute drug use in 16 sentinel hospital Emergency Rooms in 10 countries.

Demographics of presentations
Most of the reports involved males (75.4%) who were residents of the city (73.9%) in which the Euro-DEN centre was based, the overall median age was 31 years (range 11-90 years). Although the location of
the drug use was not recorded in the majority of presentations, when it was it was most frequently at home or in the street, rather than at bars or nightclubs. There was some variation of the drugs used by location; on the street heroin and cannabis use were most common; at nightclubs and festivals MDMA and cocaine were most common; and at home and in other private locations cannabis and cocaine were most common. However, despite this the two main drug categories of stimulants and depressants were seen in all locations and therefore there is little difference in pre-hospital service provision and prevention requirements. The frequency of heroin presentations from home, the street and other private locations further supports initiatives to increase public availability of naloxone. Almost a fifth of individuals were not resident in the city in which they attended hospital and this has significant implications for discharge planning particularly as presentations are most common during the night.

Patterns of drugs associated with presentations
The mean number of drugs (excluding alcohol) per presentation was 1.6, with over 60% of presentations involving only a single drug. Classical recreational drugs were most commonly reported drugs and heroin was the most common. Heroin was reported by all centres with the exception of the two centres in Estonia - this is likely to reflect the pattern of opioid use in Estonia, with predominant availability and use of fentanyl (EMCDDA 2014 a). Cocaine and cannabis were the second and third most common classical recreational drugs and were reported in all centres. GHB/GBL was the fourth most common drug overall; however 85% of presentations associated with GHB/GBL were from the London, Oslo and Barcelona centres showing that presentations related to acute GHB/GBL toxicity are more clustered than other drugs. This may reflect a number of different factors including localised patterns of use.

Prescription/OTC drugs were associated with over 25% of Euro-DEN presentations. The most common drugs within this category were the benzodiazepines and opioids, with only a small number of cases related to other drugs. Fentanyl presentations were predominantly from the Tallinn and Munich centres; this mirrors data from the EMCDDA Trend Spotting Meeting 2012 and the European Drug Report 2014 on the patterns and availability of opioids in these countries (EMCDDA 2014 a). Buprenorphine presentations were predominantly in the Munich, Oslo OAEOC and Paris centres which may reflect variation in European opioid substitution programmes. The benzodiazepines were the second most common group of drugs in the overall Euro-DEN dataset. Some of the benzodiazepines e.g. diazepam, clonazepam and alprazolam were seen across the majority of centres, although there was variability in the number per centre. Others such as bromazepam and oxazepam were only seen in a minority of centres. Further work is required to understand the reasons for these patterns, including comparison with prescribing data to be able to inform appropriate geographically targeted prevention activity.

NPS were less frequently seen than classical recreational drugs and prescription / OTC medicines. The group of NPS most frequently reported in presentations was the cathinones, with mephedrone being the most common NPS. Presentations associated with the use of NPS were concentrated in a few centres, especially those in Gdansk, the UK (London and York), Dublin and Munich; in contrast there were three centres (Pärnu, Tallinn and Drogheda) that had no presentations with NPS use. There may be reduced recognition of NPS in areas with lower numbers of presentations. However, the pattern seen mirrors data from the UNODC and EMCDDA on other indicators related to NPS including prevalence of use and availability (EMCDDA 2014 a, UNODC 2013).

Strengths and Limitations of the Euro-DEN Project
The departments participating in the Euro-DEN project are sentinels centres and they are not necessarily representative of the countries in which they are based. However they are specialist centres with an interest in the acute toxicity of drugs and therefore have both the expertise and interest to collect the data. The centres serve different sizes and types of population (from urban to semi-rural) and there are variations in their functions. Most are in hospitals with general Emergency Departments, but the OAEOC in Oslo offers primary care assessments with admission to another hospital if necessary, whilst the
centre in Gdansk acts only as a tertiary referral centre. There was disparity in the number of presentations reported by the centres (ranging from 15 to 1478) so a few centres contributed large numbers of cases to the overall dataset. However the proportion of presentations related to recreational drugs, compared to the total ER attendances, was similar in across the Euro-DEN centres. Whilst the variation in the absolute numbers between the centres can be seen as a limitation, it is also a strength as it provides insights into presentations from a variety of different settings. Finally there is the potential that some of the patterns seen, such as the variations in drugs involved in presentations, may reflect the sentinel nature of the centre and local patterns of use and availability. An example of this is the high proportion of GHB/GBL use in the London, Barcelona and Oslo centres. However, some of the patterns seen in the Euro-DEN dataset are similar to those seen in other indicators such as general population surveys and treatment data. For example, the pattern of stimulants in Euro-DEN presentations is similar to data from the European Drug Report with higher proportion of cocaine use in presentations to the Spanish and UK centres compared to a higher proportion of amphetamine use in presentations to the Norwegian and Polish centres.

The Euro-DEN dataset is based on patient self-report and clinical interpretation of the drugs used. Routine comprehensive laboratory analysis was only undertaken in a minority of presentations and typically this was with immunoassay. This is representative of international best practice in recreational 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. Whilst it may be desirable for full toxicological screening with a comprehensive technique to be undertaken in all presentations, this would be expensive, logistically difficult and ethically challenging. Future studies should consider targeted screening for either a focused range of drugs in all presentations or comprehensive screening in a representative cohort. This would require analytical expertise, appropriate funding and careful consideration when interpreting the results.

The data collection for the project was based on the information collected as part of the routine clinical records made at the time of presentation. This is important as it means that the information collected is representative of contemporaneous clinical practice and patient management. It does mean that some parameters were not available for some presentations. A prospective data collection proforma may enable more complete data collection on individual cases; this would require additional ethical and administrative approval. Additionally, from a practical perspective this would be so demanding to perform in a busy ER setting that the overall participation would be significantly reduced.

Implications for acute medical services
When compared to the total attendances to the ERs, acute recreational drug/NPS toxicity accounted for a small proportion of total presentations to the ER (median of 0.3%). Serious or potentially life threatening clinical features were not seen in the majority of presentations and almost 90% of patients were discharged within 24 hours. However, over a quarter of presentations were associated with agitation, over 10% with coma and 6% with psychosis. Almost 70% of presentations were brought to hospital by ambulance; over 10% had pre-hospital naloxone, but it is likely that this is an under-representation of the use of pre-hospital naloxone as the data was collected from ER records. Overall, more than 50% of presentations received some form of treatment (including over 20% requiring sedation) and 6% required critical care admission. There were 35 cases who presented in cardiac arrest of whom 19 died; in addition there were a further 8 in-hospital fatalities. The most common time of presentation was overnight and at weekends when staffing numbers may be lower and less experienced staff may be on duty. Therefore these presentations represent a substantial and disproportionate clinical workload with associated resource implications for both pre-hospital and hospital acute medical services.
Implications for public health
From a public health perspective, data on patterns of harms associated with drug/NPS use and where it occurs, along with demographic data such as age, gender and home location is useful for deciding where to provide specialist treatment and target interventions. Although there is often media interest in NPS, data from the Euro-DEN project suggests that classical recreational drugs are most commonly associated with ER presentations and severe toxicity including deaths. This is mirrored by other EMCDDA indicators of high risk/problem drug use, such as estimates of the numbers of users, data from treatment facilities and data on fatal and non-fatal intoxications. Over a quarter of the drugs associated with presentations were prescription/OTC medicines and further work is required to understand patterns of recreational misuse of these drugs in Europe to inform prevention work to prescribers, the public and other key stakeholders in this area.

As a means of raising public awareness of the health emergencies related to recreational drug use and to improve early recognition and management of recreational drug toxicity in the pre-hospital environment, a training package was developed for staff working in the night-time economy, such as bars and nightclubs. The local characteristics of patterns of drug use were used to make the training package more relevant to those being trained in the different cities, whilst a common format enabled the results from each centre to be compared. The training was well received and participants felt more confident in the assessment of individuals with drug toxicity after the training. Guidelines on when to call the emergency services have been developed and are now available on the EMCDDA best practice portal and are being submitted for publication in the peer-reviewed literature to further increase their dissemination and use in the field.

Continuation of the Euro-DEN Project: Euro-DEN Plus
The Euro-DEN project has demonstrated the value of data collection from sentinel centres across Europe in documenting the acute toxicity associated with recreational drugs and NPS. Following the completion of Workstream 1 Activity 3 data collection in September 2014, all of the Euro-DEN sentinel centres have agreed to continue collecting data. In addition, two further centres have joined the project – these are in Ekaterinburg, Russia and Roskilde, Denmark. This ongoing data collection network will be referred to as the Euro-DEN Plus project. Currently this is unfunded but the centres are all happy to continue as they feel that there is significant value in continuation of the project. The EMCDDA will continue to provide support to the project and the lead Euro-DEN centre in London will continue to collate, analyse, and facilitate dissemination and reporting of the data.

The Euro-DEN Steering Group have reviewed the minimum dataset developed in Workstream 1 Activity 2 and determined that some data fields, particularly those for which data was not routinely available in the hospital records, should be removed for the Euro-DEN Plus minimum dataset. All of the key variables which enable description of the main demographic, clinical and outcome parameters related to acute recreational drug and NPS toxicity remain.

Euro-DEN Plus will enable us to build on the strength and size of the Euro-DEN dataset, further examine geographical and time trends and continue to monitor evolving changes in this important area in which there is a paucity of reliable, systematic data. The sentinel centres are committed to continuation of data collection and this will be presented at conferences, disseminated to key stakeholders such as REITOX Focal Points and the EMCDDA and submitted for publication in the peer-reviewed literature. Further grant and/or core funding will be sought to enable further development and sustainability of the Euro-DEN Plus network.
Suggestions for the future
The guidelines developed on when to call the emergency services for an individual with acute recreational drug / NPS toxicity were launched through the EMCDDA Best Practice Portal in February 2015. The associated training package was successfully delivered in three European countries. Feedback after the training sessions received from those working in the night-time economy suggested consideration of more practical and interactive training. This could be undertaken using simulation training, similar to that used for training healthcare professionals. In addition, there would be the potential to consider development of a training video to enable wider dissemination at lower cost. The feasibility study undertaken in Euro-DEN has shown that the training improves confidence in the management of acute recreational drug and NPS toxicity. Both of these further developments would enhance the training package to enable more widespread and effective improvement of pre-hospital assessment of European citizens with acute recreational drug and NPS toxicity.

There are a number of further developments that could add value to the Euro-DEN Plus data collection system and its outputs. As noted above, the Euro-DEN network has already included two further centres, including one in Russia. The Euro-DEN Plus network has 18 centres in 11 countries and is representative of the primary stimulant use across Europe as reported by the ECMDDA. Further expansion of the network will be explored to include at least one sentinel centre in all European Union and neighbouring countries. In addition to expansion of the network, as discussed in detail above, there should be consideration of enhanced toxicological screening of biological samples in acute recreational drug/NPS toxicity presentations. Whilst this is not clinically justified nor routinely feasible and whilst it would require significant additional resource and analytical capacity there is the potential that screening, particularly of selected relevant cases, would add value to the self-reported and clinician ascribed drug(s) associated with presentations.

The Euro-DEN Plus system will provide comprehensive and detailed data on the overall picture of acute recreational drug and NPS toxicity in presentations to sentinel centres. Whilst it is feasible to increase the number of centres within the network to improve the European coverage, data collection of the complete minimum dataset is only feasible in specialist centres with an interest in acute drug toxicity. A complimentary approach that would allow data collection from a larger number of centres within each European Union and neighbouring country would be to use a snapshot methodology. This has been used successfully in providing widespread representative data that has resulted in improvements in the health of European citizens in other areas including sepsis and trauma. The snapshot methodology could involve collecting a subset of key data parameters from the Euro-DEN Plus minimum dataset. This could be undertaken over a shorter period of time, for example a week, every three to six months. This would enable regular reporting of data using a standardised reporting structure to the EMCDDA and other key stakeholders including legislative bodies and policy makers. The Euro-DEN minimum dataset includes over 60 data parameters, this methodology would involve 10-15 essential data parameters that would capture drugs involved and demographics together with indicators of severity of toxicity and outcome.

The benefit of the snapshot methodology is that it provides data from a large number of ERs enabling a richer, repeatable and more representative picture of geographical patterns and trends within individual centres. This is complimentary to the Euro-DEN Plus dataset which provides more comprehensive data on the patterns and severity of toxicity together with capture of information on rare or less frequently encountered drugs and NPS. The snapshot methodology could also be employed to inform Risk Assessment of new and emerging NPS by targeting data collection to areas in which there were signals generated from other key indicators and reports to the European Union Early Warning System.

Workstream 1 Activity 1 of the Euro-DEN Project confirmed that there is limited systematic data being collected in Europe on acute recreational drug and NPS toxicity. This is a significant gap in the Public Health implications of drug and NPS use in Europe. The ultimate aim of the further development of the Euro-DEN Plus sentinel network system together with the snapshot methodology would be to contribute
to a new key indicator on acute recreational drug/NPS toxicity, complimentary to the existing key indicators currently reported to the EMCDDA by REITOX Focal Points in European Union and neighbouring countries. This would address the gap in the Public Health understanding of the harms of recreational drugs and NPS, leading to a more complete picture on the implications of drug use in Europe.

Conclusions
The Euro-DEN project is a European Commission funded project that has delivered all of the stated objectives in the grant. The project has developed and delivered training for staff in recreational settings and published European guidelines on the assessment of individuals with acute drug/NPS toxicity in night-time economy settings. The minimum dataset developed has been used to demonstrate that data can be successfully collected by sentinel centres across Europe. The data on 5529 presentations over a 12 month period provides a unique insight into the drugs associated with acute drug toxicity in Europe, and the patterns and implications of this. Case-based data collection from sentinel hospital Emergency Rooms will continue in the Euro-DEN Plus Project and the group plan to build further on this and look at further developing of training for the night-time economy. This will lead to improvements in the health and wellbeing of European citizens in this key area of Public Health need.
References


Appendix 1: Descriptions of Euro-DEN centres

Barcelona
Emergency Area, Clinical Toxicology Unit, Hospital Clinic, Barcelona, Spain.
The Hospital Clinic is a 600 bed teaching hospital in central Barcelona serving a population of over 550,000. In 2013 there were almost 115,000 attendances at the ER of which approximately 2000 were due to poisoning. Poisoned patients are treated in the emergency area, intensive care or general medical wards.
Euro-DEN Contributors: Oscar Miro, Miguel Galicia

Basel
Division of Clinical Pharmacology and Toxicology, University Hospital Basel, Basel, Switzerland
The University Hospital Basel serves as primary care and referral centre for north-western Switzerland, a population of about 1 million. In 2014, there were approximately 48,000 attendances at the ER of which approximately 1000 were associated with intoxications. Poisoned patients are seen by the emergency physician with the clinical pharmacologist & toxicologist on-call when specialised advice is needed.
Euro-DEN Contributors: Matthias Liechti; Evangelia Liakoni

Copenhagen
Bispebjerg Hospital, Copenhagen, Denmark
Bispebjerg Hospital is part of the Copenhagen University Hospital. The hospital serves approximately 400,000 citizens from the Municipality of Copenhagen and Frederiksberg. In the period from October 2013 to September 2014, there were over 72,000 attendances to the ER, approximately 600 due to poisoning. Clinical toxicology is not a medical specialty in Denmark. Poisoned patients are typically seen by internists or anesthesiologists in the ER. The Danish Poison Information Centre (Giftlinjen), based at Bispebjerg Hospital, provides advice on more complex, rare or unusual cases of poisoning, but has no day-to-day responsibility for patient care in the ER.
Euro-DEN Contributors: Gesche Jurgens; Carsten Boe Pedersen; Katrine Elisabeth Moller Mortensen

Drogheda
Emergency Department, Our Lady of Lourdes Hospital, Drogheda, Republic of Ireland
Our Lady of Lourdes hospital is the regional hospital in the North East of the Republic of Ireland and serves a mixed urban and rural population. The department has 54,000 patient attendances per annum of which 300 have poisoning as their presenting complaint.
Euro-DEN Contributors: Niall O’Connor; Gerard Markey; Sarah Jane Yeung

Dublin
Emergency Department, The Mater Misericordiae University Hospital, Dublin, Republic of Ireland
The Mater Misericordiae University Hospital is a 600 bed teaching hospital located in the north inner city serving a domiciled population of approximately 185,000 people. The emergency department saw approximately 50,000 patients in 2014 with just over 8,000 seen in the aligned minor injuries unit. Initial management of toxicological emergencies is in the emergency department with admission under general medicine or critical care if required.
Euro-DEN Contributors: Adrian Moughty; Ciara Daly; Alan Blake; Stuart O’Flanagan; Carla Hopper; Andy Neil; Ryan Boyd Moffatt; Aaron Donnelly

Gdansk
Pomeranian Centre of Clinical Toxicology, Gdansk, Poland
Pomeranian Centre of Clinical Toxicology (PCT) is a specialist hospital located in centre of Gdansk, north of Poland and serves as a toxicology reference hospital for three regions with a combined population of about 5.8 million. There are about 1300 admissions to the PCT every year of intoxication or severe
withdrawal syndrome in intoxicated patients. The PCT operates 24/7 and consists of 17 beds including 7 intensive care beds with facilities for mechanical ventilation and renal replacement therapy. The staff specialises in Internal Diseases, Clinical Toxicology and Emergency Medicine and the PCT is a teaching facility for Medical University of Gdansk. Additionally PCT serves as a Poison Control Centre and Toxicological Information Centre. Euro-DEN Contributors: Jacek Sein Anand; Piotr Maciej Kabata; Wojciech Waldman

London STH
Clinical Toxicology Service, Guy’s & St Thomas’ NHS Foundation Trust, London UK
Guy’s and St Thomas’ NHS Foundation Trust (GSTT) is a 1100 bed teaching hospital in central London serving a population of over 1.6 million. In 2013 there were almost 137,500 attendances at the ER, of which approximately 2000 were due to poisoning. These patients are seen by the Clinical Toxicology service during office hours in the ER, intensive care or general medical wards and out of hours a consultant toxicologist is on-call. The clinical toxicology service collects detailed data on a purpose designed database all poisoned patients, not just those with recreational drug/NPS toxicity. Euro-DEN Contributors: Paul I Dargan; David M Wood; Alison M Dines; Maeve McParland

London KCH
Emergency Department, King’s College Hospital NHS Foundation Trust, London UK
King’s College Hospital (KCH) is a 900 bed teaching hospital in south east London serving a similar population to that of GSTT. In 2013 there were almost 135,000 attendances at the ER, of which approximately 1600 were due to poisoning. There is no formal toxicology service at KCH but there are strong links with the service at GSTT. The GSTT clinical toxicology service collects detailed data on a purpose designed database all poisoned patients at KCH, not just those with recreational drug/NPS toxicity. Euro-DEN Contributors: Paul I Dargan; David M Wood; Alison M Dines; Melvin Lipi

Mallorca
Emergency Department and Clinical Toxicology Unit, Hospital Universitari Son Espases, Palma de Mallorca, Spain.
Son Espases is a 750 bed teaching hospital serving as a primary hospital for a resident population of about 400,000 and as a reference hospital for over a million people. As Mallorca is a leading tourist destination there is a large migrant population of tourists and seasonal workers especially during summer months, with over 8 million foreign tourists each year. In 2013 there were almost 89,000 attendances at the ER with approximately 1500 due to poisoning. The ER treats poisoned patients on arrival; poisoned patients are reviewed by a member of the Clinical Toxicology Unit when on-duty or during office hours. No formal reference consultant is on-call for toxicology. Euro-DEN Contributors: Christopher Yates; Jordi Puiguriguera; Catalina Homar

Munich
Department of Clinical Toxicology, Klinikum rechts der Isar, School of Medicine of the Technical University Munich, Germany
The School of Medicine of the Technical University Munich is a 1,100-bed tertiary university teaching hospital. During the study period between October 2013 and September 2014, there were over 12,250 attendances at the medical ER, of which over 1500 were due to poisoning. Poisoned patients are admitted directly and treated separately from the general medical ER at our department of Clinical Toxicology which has 28 beds; 5 in a fully equipped ICU, 13 in a high dependency unit and 10 in a general ward. Additionally, it provides a toxicological laboratory service and the Munich’s Poison Control Center with about 36,000 inquiries per year. Poisoned patients are seen by the Clinical Toxicology stuff during office hours, intensive care stuff during the night shift and there is 24 hours/7 days a consultant
toxicologist on-call. A team of qualified social education workers, psychologists, an art-therapist and a psychotherapist work in the specialized addictive clinic.

**Euro-DEN Contributors:** Florian Eyer; Stefanie Geith

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**Oslo OAEOC**

**Oslo Accident and Emergency Outpatient Clinic (OAEOC), Norway**

The Oslo Accident and Emergency Outpatient Clinic (OAEOC) is the main casualty clinic in Oslo. It is a primary care emergency institution, serving the entire city (population 650,000) at all hours. The OAEOC has facilities for short time observation, but diagnostic tools and treatment options are limited. In Norway, patients cannot present directly to hospitals, but have to be assessed in primary care or by the ambulance service first. The OAEOC has nearly 200,000 consultations a year, among them about 3000 due to acute poisoning. One in five poisoned patients presenting to the OAEOC are referred to hospital. Poisoned patients are treated at the Emergency General Practice Department, mostly by registrar/resident-level general practitioners.

**Euro-DEN Contributors:** Odd Martin Vallersnes

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**Oslo Ullevaal**

**Department of Acute Medicine, Oslo University Hospital, Oslo, Norway.**

The Department of Acute Medicine is based in the Oslo University Hospital (OUH), an emergency hospital with local, regional and national responsibility of a variety of assignments. The Department consists of an observational unit of 17 beds with a medical intensive care unit of 12 beds and it hosts the Norwegian CBRNe Centre of Medicine. The Department treats approximately 600 poisonings per year; among those the most severely poisoned ones from a catchment area of approximately 3 million people. All five clinical consultants for the National Poison Control Centre are also employed at the same department.

**Euro-DEN Contributors:** Knut Erik Hovda; Fridtjof Heyerdahl; Per Sverre Persett

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**Paris**

**Emergency Department, Lariboisière Hospital, Assistance Publique – Hôpitaux de Paris, Paris, France**

Lariboisière–Fernand Widal Hospital is a 1,200 bed teaching hospital in central Paris serving a population of over 3 million. In 2013, there were almost 141,000 attendances at the ER of which approximately 5000 were due to poisoning. Poisoned patients are seen by the Emergency Medicine Physicians on a 24/7 day-basis. Specialists on-call from the Paris Poison Centre and the medical and toxicological intensive care unit at the same hospital are consulted if required for any specific or severe case, respectively.

**Euro-DEN Contributors:** Bruno Mégarbane; Lucie Chevillard

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**Pärnu**

**Pärnu Hospital, Estonia**

Pärnu Hospital is a 330 bed hospital in western part of Estonia serving a population of about 100,000, which increases significantly in the summer with tourists from other parts of Estonia and abroad. In 2013 there were almost 30,000 attendances to the ER of which more than 300 were due to poisoning. Poisoned patients are initially managed within the ER and, if further treatment is needed, may be admitted to the general medicine wards or intensive care unit.

**Euro-DEN Contributors:** Raido Paasma

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**York**

**York Teaching Hospital NHS Foundation Trust, York, UK**

York Teaching Hospital NHS Foundation Trust provides services to a semi-rural population of around 800,000 people that living in or near York and North Yorkshire. York Hospital has 700 inpatient beds and the ER receives about 80,000 attendances per year that include around 900 poisoned patients. Toxicology patients are managed initially within the ER and, if needed, may be admitted to the Acute
Medical Unit or critical care areas under the care of a General Physician, with support from a local liaison psychiatry team.

**Euro-DEN Contributors:** W Stephen Waring

**Tallinn**

**North Estonia Medical Centre, Tallinn, Estonia**

The North Estonia Medical Centre is a 1,230 bed hospital. In 2013 there over 75,800 attendances to ER of which approximately 1,300 were due to poisoning. The poisoned patients are initially treated by the emergency medicine doctors in ER and if further treatment is needed, the patients are transfered to intensive care or general medicine wards.

**Euro-DEN Contributors:** Andrus Remmelgas; Kristiina Põld
Appendix 2: Euro-DEN papers, invited keynote presentations, abstracts and other outputs


Invited keynote presentations relating to Euro-DEN

Wood DM. The role of the European Drug Emergencies Network (Euro-DEN) in the toxicovigilance of NPS.
Invited oral presentation: EMCDDA Expert meeting on the toxicovigilance of new psychoactive substances, Lisbon, Portugal, December 2014


Wood DM, Dines A, Dargan PI on behalf of the Euro-DEN project. Emergency Department Presentations with Acute Cannabis Toxicity in Europe: Data from the Euro-DEN Project.
Invited oral presentation (Wood DM): EMCDDA, Annual expert meeting on Drug-related deaths (DRD) and Drug-related infectious diseases (DRID), Lisbon, Portugal, October 2014

Dargan PI.
Novel Psychoactive Substance Toxicity: Bench to Bedside.
Invited Keynote Lecture (Dargan PI). Asia Pacific Association of Medical Toxicology Conference, Shenyang, China, September 2014.

Wood DM. Novel sources of data on novel psychoactive substances/recreational drugs
Invited lecture as part of the Continuing Education Course: EuroTox congress, Edinburgh, UK, September 2014.

Wood DM. Development of guidelines to be used by non-specialist staff on appropriate management and when to involve ambulance services/referral to the emergency department.
Invited lecture: 13th Annual CARES conference, Dundee, UK, June 2014

Invited keynote lecture: EAPCCT, Brussels, Belgium, May 2014

Dargan PI.

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Recreational Drug Toxicity: Novel Drugs
Invited Keynote Lecture (Dargan PI). International Conference on Emergency Medicine, Hong Kong, June 2014.

Dargan PI.
Recreational Drug Toxicity

Dargan PI.
Assessing the pattern of acute toxicity associated with NPS: problems, solutions and the Euro-DEN project.
Research and Advances in Psychiatry 2014; Suppl 1:17
Invited Keynote Lecture (Dargan PI), 3rd International Conference on Novel Psychoactive Substances, Rome, May 2014

Yates C. Clinical features of Emergency Department presentations with acute toxicity from novel drugs of abuse: insights from the Euro-DEN Project.

Wood DM. Novel psychoactive substances – epidemiology and toxicology.
Invited keynote lecture: HATS Scientific Conference 2013 – Metropolitan Poisoning, Hong Kong, China, November 2013

Invited presentation: EMCDDA, Annual expert meeting on Drug-related deaths (DRD) and Drug-related infectious diseases (DRID), Lisbon, Portugal, October 2013

Conference abstracts
Poster presentation: EAPCCT, St Julian’s, Malta, May 2015

Poster presentation: EAPCCT, St Julian’s, Malta, May 2015

Poster presentation: EAPCCT, St Julian’s, Malta, May 2015
Poster presentation: EAPCCT, St Julian’s, Malta, May 2015

Poster presentation: EAPCCT, St Julian’s, Malta, May 2015

Oral communication (Dargan PI): EAPCCT, St Julian’s, Malta, May 2015

Poster presentation: NACCT, New Orleans, USA, October 2014

Poster presentation: EAPCCT, Brussels, Belgium, May 2014

Other
The guidelines on when to call the emergency services have been published on the EMCDDA Best Practice Portal (http://www.emcdda.europa.eu/news/2015/euro-den).
### Appendix 3: Spreadsheet with minimum dataset

#### SHEET 1: 1) Demographic and outcome details

**Total ER attendances for month:**

<table>
<thead>
<tr>
<th>Euro-DEN Number</th>
<th>Date and time of presentation</th>
<th>Day of presentation select</th>
<th>Age (years)</th>
<th>Sex select</th>
<th>Home location select</th>
<th>Home location OPTIONS:</th>
<th>Discharge from ER select</th>
<th>Discharge from ER OPTIONS:</th>
<th>Died in hospital? select</th>
<th>Date and time of discharge dd/mm/yyyy HH:MM</th>
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</thead>
<tbody>
<tr>
<td>16-01-0001</td>
<td>16-01-0001</td>
<td>Local</td>
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<td></td>
<td></td>
<td></td>
<td>Medically discharged</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-01-0002</td>
<td>16-01-0002</td>
<td>National</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Self discharge</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>International</td>
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<td>Admit critical care</td>
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</tr>
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<td></td>
<td></td>
<td>Not recorded</td>
<td></td>
<td></td>
<td>Unknown</td>
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<td>Admit psych</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Death</td>
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<td></td>
<td>Not recorded</td>
<td></td>
<td>Death</td>
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</table>

#### SHEET 2: 2) Exposure details

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<tr>
<th>Euro-DEN Number</th>
<th>Ambulance to ER? Select</th>
<th>Location of use select</th>
<th>Time from use to presentation select</th>
<th>Ethanol co-ingested? select</th>
<th>Body packer or stuffer? select</th>
<th>Agent1 free text</th>
<th>Type of preparation select</th>
<th>Route of use select</th>
<th>CONTINUES FOR 6 AGENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-01-0001</td>
<td>Yes</td>
<td>Home</td>
<td>&lt;1 hour</td>
<td>Yes</td>
<td>Packer</td>
<td>Tablet</td>
<td>Oral</td>
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<tr>
<td>16-01-0002</td>
<td>No</td>
<td>Other private location</td>
<td>1-4 hours</td>
<td>No</td>
<td>Stuffer</td>
<td>Capsule</td>
<td>Insufflated</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Bar/nightclub</td>
<td>5-12 hours</td>
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<td>No</td>
<td>Powder/crystalline</td>
<td>Inhaled</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>Street</td>
<td>13-23 hours</td>
<td></td>
<td></td>
<td>Liquid</td>
<td>Inject</td>
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<tr>
<td></td>
<td></td>
<td>Festival</td>
<td>&gt;24 hours</td>
<td></td>
<td></td>
<td>Gas</td>
<td>Rectal</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Police/prison</td>
<td>Unknown</td>
<td></td>
<td></td>
<td>blotter</td>
<td>Vaginal</td>
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<tr>
<td></td>
<td></td>
<td>Other</td>
<td>herbal</td>
<td></td>
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<td>herbal</td>
<td>Other</td>
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<td>packet</td>
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### SHEET 3
3) Observations at presentation

<table>
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<th>Euro-DEN Number</th>
<th>In cardiac arrest?</th>
<th>Lactate mmol/L</th>
<th>Temperature degrees C</th>
<th>Glucose (molar) mmol/L</th>
<th>Glucose (mass) mg/dL</th>
<th>Conscious level GCS or Alert/Drowsy/Coma</th>
<th>Heart rate bpm</th>
<th>Systolic BP mmHg</th>
<th>Diastolic BP mmHg</th>
<th>Resp rate per min</th>
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</thead>
<tbody>
<tr>
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<td></td>
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</table>

OPTIONS:  
- Yes  
- No

### SHEET 4
4) Clinical features present during the presentation

<table>
<thead>
<tr>
<th>Euro-DEN Number</th>
<th>Vomiting select</th>
<th>Dyspnoea select</th>
<th>Hyperthermia select</th>
<th>Headache select</th>
<th>Anxiety select</th>
<th>Hallucinations select</th>
<th>Agitation/Aggression select</th>
<th>Psychosis select</th>
<th>Seizures select</th>
<th>Cerebellar features select</th>
<th>Palpitations select</th>
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OPTIONS:  
- Yes  
- No

Row continues:  

<table>
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<tr>
<th>Hypertension select</th>
<th>Hypotension select</th>
<th>Arrhythmias select</th>
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<th>QRS ms</th>
<th>QTc ms</th>
<th>Peak creatine kinase IU/L</th>
<th>Peak creatinine mmol/L</th>
<th>Peak creatinine mg/dL</th>
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OPTIONS:  
- Yes  
- No
### SHEET 5  5) Treatment and outcome

<table>
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<tr>
<th>Euro-DEN Number</th>
<th>Treatment required select</th>
<th>Intubated select</th>
<th>Vasopressors/ inotropes select</th>
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<th>Flumazenil select</th>
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<th>Analytical confirmation select</th>
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</table>

**OPTIONS:**
- Yes pre-hospital
- Yes hospital
- No

### SHEET 6  6) Sedation

<table>
<thead>
<tr>
<th>Euro-DEN Number</th>
<th>Sedation select</th>
<th>Barbiturates select</th>
<th>Benzodiazepines select</th>
<th>Chlorpromazine select</th>
<th>Clonidine select</th>
<th>Dexmedetomidine select</th>
<th>Droperidol select</th>
<th>Haloperidol select</th>
<th>Ketamine select</th>
<th>Olanzapine select</th>
<th>Propofol select</th>
<th>Other free text</th>
</tr>
</thead>
<tbody>
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**OPTIONS:**
- Yes pre-hospital
- Yes hospital
- Yes both
- No
Appendix 4: Training presentation – slides with trainers’ notes

Slide 1:

Recreational Drugs
How to recognise toxicity and when to call 999

Dr Paul Dargan and Dr David Wood
Guy's and St Thomas’ NHS Foundation Trust

Euro-DEN club training v1 UK: 13/06/2014

Put names of the people running the session on this title slide and at XXX the 3-digit telephone number for the emergency services

Points to cover:
Introductions
As part of Euro-DEN, an EU funded project, we have developed this training package about the problems which can occur when people use recreational drugs. The same training is being run in London, Oslo, Mallorca and Estonia. We would like to find out if you find it helpful and how it could be improved.

Materials to take:
Copies of pre and post questionnaires
Pens
Signing in sheet for names (especially for certificates) and contact details (for one month questionnaire)
Copies of ambulance guidelines
Certificates
Mat/towels to lie on for demo of recovery position
Slide 2:

Contents of training session

- Pre-training questionnaire
- Types of drugs commonly used
- Examples of acute recreational drug problems
- Putting someone into the recovery position
- When to call the emergency services (999)
- Post-training questionnaire and certificate

- Before we start please answer the pre-training questionnaire
- We are going to look at the types of drugs that are commonly used [locally] and the effects they can cause
- Using examples we will discuss the serious effects you should look for
- We will practise how to put someone in the recovery position
- We will discuss what signs of toxicity should make you call an ambulance
- We would like you to answer a questionnaire at the end of the session and in one month’s time to look at the impact of this training session
- We’ll give you a certificate of attendance for today at the end of this session (when you’ve completed the questionnaire!)
Slide 3:

Types of recreational drugs used

- “Classical” recreational drugs
  - Cocaine, MDMA, amphetamines, ketamine etc

Form and administration of drugs:

MDMA, amphetamine and ketamine are usually used in tablet or powder form and ingested, snorted or injected.
Cocaine is usually powder but crack cocaine is in ‘rocks’ similar to sugar cubes which is smoked or injected.
GHB is usually a liquid in small bottles ingested NB: MOVED TO ‘NEW’ RECREATIONAL DRUG VENN DIAGRAM.
Opioids may come as tablets or as powder for injecting or smoking or as a liquid.
Hallucinogens may come as tablets, powder or liquid and LSD on squares of paper. Magic mushrooms may come as fungi or in other food.
Types of recreational drugs used

- Change in the drugs used in the last 5-10 years
  - New psychoactive substances (NPS)
  - Often called ‘legal highs’

Available over the Internet, in head shops and from dealers

Rapidly changing field - over 70 new drugs per year in Europe

Lots of drugs with long complicated scientific names. Often sold as “bath salts” or “plant food” or under trade names (give some local examples and substitute these pictures)

Generally cause the same sorts of problems as the classical recreational drugs
“Classical” recreational drugs is a term used to cover drugs that have been used for decades.

Stimulant drugs ‘stimulate’ the body systems.
Common effects include hyperactivity, restlessness, talkativeness, anxiety, teeth grinding, sweating and large (dilated) pupils.
Complications include severe agitation and aggression, fast heart rate (tachycardia), high blood pressure (hypertension), convulsions (seizures/fits), strokes, heart attacks and dangerously high body temperature (hyperpyrexia).

Depressant drugs ‘depress’ the body systems.
Common effects include an initial high, sometimes associated with agitation, sleepiness, vomiting and small (constricted) pupils.
Complications include convulsions (seizures/fits) and vomit getting into the lungs (aspiration), severe drowsiness with decreased breathing rate and swallow breathing or breathing may stop.

Hallucinogenic drugs cause hallucinations (visual and/or auditory).
Common effects include an altered sense of reality, ‘out of body’ experiences, hallucinations and feelings of persecutions and paranoia. In addition some hallucinogens (e.g. ketamine) can also cause aggression and more rarely sleepiness, breathing problems and high blood pressure. Serious complications are rare but the effects can be unpleasant and people may act in a dangerous way.

Note that:
• There can be some overlap in the effects of the different types of drugs
• Some people may use several drugs (polydrug use) at the same time or over a period of time
• Some people may not know what drug(s) they have used.
“New” recreational drugs are being regularly developed.
More than one new drug per week in Europe
Effects as before – although some overlap (particularly stimulant and hallucinogenic drugs) and some people may use drugs from different classes
Case 1

- One of the security team asks for your help because a man has become very agitated
- When you see him, the man is sweating and is shouting and pushing people away
- What sort of drug do you think he has taken?
- How would you assess him?
- What other drug related problems would you be worried about?

Points to cover:

- Serious signs include
  - High temperature - discuss if measurement will be possible at the venue
  - High blood pressure – discuss if measurement will be possible at the venue
  - High heart rate – discuss how to measure the pulse
  - Chest pain – mention common descriptions of chest pain
- Urgent transfer to hospital
- Cooling methods
Slide 8:

Case 2

- Someone tells you his friend has used some drugs and he is becoming anxious and acting strangely
- What sort of drug do you think he has taken?
- How would you assess him and what would you be looking out for?

Points to cover:

- Check that he doesn’t have any ‘worrying’ problems discussed in the previous case
- Ask him whether he is having hallucinations (seeing or hearing things)
- How to decide if they are safe to leave
  - Can anyone else accompany him?
  - Does he know how to get home and will there be someone at home or someone who can stay with him?
  - What is the weather/ambient temperature?
- How to obtain more information from an agitated person – see next slide
Talking to and assessing an agitated person

- Try and find a quiet area, away from other people
- Talk in an even, calm tone of voice
- Use the person’s name
- Listen to the person
- Use open-ended questions
- Avoid negative language
- Avoid too much eye contact
- Allow the person as much personal space as possible

- How to obtain more information from an agitated person (a verbal de-escalation strategy!)
  - Act in a calm and confident manner
  - Try and take the person to a quieter area; unexpected stimuli like loud noises or sudden movements can make the situation worse
  - People affected by stimulant/hallucinogenic drugs are more likely to respond positively to communication that is not perceived as hostile, threatening or confrontational so try to:
    - Listen to the person
    - Use the person’s name to personalise the interaction
    - Speak in an even, calm tone of voice – even if the person becomes hostile
    - Use open-ended questions to find out the cause of the behaviour e.g. “How did....”
    - Avoid negative, ‘no’ language which may cause an aggressive outburst. Use phrases such as: “I’m sorry our policy does not allow me to do that but I can offer you other help like.....”
    - Allow the person as much personal space as possible whilst still maintaining control of the situation
    - Avoid too much eye contact as this can increase fear or promote aggressive outbursts in some hostile or paranoid individuals
Case 3

- Someone tells you his girlfriend has collapsed and she’s with some friends who are trying to wake her up
- What sort of drug do you think she has taken?
- How would you assess her and what would you do?

Points to cover:

1. Assess how alert / drowsy she is ... talk about the AVPU scale
   A=Alert
   V=Responds to voice i.e. talking to
   P= Responds to painful stimuli only (e.g. pressure across a finger nail)
   U=Unconscious

2. Big problem in someone who is unconscious is that they are not breathing enough and not protecting their airway
   - Reduced rate/swallow breathing
   - Vomit into lungs

3. Recovery position
   (see next slide)
Slide 11:

Points to cover:

Demonstrate recovery position and get participants to try it on each other

Take a towel or mat so you don’t have to lie on a dirty floor!

Slide 12:

Points to cover:

Distribute copies of the guideline.
Go through each point, clarifying how to assess them
Slide 13:

**Summary**

- Drugs can be classed as stimulants, hallucinogens or depressants
- Use the guidelines on when to call 999
  - Early hospital assessment of those with severe toxicity is important
- If someone is unconscious, put them in the recovery position and get help

Points to cover:
- Notes re overlap and polydrug use
- Make sure questionnaires are completed by participants and trainers
- Distribute certificates (or send later?)
- Ensure have contact details for one month post training evaluation

Slide 14:

**THANK YOU!**

**ANY QUESTIONS?**

Please answer our post training questionnaire!
The Euro-DEN Project
Guidelines on when to call the Emergency Services 999 for unwell recreational drug users

Call 999 if ANY one of the following is present:

- Unconsciousness – if the patient does not respond to vocal commands, requires painful stimulus (e.g. pressure across the fingernails) to respond or does not respond at all
- Significant agitation (e.g. pacing around the room) or aggression not settling within 15 minutes
- Seizures (e.g. a convulsion similar to an epileptic fit)
- Breathing difficulties, such as fast breathing rate, not settling within 5 minutes
- Heart rate over 140 beats per minute not settling within 5 minutes
- Temperature over 38.5°C not settling after about 5 minutes of rest, or if very flushed and feels very hot if no thermometer is available
- Blood pressure: Systolic ("upper pressure") over 180mmHg, or Diastolic ("lower pressure") over 110mmHg on 2 repeated blood pressure measurements
- If there are any other concerns (e.g. severe headache, chest pain)

IF IN DOUBT CALL 999!
Glossary
Arrhythmia – abnormal heart rhythm
Aspiration pneumonia – chest infection following inhalation of stomach contents
ATS – amphetamine-type stimulants
Cellulitis – infection of the deeper layers of the skin
Cerebellar features – clinical signs related to dysfunction of the cerebellum (such as unsteadiness, tremor, oscillating eye movements and slurred speech)
Creatine kinase – an enzyme measured in the blood and used to indicate muscle damage
Creatinine – a breakdown product measured in the blood and used indicate kidney function
Dyspnoea – difficulty in breathing
Dystonic/choreiform movement disorders – involuntary muscle movements
EMCDDA – European Monitoring Centre for Drugs and Drug Addiction
Endocarditis – infection of inner lining (endocardium) of the heart
ER – Emergency Room
Euro-DEN – European Drug Emergencies Network
GHB/GBL – gamma-hydroxybutyrate and gamma-butyrolactone
GCS – Glasgow Coma Score, a measure of the level of consciousness
HIV – human immunodeficiency virus
HBV – hepatitis B virus
HCV – hepatitis C virus
HPLC – high performance liquid chromatography
Hypertension – high blood pressure
Hyperthermia – high body temperature
Hypotension – low blood pressure
Intracranial haemorrhage – bleeding within the skull
Intubation – insertion of tube into the windpipe (trachea) to maintain an open airway
LC-MS/MS – liquid chromatography – mass spectrometry
Methaemoglobinaemia – the presence of methaemoglobin in the blood. This does not transport oxygen as effectively as haemoglobin and may cause breathlessness
MDMA - 3,4-methylenedioxy-methamphetamine
MDPV - Methyleneoxyprovalerone
MS – mass spectrometry
MSM – men who have sex with men
NPS – new psychoactive substance
OAEOC - Oslo Accident and Emergency Outpatient Clinic
SCRA – synthetic cannabinoid receptor agonist
SOP – standard operating procedure
Systolic blood pressure – the upper of the two blood pressure reading
Vasopressors – drugs which constrict the blood vessels and are used to increase blood pressure
WS – workstream, the project was divided into three workstreams which were made up of different activities (A) e.g. WS1A1