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for Drugs and Drug Addiction

RAPID COMMUNICATION

High-risk drug use and new psychoactive substances

Results from an EMCDDA trendspotter study

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European Monitoring Centre
for Drugs and Drug Addiction

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

Contents

EMCDDA authors/contributors: Jane Mounteney, Manuel Ruiz, Alessandra Bo, Teodora Groshkova, João Matias, Liesbeth Vandam, Feline Cardoso, Rachel Christie, Linda Montanari, Isabelle Giraudon, Paul Griffiths

Study rationale and methods

In recent years, environmental signals from both formal and informal research and monitoring sources have been indicating critical new developments within Europe's new psychoactive substances (NPS) market. These include signs of increased and problem use of NPS among a range of demographic groups, including the use of synthetic cathinones by opioid and amphetamine injectors, the injection of synthetic cathinones by certain subgroups of men who have sex with men, reports of potent new synthetic opioids found in heroin products, and the use of synthetic cannabinoids by marginalised populations in some countries.

To investigate the circumstances and impact of these developments, a targeted rapid information assessment or 'trendspotter' study was initiated by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and carried out between July and October 2016.

The study aimed to map and increase understanding of high-risk drug use and NPS in Europe, including the range of forms this may take, the underlying facilitating factors, and associated harms and consequences. Specifically, it aimed to explore:

- the main high-risk user groups and their characteristics;
- clusters, patterns and trends in use;
- primary substances/products used and their effects;
- associated harms and deaths;
- external triggers and motivations for use.

In terms of methodology, the study was divided into two phases. The first phase involved a round of data collection by an EMCDDA team, including a literature review and the conducting of online surveys. The second phase centred on data collection and analysis. The analysis took place during an expert meeting, held in Lisbon on 20–21 October 2016. This event was attended by 15 invited experts from 11 countries, who shared information and contributed to an in-depth analysis of the topic, providing insights from a range of perspectives including drug research and monitoring, front-line service provision, forensics, law enforcement and health.

The trendspotter study methodology utilises a range of different investigative approaches and data collection from multiple sources (Mounteney et al., 2015). This study incorporated three internet surveys (one among national focal points in 30 countries; one among experts attending the meeting; and one in an EMCDDA trendspotter network), ad hoc data collection among prison experts, a non-systematic review of the international literature, grey literature and available monitoring data, 15 expert presentations, and findings from three facilitated working groups. Analysis was based on triangulation of these information sources, with a view to providing as complete

Definitions used in this study

High-risk drug use definition — the study took as a starting point a focus on NPS use among:

a) high-risk users of opioids, stimulants and cannabis ([1]) who switch to NPS use or incorporate NPS in their polydrug use patterns;
b) people who inject NPS or use them in other potentially harmful ways (including slamming);
c) people experiencing problems/entering treatment for NPS-related problems;
d) marginalised or vulnerable drug-using populations (including homeless people, prisoners, people with mental health problems etc.).

Exclusion criteria — experimental use, occasional use, psychonauts, use not associated with health and social problems.

New psychoactive substance definition — the study took as a starting point a focus on non-controlled and recently controlled new psychoactive substances, in particular (but not exclusively) synthetic cathinones, synthetic cannabinoid receptor agonists (SCRAs), new synthetic opioids and new benzodiazepines.

Exclusion criteria — established illicit drugs including GHB (gamma-hydroxybutyrate), GBL (gamma-butyrolactone) and ketamine (unless reported in problem polydrug use patterns with NPS). Fentanyl (as either a medicinal product or an illicit drug) is excluded, although many fentanyl derivatives are included as NPS.

([1]) See the EMCDDA website: emcdda.europa.eu/activities/hrdu

EU Early Warning System on new psychoactive substances

By the end of 2016 the European Early Warning System (EU EWS) was routinely monitoring over 620 substances in EU Member States, Norway and Turkey. In 2016, 66 NPS were formally notified for the first time.

The largest substance categories monitored by the EU EWS are the synthetic cannabinoids or SCRAs (over 160 substances, including 11 new cannabinoids reported in 2016), followed by the synthetic cathinones (over 100 substances, 14 reported for the first time in 2016). Overall, 25 new opioids have been detected on Europe's market since 2009, including nine reported for the first time in 2016. Similar low-level but increasing trends have been observed with the number of benzodiazepine derivatives available in recent years: six were detected for the first time in Europe in 2016.

In 2015, almost 80 000 seizures of NPS were reported. Together SCRAs and synthetic cathinones accounted for 60 % of all NPS seizure cases in 2015 (over 47 000). The number of seizures of new synthetic opioids remains relatively low.

Information received by the EU EWS also highlights the increase in reports of serious adverse events, including mass intoxications, deaths and outbreaks of infections associated with the use of NPS. In 2015, 17 public health-related alerts (including updates) were issued to the EU EWS network, addressing public health concerns, such as deaths associated with the use of potent synthetic opioids; clusters and outbreaks of intoxications associated with SCRAs; and infections among people who inject drugs, including NPS.

and verified a picture as possible. The combination of routine and survey data with key informant reports and scientific literature provided a rich and in-depth view of a complex and differentiated phenomenon. This report summarises the study findings and conclusions. Where results are based on the literature, references are cited; otherwise findings are based on EMCDDA and national monitoring and the qualitative sources described above.

The substances: which NPS are linked with high-risk use?

Synthetic cannabinoid receptor agonists

Synthetic cannabinoid receptor agonists (SCRAs) emerged over the past decade as an alternative to cannabis. This group of substances mimics the effects of THC (delta-9-tetrahydrocannabinol), which is the substance that is primarily responsible for the major psychoactive effects of cannabis (Fantegrossi et al., 2014). However, while THC is a weak partial agonist of cannabinoid receptors in the brain, SCRAs are potent full cannabinoid receptor agonists and most are very potent cannabinoid receptor type 1 (CB_1) agonists (Seely et al., 2013).

Little is known about the pharmacological properties of SCRAs. It is possible that, apart from high potency, some could have particularly long half-lives, potentially leading to a prolonged psychoactive effect. However, because of the wide chemical diversity of SCRAs it is currently not possible to extrapolate pharmacological properties between, and potentially within, different SCRA classes (Lovett et al., 2015a).

SCRAs have sometimes been grouped under the street name 'spice' or 'spice products'. The actual substances identified vary widely even within spice products with the same name, making it hard to establish the most used SCRAS. The most commonly seized in recent years have been AM-2201, MDMB-CHMICA, AB-FUBINACA, MAM-2201 and XLR-11 (5F-UR-144).

When they first emerged SCRAs were predominantly seized as herbal smoking blends, but recently they have been increasingly seized in powder form, and they have also been found in tablet form and liquids. The powders are used to manufacture 'legal high'/spice products and small quantities may represent millions of doses. The typical amount in a packet of spice is around 3 g (Fattore and Fratta, 2011).

The present study identified the use of SCRAs among high-risk drug-using populations including prisoners in around two thirds (19) of the EMCDDA reporting countries: Belgium, Bulgaria, Croatia, the Czech Republic, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Poland, Portugal, Romania, Slovenia, Sweden, Turkey and the United Kingdom.

Synthetic cathinones

Synthetic cathinones were first detected in Europe in 2008 and have emerged in recent years as a new class of stimulant drug in many European countries. These substances are ring-substituted phenylethylamines with a substitution of a ketone group at the β-carbon position. Different R-group substitutions give rise to a large list of synthetic cathinones, and many of them are identical except for the β-carbon ketone group (Spiller et al., 2011). These substances are often seen as an alternative to MDMA, amphetamines and cocaine because of their stimulant psychoactive effects. Very little is known about the pharmacokinetics and pharmacodynamics of synthetic cathinones, although, like amphetamines and cocaine, they are thought to act on the central nervous system, promoting release of monoamine neurotransmitters, and most likely inhibit their reuptake (Baumann et al., 2013; Dorairaj et al., 2012).

In Europe, synthetic cathinones have been sold online and in shops labelled as 'plant food' and 'bath salts' so that sellers can circumvent sales regulations. The most widely used synthetic cathinones in the context of problem drug use (as well as in recreational settings) in Europe are mephedrone (4-MMC), 3-MMC (closely related in structure to mephedrone), 4-MEC, pentedrone, and pyrovalerone derivatives such as MDPV or alpha-PVP. The most commonly seized synthetic cathinone in recent years include mephedrone and its isomers 3-MMC and 2-MMC, as well as pentedrone and alpha-PVP.

This analysis identified reports of the problematic use of synthetic cathinones in half of the countries reporting to the EMCDDA (Belgium, Czech Republic, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Poland, Romania, Slovenia, Spain, Sweden and United Kingdom).

New synthetic opioids

Synthetic opioids are a broad family of pain relievers and anaesthetics acting predominantly at the mu (μ) opioid receptor, but also at the sigma (δ) and kappa (κ) opioid receptors. Like opiates (e.g. heroin, opium and morphine) and semi-synthetic opioids (e.g. hydrocodone, hydromorphone, oxycodone and oxymorphone), synthetic opioids produce effects such as respiratory depression, analgesia, hypothermia, sedation, euphoria, drowsiness and miosis. The strength of physiological and psychological effects differs depending on the particular synthetic opioid and the type of receptor that is activated or inhibited.

In Europe, new synthetic opioids may be sold as heroin to unsuspecting users or as 'synthetic heroin' or 'research chemicals'. The main new synthetic opioids currently being identified are fentanyl derivatives (e.g. acetyl fentanyl, acryloylfentanyl, carfentanyl and furanylfentanyl) and other opioids such as AH-7921, MT-45 and U-47700. Specific recent examples include seizures of carfentanyl found with heroin, and ocfentanil (with caffeine and paracetamol) sold as heroin. Acetyl fentanyl has also been found in the form of a nasal spray. MT-45 has been found in Belgium, Germany and Sweden, mostly in powder form, but also in herbal smoking mixtures along with a SCRA. Information about 42 deaths associated with acryloylfentanyl was reported in 2016 to the EMCDDA by four Member States: Denmark (1 case), Finland (1), Latvia (1) and Sweden (39).

New synthetic opioids have been identified by forensic analysis (seizures and deaths) in almost two thirds of reporting countries (Belgium, Bulgaria, Croatia, Cyprus, Estonia, Finland, France, Germany, Hungary, Ireland, Latvia, Luxembourg, Norway, Poland, Portugal, Slovakia, Spain, Sweden, United Kingdom).

Benzodiazepines

Benzodiazepines are a class of psychoactive drugs that enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at the $GABA_A$ receptor, resulting in sedative, hypnotic (sleep-inducing), anxiolytic (anti-anxiety), anticonvulsant and muscle-relaxant properties.

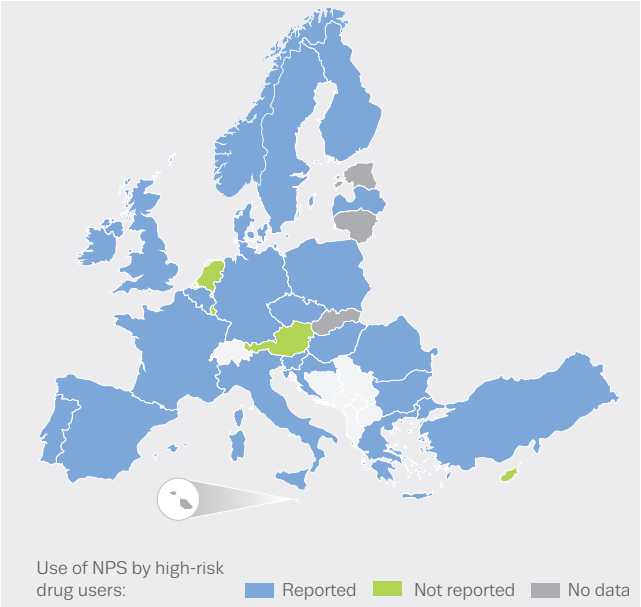
The EU EWS monitors more than 20 new and controlled benzodiazepines. New benzodiazepines are sometimes used by counterfeiters to produce fake medicines that are sold in Europe. Examples of this practice include fake alprazolam tablets, intercepted in 2015, that were found to contain flubromazolam, and fake diazepam tablets which contained phenazepam. In some European countries, these counterfeit medicines have become an important part of the illicit drug market. In the United Kingdom, etizolam, a benzodiazepine-type NPS, is reported to be available on the illicit market.

NPS use among high-risk drug users

NPS use among groups of high-risk drug users such as opioid and stimulant injectors was a primary focus for this study. This group is often in touch with treatment or low-threshold services and consequently some limited information may be available. In addition, patterns of NPS use among marginalised, vulnerable or socially disadvantaged groups, including homeless people, unemployed people and people with mental health problems, were also of concern. Overall, information on the use of NPS among these populations is

FIGURE 1

Use of NPS by high-risk drug users in the European Union, Norway and Turkey (2016)



very fragmented and incomplete, and the availability of data on NPS use by these populations is scarce.

It is important to clarify that, overall, reports of use of NPS among high-risk drug users are rare in Europe, suggesting that prevalence is likely to be low. Nevertheless, 22 of the 30 countries monitored by the EMCDDA do report the existence of some form of NPS use among their high-risk drug-using populations. Four countries (Austria, Cyprus, Luxembourg, Netherlands) report no documented NPS use among their high-risk drug users, while no information was available for four countries (Estonia, Lithuania, Malta, Slovakia) (Figure 1). From the available information, the NPS most commonly used among high-risk drug users appear to be synthetic cathinones, more specifically mephedrone, MDPV, alpha-PVP, pentedrone and 3-MMC. The second most frequently reported category of NPS is SCRAs, followed by synthetic opioids.

Prevalence of NPS use among high-risk drug users

No Europe-wide estimates exist for current or lifetime use of NPS among high-risk drug users, and only a small number of countries, including Belgium and the Czech Republic, have national estimates of the prevalence of NPS use among high-risk drug users. In Belgium, last year NPS prevalence in high-risk drug users was on average 26 %, with SCRAs (19 %) and mephedrone (12.5 %), 2C-B (9 %), methoxetamine (MXE, 6 %), MDPV (4.7 %) and 4-fluoroamphetamine (4-FA, 4.3 %) the most frequently used by the needle and syringe programme population (Windelinckx, 2015). In the Czech Republic, one third of high-risk drug users have reportedly used a cathinone or phenethylamine at least once (and 10.5 % used them in the last 12 months) but a very low proportion report them as their primary drug (0.2 %). In Hungary, before 2010, approximately half of the clients of needle/syringe programmes injected heroin and half injected amphetamine. By 2014, over two thirds (68 %) of them reported injecting an NPS as their main drug.

In the United Kingdom, 5.9 % of those participating in the Unlinked Anonymous Monitoring Survey during 2014 reported that they had injected mephedrone during the preceding month, and 8.9 % had injected this drug at some point during the preceding year (PHE, 2015). In Scotland, a recent study explored NPS use among vulnerable populations (mental health service users, homeless people, people who injected, at-risk young people and men who have sex with men) (n = 424) and found use of NPS to be widespread, with 59 % of respondents reporting that they had ever used NPS (MacLeod et al., 2016). Of those, 74 % reported having used NPS within the last six months. The most commonly used NPS were SCRAs (41 %) and benzo-type NPS (41 %), while approximately one fifth reported taking stimulant-type NPS (21 %) and mephedrone (19 %).

Lifetime experience of NPS use has also been measured in high-risk drug using populations in some countries. A study

Prevalence of NPS use among young people

Some insights into drug use prevalence among young people (aged 15–24) in Europe are provided by the 2014 Flash Eurobarometer, which reports NPS lifetime prevalence of 8 % and last year use of 3 % (European Commission, 2014). Last year prevalence of NPS use ranged from 0 % in Poland to 9.7 % in Ireland (EMCDDA, 2016a). Reported prevalence levels of NPS use among European students aged 15–16 years is provided by the 2015 European School Survey Project on Alcohol and Other Drugs (ESPAD) study. Overall, lifetime prevalence was reported to be 4 % and last year prevalence 3 %. Last year prevalence of NPS use ranged from 1 % in Belgium (Flanders), Denmark, Finland, the Netherlands, Norway and Portugal to 8 % in Estonia and Poland (ESPAD, 2016). It is notable that results from these two studies show no consistency within countries in terms of reported levels of NPS use.

of opioid users in Croatia reported a lifetime prevalence of 2.3 % for mephedrone, 2.9 % for SCRAs and 14.9 % for other new drugs, and this study concluded that opioid users did not transfer to NPS (Doležal, 2011).

In some European countries no evidence was found to support the existence of NPS use among high-risk drug users. In Luxembourg, for example, Grund et al. (2016) found no data to suggest that high-risk drug users using established drugs, such as heroin, had used NPS.

Data on treatment entrance can also provide some insight into people experiencing problems with drug use, including with NPS. However, the data here are sparse and under-reporting in this area is likely. In 2015 around 3 200 clients, or fewer than 1 % of European clients entering specialised drug treatment, reported problems related to NPS. In the United Kingdom, around 1 500 clients entering drug treatment (or around 1 % of all drug clients) reported primary use of synthetic cathinones; Hungary and Romania also report relatively high numbers of NPS users entering drug treatment. On the basis of the estimates from the treatment units participating in the Hungarian national focal point 2015 treatment facility survey, at least 26 % of clients treated had a SCRA problem, and 21 % reported problems linked to new stimulants, mainly synthetic cathinones. In Croatia, in 2014, the first year on which data on selected NPS use were collected from the clients in drug treatment, only four clients were registered for primary use of NPS, SCRAs in all cases.

Patterns of NPS use among high-risk drug users

The ways NPS are administered vary, and routes of administration tend to be both substance and context specific. In many countries injection of synthetic cathinones is reported as a common route of administration among groups who otherwise inject opioids or stimulants. Such patterns of intravenous NPS use have been documented in Austria, Finland, Germany Hungary, Latvia, Slovenia, Sweden and the United Kingdom. SCRAs are most commonly smoked as herbal mixtures, but there are reports of these drugs being snorted, consumed in tablet form or used in vaporisers (as c-liquids).

Two important factors emerge with regard to the use of NPS among high-risk drug users. Firstly, NPS use mainly occurs in a context of polydrug use. This means that the drugs are used in combination with or in the same session as other substances including illicit opioids, stimulants and benzodiazepines and alcohol. For example, in Slovenia, a 2014 study found that 3-MMC tended to be used simultaneously with other opioids (Sande, 2016).

Secondly, in most but not all cases, new psychoactive substances are very rarely reported to be the primary drug used by high-risk drug-using groups. More often they are a secondary or tertiary drug, for example when the preferred substance is not available or to heighten the effect of other drugs. This means that it would be uncommon to find many high-risk NPS users per se, with the exception of specific groups in Hungary and some areas of the United Kingdom.

The substitution of an established illicit drug (usually heroin or amphetamines) with an NPS is another pattern of use reported among high-risk drug users. Poor availability, low purity and high prices may play a role here. This development has been observed in Hungary and United Kingdom, for example, during periods of heroin shortage. Here the replacement of established drugs with synthetic cathinones has been relatively well documented. An analysis of client data from Hungary's biggest needle/syringe programme reveals that heroin was mainly substituted with synthetic cathinones such as mephedrone, MDPV and pentedrone (Tarján, 2017). In Slovenia, the use of 3-MMC as a replacement for cocaine is also reported among intravenous opiate users (Sande, 2016). Interestingly, reports from needle exchanges in the United Kingdom indicate that many of the heroin users who migrated to injecting stimulant NPS returned to heroin injection after a period, in response to the negative effects of the NPS.

NPS are also used as a complement or in addition to other licit or illicit substances. In Finland high-risk drug users have reportedly been using NPS intravenously, including the synthetic cathinones alpha-PVP and MDPV, alongside established substances (Tammi et al., 2011). For many of this group, MDPV is administered together with and in addition to amphetamines, alcohol, and medicinal products (Grund et al., 2016).

SCRAs and marginalised groups

Whereas first-generation SCRAs or 'spice products' have been on the European drug markets since around 2008, largely associated with recreational use and 'legal highs' smoking mixtures, a more recent trend has seen a rise in the use of SCRAs in vulnerable groups, including treatment population, homeless people and prisoners. This new phenomenon has been reported in more than half of European countries. Examples cited by experts include the use of SCRAs among homeless and vulnerable groups in Dublin (and rural areas of Ireland), Scotland and London, and use by Roma populations in Finland.

In addition, the problem use of SCRAs by vulnerable young people was highlighted by experts involved in this study and is a particular cause for concern. In Finland, there are reports of very young people injecting SCRAs, and the internet market — with the relative ease of online purchases — is mentioned as playing an important role in this early onset. In Sweden, SCRAs or spice have received media attention, with older drug users reportedly appearing on national television to warn younger users of the serious adverse consequences of these drugs.

NPS use in prison

NPS use among prisoners is a relatively new but rapidly developing phenomenon and empirical data are currently scarce and patchy. Monitoring drug use among prisoners in general, and NPS use in particular at the European level, is complicated. There is a lack of common definitions, and different methodologies and study designs are applied.

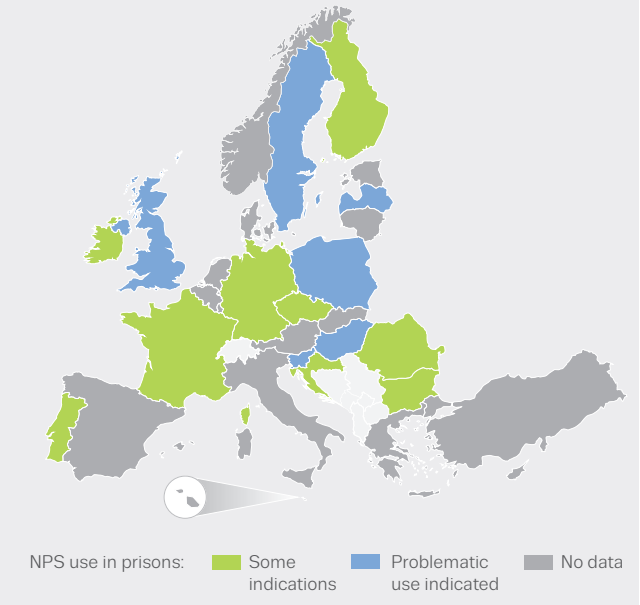
There is, however, growing evidence to show that the use of SCRAs has become a serious problem in prisons in the United Kingdom, where the issue (including violence and non-fatal and fatal intoxications) is relatively well documented. Information on the situation in other EU countries is largely anecdotal. Drug-related and other problems inside prisons (e.g. assaults and suicides) have risen to record levels in the United Kingdom (HMIP, 2015; User Voice, 2016), and a large part of the disruptive behaviour has been linked to the harms caused by the use of NPS, in particular SCRAs (Centre for Social Justice, 2015; HMIP, 2016).

In total, this study identified reports of NPS use amongst prisoners from 15 European countries. In addition to the United Kingdom, there is some evidence to suggest that NPS use in prison settings is a problem in Hungary, Latvia, Poland, Slovenia and Sweden. Anecdotal reports also document NPS use in prison in Bulgaria, Croatia, the Czech Republic, Germany, Ireland, Finland, France, Portugal and Romania. For other European countries, it remains unclear whether there is no NPS use in prison or no information is available (Figure 2).

The limited information available indicates that SCRAs are responsible for a large share of drug-related problems in prison in the United Kingdom and to some extent in other countries, including Hungary, Latvia, Slovenia and Sweden. SCRAs or spice were first identified by Her Majesty's Inspectorate of Prisons (HMIP) as a serious problem in the United Kingdom in December 2011, but were not identified as a widespread issue until 2013 (HMIP, 2015). HMIP's thematic survey (2015) found that 10 % of respondents

FIGURE 2

Use of NPS among prisoners in the European Union, Norway and Turkey



had used spice in their current prison, compared with 13 % who had used cannabis. Spice was found to be the only drug whose self-reported prevalence of use was higher in prison than in the two months before prison (HMIP, 2015). A survey carried out by User Voice among 684 prisoners in England found that one in three prisoners reported use of spice in the last month, making it the most popular drug (User Voice, 2016).

It is not possible to compare estimates across countries, as different definitions and methodologies are used. The prevalence estimates for NPS use in prison among countries for which data are available range from less than 2 % in Portugal to over 30 % in some prisons in the United Kingdom (User Voice, 2016), often depending on the type of prison involved. There are indications that NPS use in prison may be higher in men's prisons than in women's prisons, higher in remand prisons and lower in high-security prisons.

The HMIP report highlights that different types of NPS user are identifiable in UK prison settings, including those with long drug careers, often homeless and in regular contact with the criminal justice system, as well as a group of young, relatively inexperienced users who may be initiating NPS use in prison (HMIP, 2015). The report notes cases in which prisoners, referred to as 'spice pigs', are used to test new SCRA products, to find out what quantities are safe and what effects can be marketed.

There are anecdotal reports about supply of SCRAs in a number of European prisons, including dealers throwing

packages over the prison wall, sometimes using drones or hiding the substances inside dead birds. Staff, prisoners and visitors are seen to play an important role in the supply of SCRAs in prison, including using body cavities or bringing it into prison in the form of saturated rice-paper. Recently there have been reports that SCRAs are sprayed on letters or children's drawings and enter the prison by post.

The emergence of SCRA use in prisons in Europe raises a multitude of issues, including challenges on appropriate healthcare responses and the adequacy of detection techniques. There is an urgent need for a better understanding and monitoring of this situation, alongside training of staff to be able to handle SCRA-related problems, both health and behavioural, and the establishment of appropriate treatment and harm-reduction programmes in prisons. A recent training tool on NPS management has been published by Public Health England, identifying the main issues to deal with to tackle NPS-related problems for prison staff, and mandatory drug-testing procedures have been revised for English prisons (PHE, 2015).

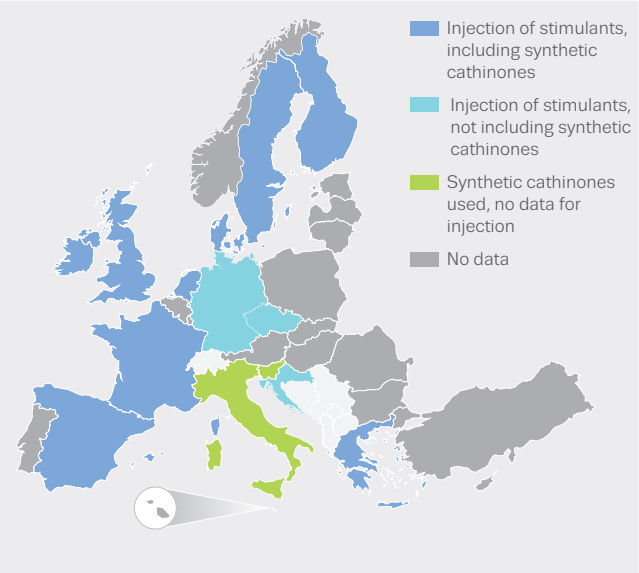
NPS and injection among men who have sex with men/slamming

The practice of stimulant drug injection, sometimes including synthetic cathinones, by a subgroup of men who have sex with men has raised public health concerns in recent years. This injection behaviour, generally referred to as 'slam' or 'slamming', primarily takes place in the context of sex parties (Batisse et al., 2016; Kirby and Thornber-Dunwell 2013a,b; Stuart, 2013). Synthetic cathinones, such as mephedrone, are sometimes used in combination with other drugs such as GHB (gamma-hydroxybutyrate), GBL (gamma-butyrolactone), crystallised methamphetamine, cocaine and sildenafil, with the purpose of reducing inhibition and enhancing sexual experience (Abdulrahim et al., 2016; Bourne et al., 2014). 'Chemsex' parties can last from a few hours to several days and participants usually engage in risky sexual practices with multiple partners, sometimes exchanging syringes and not using condoms, with a consequent increase in the risk of contracting sexually transmitted diseases and other blood-/body fluid-borne viral infections (McCall et al., 2015; Peyrière et al., 2013).

At the time of writing, a small number of studies documenting slamming practices have come from France, Spain and the United Kingdom. A recent survey of HIV-positive patients attending 30 HIV clinics in England and

FIGURE 3

Reports of injection and stimulant use among men who have sex with men in the European Union, Norway and Turkey



Wales found that among the men who have sex with men, nearly a third (29 %) reported engaging in chemsex in the past year and 1 in 10 reported slamming (Bourne et al., 2015; Daskalopoulou et al., 2014; Pufall et al., 2016). Studies have also been conducted in French cities (Batisse et al., 2016; Foureur et al., 2013). In addition, experts involved in this analysis report that the injection of NPS among men who have sex with men also occurred in Ireland, the Netherlands and Sweden.

Reports of slamming practices are also available from other European countries. In both the Czech Republic and Germany, the injection of stimulants among small populations of men who have sex with men is confirmed, but synthetic cathinones do not appear to be part of the cocktail of substances used. In Denmark, Finland and Greece, anecdotal evidence also suggests that some stimulant injection might be occurring among men who have sex with men. In Italy and Slovenia, mephedrone is reportedly available and used in the men who have sex with men scene but there is no clear evidence that it is being injected (see Figure 3).

There are concerns that the small group of men who have sex with men who may be experiencing problems linked to chemsex and slamming seem to be 'off the radar' of national drug agencies and community-based drug services (Pirona et al., 2017). Evidence suggests that those among this group with drug problems are more likely to be in contact with sexual health clinics or HIV/AIDS checkpoints, and rarely access drug treatment services

(Lovett et al., 2015b). In this area, responses require a multidisciplinary approach to address the psychosocial aspects of drug-taking behaviours, in collaboration with healthcare professionals experienced in the management of sexual health problems. Research highlights the importance of screening and brief intervention, as well as effective referral processes to specialised drug treatment, as appropriate strategies to reduce harms related to drug use in this setting (Abdulrahim et al., 2016; Bourne et al., 2015; PHE, 2015).

NPS-related harms and deaths

In the absence of clinical trials establishing the physical and psychological harms caused by NPS consumption, this study relies on data from NPS hospital emergency presentations, post-mortem toxicology examinations reported by special mortality registers, fatal and non-fatal intoxications reported to the EU EWS, data from user surveys, regional and national poison information services, single-case or cluster reports and published scientific studies. In many cases it is almost impossible to assess the impact or role played by NPS compared with the impact of other substances, for example in acute emergencies or deaths where multiple substances are present.

General acute NPS toxicity

A number of NPS may potentially cause acute intoxications leading to serious consequences, which might be aggravated in the context of high-risk drug use. Pharmacologically, these substances interact with various neurotransmitter targets affecting both the central and the peripheral nervous system.

Adverse effects linked with synthetic cathinones are similar to the monoamine dysfunction observed in stimulant (amphetamines, cocaine) users (EMCDDA, 2011; German et al., 2014). The general pattern is characterised by agitation, paranoia, hallucinations, psychosis, myoclonus, headaches, hyperthermia, hypertension, tachycardia, hyponatremia, nausea, vomiting and chest pains (Capriola, 2013). In addition, stimulants such as ethylphenidate mimic the effects of the stimulant medicine methylphenidate and have been linked with a range of harms in the United Kingdom (ACMD, 2015; PHE, 2015). New synthetic opioids tend to produce the toxic effects typical of opioids such as heroin, including respiratory depression and respiratory arrest, loss of consciousness and coma, miosis, nausea, and drowsiness (EMCDDA, 2016a; Helander et al., 2016). Designer benzodiazepines produce the traditional benzodiazepines' analogue sedative, hypnotic, anxiolytic and muscle-relaxant effects. Their combination with opioids potentiates the clinical features seen, including extreme sleepiness, respiratory depression, increased risk of overdose (Park et al., 2015), coma and death. SCRAs appear to have the potential for more severe and unusual effects than THC; in addition to the expected effects on the central nervous system, some SCRA compounds have been associated with stimulant-like features (including psychosis, seizures, tachycardia and autonomic hyperactivity), along with effects including kidney damage and suicidality (Gurney et al., 2014).

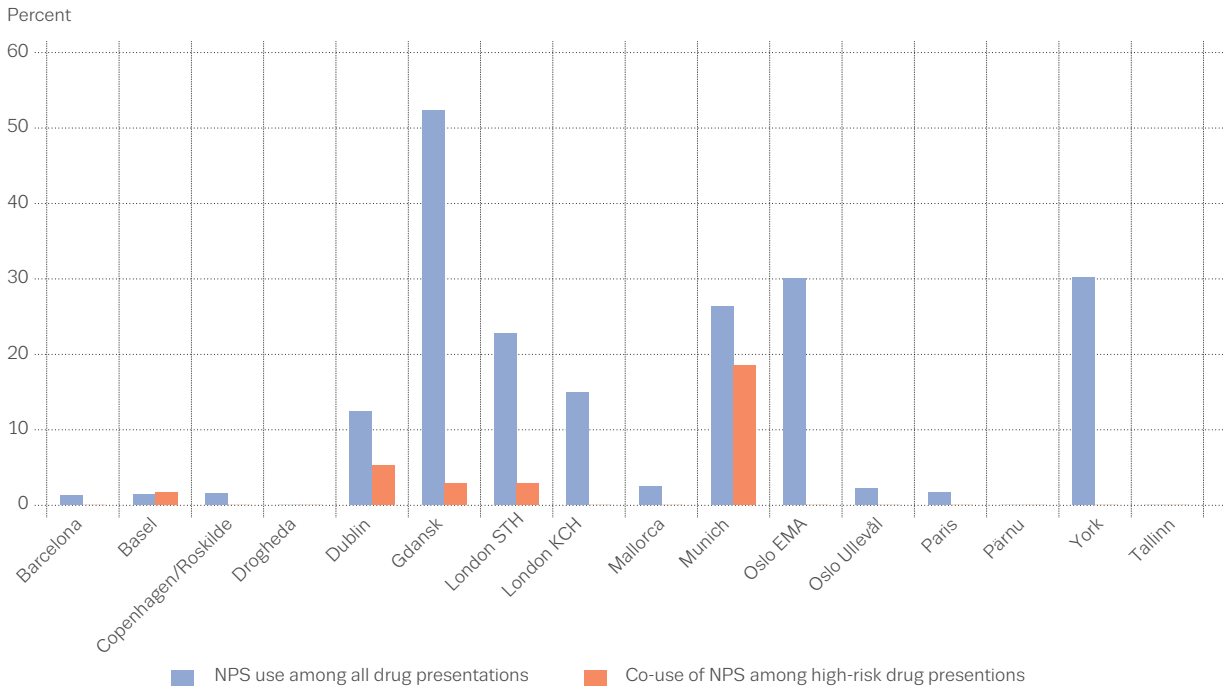
Hospital emergencies and poisonings

Important insights into patterns and trends in acute health harms related to NPS use come from hospital emergency settings. Since 2013 the European Drug Emergencies Network (Euro-DEN) project has been collecting systematic data on the drug-related acute toxicity presentations to the emergency departments across Europe. Between October 2013 and September 2015, the original 16 sentinel centres in the Euro-DEN Plus network reported 10 956 emergency presentations directly related to the use of illicit drugs or NPS. Of these, 3 288 (30 %) involved the use of a substance potentially associated with high-risk drug use (buprenorphine, fentanyl, crack cocaine, heroin, methadone). Among these potential high-risk drug use cases, just 67 (2 %) involved the concomitant use of NPS. Looking at the characteristics of this small group, approximately 60 % of patients were male and the median age was 33 years. Their median stay in hospital was 13 hours 30 minutes.

Almost all of the 67 cases were recorded in Munich, Dublin and London South (Figure 4). As shown in Figure 4, in the hospitals reporting higher proportions of NPS-using patients (Gdansk, York etc.), co-use of NPS was not necessarily common among those who had used high-risk drugs. In addition, other centres found no cases of co-use of NPS and high-risk drugs. Included in this group is York, where 30 % of the 405 presentations were related to NPS and a further 30 % were related to high-risk drugs. Also in the group are the Oslo centres, where the prevalence of NPS cases was less than 1 % and high-risk drugs accounted for 1 636 out of a total of 3 515 drug-related presentations. The types of NPS used along with high-risk established drugs varied between locations. Munich recorded presentations with synthetic cathinones and 4-MPA. In Dublin, mephedrone was the only NPS used alongside high-risk drugs.

FIGURE 4

Hospital presentations related to NPS and co-use of NPS among high-risk drug presentations at Euro-DEN sentinel centres, October 2013 to September 2015



Some data are also available on national reports of acute intoxications sent to the EMCDDA and in the scientific literature. These indicate that a range of synthetic cathinones — MDPV, alpha-PVP, mephedrone and 5-IT — were associated with acute intoxications in Germany, Finland, Hungary, Poland, Sweden and the United Kingdom between 2010 and 2015. Serious intoxications associated with SCRAs have also been reported to the EU EWS since 2015, including an outbreak in the Polish Silesia region (483), as well as intoxications in Sweden (10), Austria (7) and Germany (7) (EMCDDA and Europol, 2016a). Sweden also reported a number of acute intoxications linked to synthetic opioids between 2013 and 2015: MT-45 (12), AH-7921 (6) and acetylfentanyl (6) (EMCDDA, 2014, 2015; EMCDDA and Europol, 2016b).

NPS-related infections: HIV and hepatitis C

People injecting stimulants report higher levels of sharing and reusing needles and syringes, of risky sexual behaviours, including unprotected sex, and increased numbers of sexual partners, resulting in an overall greater risk of acquisition and transmission of blood-borne viruses, as well as injection site infections (Wiessing and Folch, 2016). People who inject stimulant-type NPS in particular synthetic cathinones are thus a population at risk of blood-borne viruses such as HIV, hepatitis C virus (HCV) and hepatitis B virus (HBV), linked to both sex and injection. The short duration of intravenous mephedrone action has been associated with repeat dosing and a high frequency of injection (10 to 20 times per day) to maintain and prolong the effects, leading to a higher risk of blood-borne diseases and infections if infected injection equipment is shared. Besides compulsive use, other addictive elements such as craving, uncontrolled binging behaviours and withdrawal symptoms have been reported (German et al., 2014). In a recent analysis of slamming cases notified to the French Network of Addictovigilance, involving the injection of cathinones and other drugs among men who have sex with men, HIV prevalence was on average 82 %, with 50 % hepatitis C co-infection (Batisse et al., 2016).

Synthetic cathinone injection has been linked with increased HIV and HCV transmission in Ireland (Giese et al., 2015) and in the United Kingdom (Hope et al., 2016), and HCV transmission in Hungary (Horváth, 2013; Tarján et al., 2017). In the United Kingdom, Welsh services registered an increase in HCV and HIV infection rates among heroin users who were also using synthetic cathinones. In Ireland in 2015, an increase in the number of new HIV infections was reported among a group of homeless polydrug users who primarily injected alpha-PVP

(Giese et al., 2015). In Hungary in 2014, cathinone injection, mainly pentedrone, mephedrone, MDPV and alpha-PVP, was associated with HIV infection in people who inject drugs (Rácz et al., 2016). In addition, the injection of synthetic cathinones and sharing of needles have been identified as possible factors linked to recent outbreaks of HIV infection in Romania and Greece (Botescu et al., 2012; Fotiou et al., 2012).

Physical harms and mental health problems

The high number of daily injections associated with the use of synthetic cathinones can also exacerbate a range of injection-related harms, including soft tissue injuries, abscesses, gangrene, sore or open wounds at injection sites, bacterial infections and vein clotting. In 2014 in Scotland (UK), an outbreak of soft tissue infections (*Staphylococcus aureus* and *Streptococcus pyogenes*) was associated with the injection of ethylphenidate, and in Slovenia, between 2014 and 2015, use of 3-MMC among intravenous opioid users was linked with soft tissue injuries. In addition, among a range of physical harms associated with NPS use, sleep deprivation and coordination problems were the most reported physical health problems in certain studies (MacLeod et al., 2016; Winstock et al., 2011). Some NPS have shown that they are potentially liable to produce physical and psychological dependence, tolerance and withdrawal (Baumeister et al., 2015). Other mental health problems are reported in the scientific literature, including psychotic reactions, self-harm, aggression, mood alterations and worsening of pre-existing psychiatric conditions.

Mephedrone consumption has been associated with increased risk of presenting psychotic symptomatology (delusive thoughts, hallucinations or disorganised speech). Although, in most cases, psychosis resolved within a few days, there have been reports of persistent psychotic symptoms for weeks after a single consumption (Dolengevich-Segal et al., 2016). The worsening of psychiatric status among high-risk drug users who started using synthetic cathinones and SCRAs has been reported in Germany, Finland, Hungary and the United Kingdom. Welsh drug services, for example, report that heroin users experienced rapid deterioration in mental and physical health after commencing NPS use, and many subsequently returned to using heroin.

Mental health problems, including self-harm, anxiety and depression, physical health problems and strong withdrawal effects are among the harmful consequences reported as linked to SCRA use in prisons.

Social harms

Illicit drug use, particularly opioid use and injection, has historically been associated with social problems, and this is no less the case for NPS use. A number of sources highlighted social harms associated with the use of synthetic cathinones and SCRAs, including poverty, homelessness and challenges associated with users' violence and aggression. In some countries (Czech Republic, Hungary and United Kingdom), NPS are increasingly being seen as the drugs of the poor. In Hungary, the use of SCRAs is particularly linked with rural poverty. In the United Kingdom, the use of SCRAs among homeless people and marginalised youth has been high on the political agenda in recent months (MacLeod et al., 2016). Slovenia also reports the use of 3-MMC among marginalised populations including vulnerable young people and sex workers.

In Ireland, three Dublin drug treatment services have reportedly closed (and later reopened) because of problems dealing with synthetic cathinone users (mephedrone and alpha-PVP) and management of difficult client behaviour (e.g. severe agitation, aggression and violence in users). Similarly, a number of Europe's prisons are struggling with behavioural challenges among inmates. As discussed earlier, the growing level of NPS use in prisons in Europe may be linked to an increasing level of violence towards both prisoners and staff (User Voice, 2016).

NPS-related deaths

Across European countries the number of deaths where NPS are involved in the context of high-risk drug use is variable and difficult to establish. In particular, there are many limitations in the data on drug-related mortality. These include the likely under-detection and underreporting of NPS in post-mortem analysis, especially when heroin or other illicit drugs are also present. Also, lack of specific codes for NPS in general mortality registers prevents many NPS-related fatal poisonings from being identified. An unknown number of NPS-related deaths may be hidden behind cases associated with heroin, other opioids or stimulants.

A limited number of deaths among high-risk drug users have been associated with synthetic cathinones in Europe. Between 2010 and 2014, Finland, Sweden and the United Kingdom reported deaths due to synthetic cathinone use, in addition to cases where these drugs were present in the post-mortem toxicology together with other substances such as alcohol and medicines. Synthetic cathinones that have been associated with deaths in Europe include

MDPV, alpha-PVP, mephedrone, 4,4'-DMAR and 5-IT (5-(2-aminopropyl)-indole). SCRAs have also been linked with deaths. For example, between 2012 and 2014, the United Kingdom reported 19 deaths in prison in which SCRAs were suspected to have played a role; Hungary, Sweden and Turkey have also reported SCRA deaths.

Although numbers remain low, deaths in Europe related to new synthetic opioids have been reported to the EU EWS. These substances can be extremely potent, and very small doses can cause fatalities. Derivatives of fentanyl, such as ocfentanyl and acetylfentanyl, have contributed to a number of deaths in Belgium, Germany, Poland, Sweden and the United Kingdom. Other new synthetic opioids have also been associated with morbidity. More than 40 deaths were reported to the EMCDDA within months of the detection of the opioids AH-7921 and MT-45 on the European drug market. In 2016, new dangerous synthetic opioids have been detected, with 23 deaths in Sweden linked to acryloylfentanyl and four deaths in Finland linked to U-47700.

Other NPS, such as tryptamines — which are known for their hallucinogenic properties — have been associated with fatal intoxications in Europe. However, these substances are rarely linked to high-risk drug-using populations and are primarily reported in recreational contexts. In Scotland, in 2015, NPS were implicated in 74 deaths, with three where NPS were the only substance present. The NPS most commonly implicated in these 74 deaths were benzodiazepine-type NPS such as phenazepam, etizolam and diclazepam (MacLeod et al., 2016).

Motivations for use

The reasons behind new outbreaks of NPS use among high-risk drug users and the emergence of clusters of problematic use of NPS are variable and complex. Nevertheless a few common factors can be identified, including reduced availability of illicit drugs, competitive prices, the fact that NPS are hard to detect in routine drug tests, their legal status and specific qualities of the substances themselves.

Most evidence on motivation for use of NPS comes from studies of recreational users and the general population. An examination of motivational characteristics of each group of NPS (i.e. SCRAs, opioids, hallucinogens, dissociatives etc.) revealed that price, legal status, availability and non-detectability in screening tests acted as motivation for use of SCRAs more than for hallucinogens, stimulants and dissociatives (Soussan and Kjellgren, 2016). Research on the first wave of mephedrone use in the United Kingdom and Ireland (early 2009) suggested that their uptake by experienced drug users might be due to the reduced availability and low purity of ecstasy pills and powder cocaine (Measham et al., 2010).

Research on synthetic cathinones and the use of 3-MMC in Slovenia identified that low price and high purity were among the most important reasons for use and more important than legality of NPS and lack of traditional drugs (Sande, 2016). Conversely, findings from a German online survey (Werse and Morgenstern, 2012) identified legality as a major incentive for the use of SCRAs.

There is even less evidence to explain the emergence of NPS use among high-risk drug users in Europe. Nevertheless, in Hungary and the United Kingdom, use by this group has been linked to shortages of heroin in 2010/11 (Griffiths et al., 2012). In particular, ready availability and the low price of mephedrone and other cathinones are documented as reasons. The push factors behind use of mephedrone by men who have sex with men in chemsex contexts appear linked to both availability factors and the empathogenic effects of the drug (Amaro, 2016), alongside the emergence of dating websites and phone apps aimed at men who have sex with men.

A 2016 study found that Scottish users were motivated to continue using NPS by its ease of access, pleasure, compulsion, a desire to avoid going into withdrawal, and as a way to self-manage underlying mental health problems or dependency (MacLeod et al., 2016). The same study revealed that the motivations of users to stop using NPS were related to 'not liking' them or to specific harms that individuals had experienced such as negative impacts on mental and physical health. Legal status did not appear to be a key motivator for use. Conversely, the use of SCRAs by treatment clients to avoid drug tests was highlighted by German experts participating in the EMCDDA study.

Some of the motivations identified for NPS use among recreational populations may be less important for high-risk drug users. For example, the legality issue is less significant for people who are already using a range of other, illicit, substances. Online availability may not be directly beneficial for many marginalised and homeless users, who will be most likely to source their supply of substances from street dealers. However, the fact that SCRAs are difficult to detect in drug tests will be a major pull factor, for example among prisoners. Low price (cheaper than alcohol) and ready availability are both factors linked to use among low-income groups, and have been cited as reasons for rapid uptake of SCRAs among homeless populations in the United Kingdom, and Roma communities in Hungary and Finland.

NPS production, distribution and marketing

Most NPS and precursors are produced in China and bought by European distributors, often in bulk quantities, and transported to Europe by air or sea. European actors, often with links to organised crime, then package and market them either on the open market or directly on the illicit drug market. For small quantities, online orders may be placed directly with Chinese vendors or via internet smart shops. Orders are then shipped using the postal service and couriers (delivery companies).

Both online and bricks-and-mortar shops have been important sales platforms for new substances in Europe. In particular the internet plays an important role for NPS distribution (Soussan and Kjellgren, 2016) and its ease of access reaches geographically remote areas. Substances are typically marketed as research chemicals, dietary supplements or plant food, and commonly labelled 'not for human consumption' to circumvent drug control legislation. Dark net markets also provide anonymity for operators and a similar infrastructure for sellers and buyers of NPS to those provided by other online marketplaces (e.g. eBay or Amazon). Once substances have been controlled, however, they have also been increasingly supplied by traditional sources such as street dealers.

The synthesis of many NPS requires similar equipment and chemical expertise to those needed for the manufacture of illicit synthetic drugs. In a relatively recent development, market signals suggest an increase in the production and importation of precursors that can be used for the synthesis of NPS within Europe, for European markets (EMCDDA, 2016b; Europol, 2013).

Discussion

Top-level trends and developments

This analysis has focused on a new and emerging drug use problem. However, the small scale of the phenomenon is important to remember. To put things into perspective, the latest estimates are that there are around 1.3 million high-risk opioid users in Europe, most of whom use heroin (EMCDDA, 2017). There were also an estimated more than 8 400 drug-induced deaths in 2015, most related to heroin, methadone, cocaine and amphetamines. Some of these high-risk users will also include NPS in their repertoire, either regularly or occasionally. Indeed, this analysis suggests that primary NPS users are very rare and that most problem use of NPS occurs in the context of polysubstance use. Only use of SCRAs by prisoners and homeless populations appears to be less linked with other high-risk drug use patterns, although it is probably connected with alcohol and cannabis use.

At least among pockets of drug users in many European countries, it seems reasonable to state that the distinction between the use of established substances and NPS is diminishing. This is occurring in a situation characterised by rather fluid patterns of polydrug use closely meshed with substance availability, price and purity. In a number of countries, NPS are now more visible and important than chronic and more problem patterns of substance consumption. There are, however, some qualifiers and the picture is not a simple one. For a number of countries, mainly situated in the south of Europe, very little NPS use is reported. For another group of countries, a low level of problem NPS use has been identified, while for a small group of countries, notably Hungary, Ireland and the United Kingdom, this is a major issue for drug policy and a challenge for health and social responses. At least for these countries, there appear to be some common drivers, including diminishing heroin supplies and ready availability of NPS, first through shops and later through online means. Common protective factors for countries with little or no evidence of this problem may include plentiful access to other illicit substances, in particular stimulants (cocaine and methamphetamine) and cannabis.

Tribes, clusters … and implications for harm

This analysis has highlighted diverse NPS-using populations and contexts for use in Europe. The populations identified as involved in high-risk use of SCRAs and synthetic cathinones range from very young experimenters (e.g. Finland, Slovenia) and young marginalised or disaffected populations (Hungary, United Kingdom) to older polydrug users and high-risk stimulant users. A common thread is social vulnerability; in most cases we are talking about small groups of users in many cases these are socially marginalised populations, often unemployed and homeless, sometimes with coexisting mental health disorders and established criminal careers. Also highlighted are patterns

of NPS use among minority groups, including Roma communities, and geographically isolated populations, both rural and urban poor. In some cases, NPS use is integrated into the drug use repertoires of people who inject drugs in open urban drug scenes. However, our analysis shows that the settings in which high-risk NPS use occurs vary considerably, including penal institutions, where SCRAs may be preferred by those subject to drug testing, and house parties, where mephedrone is used in the context of chemsex and slamming.

This study highlights the need for a strong public health response targeted at people using NPS in a problematic way, and tailored specifically to their needs. A particular concern is the lack of appropriate treatment and harm reduction (including drug checking) services available for users experiencing problems with stimulants and SCRAs. The fact that much NPS use occurs among marginalised and hard to reach groups (socially and geographically) has implications for the delivery of appropriate responses. Responding to problems associated with acute toxicity is a clear challenge, while health problems arising from chronic toxicity remain a potentially important future issue. Issues including increased injecting and increased injecting-related risk behaviours have been highlighted as causes for concern. It is evident that the whole area of sex and use of stimulant drugs has not been well explored, including use among male and female sex workers. This analysis has also highlighted reports of particularly chaotic clients, with high levels of aggression and psychiatric comorbidity, who are harder to engage in treatment. Importantly, greater interaction is needed between drug services and other health and social intervention providers including housing, homelessness, sexual health and mental health services.

Great variation in patterns of use across Europe

The study findings reveal a dynamic and rapidly changing NPS landscape in Europe with extensive national and local variability in both substances used and problem user groups involved.

To a certain extent, pan-national patterns or clusters can be identified. For example, Hungary, Ireland and the United Kingdom report similar trends, all with a history of intravenous cathinone use developing among clusters of opioid users in the wake of the heroin shortages reported in 2010/11. In these countries, trends may have peaked around 2015, and cathinones are integrated into polydrug use and injecting patterns involving opioids, amphetamines (including ethylphenidate) and benzodiazepines.

At the national level, different substances appear to be available and used, and this is particularly evident for the cathinones. For example, this study found 3-MMC in Slovenia, pentedrone in Hungary, mephedrone in Wales and alpha-PVP in Finland. Availability is clearly a push factor here and the market shift from one cathinone to the next is well illustrated by the Hungarian syringe residue analysis, which documents how the changing use patterns may be linked to the introduction of control measures.

Northern European countries seem disproportionately affected by new synthetic opioids. While in part this may be put down to strong forensic reporting capacity in these countries, there may also be cultural factors at play, including some historical use of fentanyl and derivatives in the region. Equally of note, most southern EU countries have relatively few reports of NPS use and harms among high-risk drug users, and the reasons for this, whether related to reporting or more linked to protective factors such as good access to established illicit drugs, would certainly warrant further exploration in the future.

Wide variations in patterns of use were also highlighted within countries. For example, in Germany, high-risk use of NPS appears to be primarily restricted to Munich and Bavaria, and was not picked up as a problem in other cities. Hospital emergency data from Euro-DEN also confirm this city-level variability. The sophisticated work undertaken on syringe residue analysis in French cities (Néfau et al., 2015) is able to identify the use of different NPS at the local level, differentiating use profiles for small geographical areas where injecting equipment is collected.

How have things changed

This analysis served to highlight some of the fast-moving changes witnessed in Europe's NPS market, most of which have occurred since around 2010. Although this is a very crude simplification, a number of trends can be identified. In terms of NPS supply, we have seen a move from sale of predominantly 'legal' products in shops, whose emergence coincided with poor availability and quality of established drugs, to the current situation, which includes organised crime groups' involvement in the distribution of (often controlled) NPS, which are frequently sold alongside established drugs. By comparison with 2010, the purity and availability of established illicit drugs is now reportedly improved in many countries (EMCDDA, 2016b). In terms of product reputation, there has been a gradual shift from NPS being considered safer and weaker than established illicit drugs to being viewed as potentially more harmful and potent. NPS users at the time of mephedrone's emergence in 2010 were primarily young and neophyte, non-

marginalised experimenters, linked with recreational settings. Currently the spotlight is on more marginalised groups, experienced polydrug users and injectors, and the substances used in many arenas. Finally, there is some evidence of a shift in the role of NPS, which in the early days were seen largely to be a replacement for cannabis or recreational stimulants. In the current marketplace we see NPS also serving as replacements for opioids, sedatives and dissociatives. Today's SCRAs are probably much less likely to be used as a cannabis replacement, at least among more experienced users.

There are a number of possible drivers of the NPS phenomenon and its gradual spread among vulnerable user groups, although it is not clear what combination of supply or demand factors lie behind different availability patterns and clusters of problem NPS use and have been fuelling them.

The role played by globalisation and developments in information technology have clearly been central for the spread of NPS but are harder to pin down for high-risk drug use. Countries with aggressive drug control policies may be susceptible to the spread of legal alternatives to illicit drugs, yet, in a number of cases, prison appears to play a role as initiation vector to NPS use, in particular SCRAs. A number of questions also remain unanswered. Why has NPS use not happened in some countries? Is this merely a recording issue, or more related to sociocultural factors, drug markets, patterns of historical drug use or perhaps different law enforcement environments? Are NPS substitutes or supplements for existing illicit drugs, or both?

Definition and data: two linked problems

This study has highlighted a number of underlying problems associated with monitoring both the availability and use of NPS and the area of problem or high-risk drug use. In the first instance it is clear that existing definitions have proved unfit for purpose when exploring the area covered by this analysis. We opted to use a broad and inclusive understanding of high-risk drug use for this study in order to ensure that the boundaries were sufficiently wide to incorporate potential new problem patterns of use or at least those outside our current monitoring gaze. Nevertheless, there is clearly a need for further clarification, and the old and rather crude dichotomy of recreational and problem drug use and drug users does not make sense when looking at a complex and graduated theme such as high-risk forms of NPS use. The decline of the injecting heroin user as the norm for high-risk drug users is a major factor perpetuating the dissolving of clear definitional understandings. A range of patterns of drug use behaviours — injecting, frequent, heavy, chronic, high-risk and harmful — have been identified as linked with NPS use and related problems. In particular, the slammers, prisoners, homeless people and at-risk young people using NPS may easily be left out of a narrower problem drug use monitoring definition, and importantly we would have missed these 'edges' of the problem if we had kept to a narrow categorisation. What has been identified here is a more fluid situation, with polydrug consumption patterns and stimulant drugs seemingly playing a more central role than previously. Linked with these patterns of use are differing dimensions of harm, which provide an alternative point of focus. Here there are diverse acute and chronic health problems, social harms and dependence, and interactions between all areas.

The challenges are no less evident when it comes to pinning down a useful definition of NPS for our purposes. In the first place, NPS is an ill-defined term, with a formal legal definition that, while necessary for identification and control purposes, is less useful for exploring emerging epidemiological patterns of use and harms. Again, this analysis utilised a generous and broad definition, bearing in mind the fact that the focus includes 30 countries with different sets of NPS laws and regulations, and where the control status of substances will be constantly changing. Accordingly, several relatively old NPS such as mephedrone and MDPV feature quite heavily. The area of misuse of medicinal products and the crossover with NPS complicates matters further, in particular with regard to new synthetic opioids, where for example fentanyl is categorised as a medicine but a range of new fentanyl derivatives come under the NPS umbrella. Similarly, new benzodiazepines are clearly a major problem in some countries, and online sale of these substances is likely to increase their availability and consumption in the future.

Another tricky aspect of monitoring and researching NPS is the challenge linked to use of an umbrella term, with multiple drugs grouped together under a single heading. What may have been a useful categorisation a decade ago, at the start of this new market phenomenon, is now largely obsolete for the practical purposes of exploring patterns of use and harm. It is unlikely that anyone will self-identify or be usefully identified as an NPS user per se (never mind the fact that NPS are almost never a primary reported drug). At the user level, the street names — meph, snowblow, bath salts, spice — may be the most common identifiers, while, for purposes of understanding effects and harms, health professionals are more likely to find the generic categories of SCRAs, synthetic opioids and synthetic cathinones somewhat more helpful.

This situation is further complicated by the rapid pace of change. While the small number of NPS identified in 2008–10 largely comprised a few cathinones and cannabinoids finding their way onto the European market as legal alternatives to cannabis, MDMA and cocaine, the current situation is very different. We now have a third generation of SCRAs, a wide variety of cathinones, increasing numbers of very potent synthetic opioids appearing, and a range of medicinal NPS on the illicit market. Finally, problems are compounded by the availability of NPS in mixtures (PMMA with MDMA, fentanyl with heroin), some of which have been combined on purpose to increase potency, while others may be accidental occurrences.

Dearth of data and implications for monitoring

This is also an area where access to data and the data itself are a particular problem. Not only are few data available, but many of them are lagged, and we are particularly reliant on expert opinion and self-reports with a lack of forensic confirmation. Matters are further complicated by the high degree of temporal and geographical variation between and within countries. In addition, there have been in the past very small, localised outbreaks related to some drugs that have emerged and then completely disappeared. In theory at least, there should be routine data available on drug users already in contact with helping services, via treatment entrance, for example. However, a number of subpopulations identified in this analysis are evidently not in touch with traditional drug services and thus may be missed, both by monitoring systems and by health and social interventions. In particular, rural poor communities, slammers, homeless people and prisoners might all rather easily slip under the net. This is therefore an area where the so-called 'lamppost problem' may operate, with investigators and helpers alike seeing only what they are looking for and not what lies outside their immediate remit.

Monitoring of high-risk or problem drug use continues to be challenging, and epidemiological surveillance of NPS use is very much in its infancy in many countries. Looking at high-risk forms of NPS use is therefore always going to be a difficult endeavour. This wide-ranging investigation nevertheless confirms the importance of extending monitoring activity to embrace new substances, new populations and in some cases new technologies. The use of proactive approaches (residue testing, outreach) and open source and online monitoring will undoubtedly play an important role in the future.

Some of the emerging phenomena identified here have a global/local nature, for example slamming, which appears to be subcultural and metropolitan rather than a national phenomenon. This is also an area where information gathered at the local and city level helps inform our understanding and where in the future a model of information communities (multi-source/mutual benefit) might be well applied. Finally, it is important that toxicological and forensic information services continue to identify and warn of potentially potent new substances such as fentanyls and other new synthetic opioids.

Conclusion: an uncertain future

This analysis has demonstrated that problem use of NPS in Europe is currently linked with relatively small numbers of users but high associated levels of harm. It confirms and further maps the documented use of synthetic cathinones by pockets of opioid injectors and among slammers, while bringing to light new trends in SCRA use among prisoners in over a third of EU countries as well as developments among marginalised communities. It remains unclear, however, how and why SCRAs are becoming established as the cheapest and strongest indiscriminate intoxicants in some vulnerable social groups. Questions also remain about how this trend might play out in the longer term, and which of those NPS now present on the market will remain and become established. At a time when the distinction between the use of illicit drugs and NPS may be diminishing, highly potent new synthetic opioids appear to be emerging. Use of these is often unintentional, they raise particular concerns for public health, and fear of these substances is reportedly strong among users. Important questions to explore in the future include: will the use of new synthetic opioids, with their high potency and online availability, become more widespread; and will new benzodiazepines become more popular? Recent indications that NPS production may now be taking place in Europe are potentially a game changer, and provide strong motivation to keep a close watch on emerging trends in this rapidly evolving area.

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Rapid communications bring you the latest findings and discussions in key areas in the drugs field. This report provides a first look at the emergence of more problematic forms of use of new psychoactive substances in the European Union, Norway and Turkey.

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

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