Novel Psychoactive Treatment UK Network

NEPTUNE

Guidance on the Clinical Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances

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Inspiring Improvement

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The guidance is based on a combination of literature review and expert clinical consensus and is based on information available up to March 2015. We accept no responsibility or liability for any consequences arising from the use of the information contained in this document.

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Chapter 1

Introduction

1.1. This document

For the purposes of this document, 'club drugs' is a short-hand term used for convenience to refer to a group of psychoactive substances typically used in dance venues, house parties, music festivals and sometimes in a sexual context. The term therefore describes a diverse group of substances with different actions. They include substances with primarily stimulant effects, those with primarily hallucinogenic effects, as well as some central nervous system depressants and synthetic cannabinoids. Club drugs include substances well established in the UK such as MDMA (ecstasy), as well as the rapidly expanding range of novel psychoactive substances (NPS) such as synthetic cannabinoids, synthetic cathinones and a range of other amphetamine-type stimulants. Some club drugs are sold on the illicit market, whilst others are sold as so-called 'legal highs'.

This document provides guidance on the clinical management of harms resulting from acute intoxication and from the harmful and dependent use of club drugs and NPS. It categorises club drugs broadly according to their clinical effects:

- **depressant**;
- **stimulant**;
- **hallucinogenic**.

In addition, the **synthetic cannabinoids** are treated as a separate category, largely for reasons relating to their clinical management but also because they do not fit neatly into that threefold categorisation.

The guidance is based on available evidence and clinical consensus. It is a response to the current gap in knowledge and experience in the management of these drugs across the UK and beyond.

Guidance is aimed in particular at clinicians in a range of settings, specifically:

- specialist drug treatment services
- hospital emergency departments (EDs)
- general practice/ primary care
- sexual health clinics

This document provides **guidance**, *not* **guidelines**. Together with the recommendations of its reviews, technical appraisals and standards, national guidelines produced by the National Institute for Health and Care Excellence (NICE) determine the wider

principles within which treatment and care should be provided within drug services, EDs, primary care, sexual health and mental health services. However, these guidelines do not relate specifically to NPS. NEPTUNE guidance must be used within the wider principles of these national guidelines.

This guidance does not aim to replace the role and resources of the National Poisons Information Service (NPIS) and its online toxicology database and telephone enquiry service TOXBASE® for advice on the clinical assessment and management of acute toxicity within hospital EDs, primary care and other healthcare facilities (Box 1.1). Clinicians should consult TOXBASE®, and where necessary call the NPIS for up-to-date information. It is highly recommended that clinicians and departments be registered to be able to use these facilities. Readers should also consult TOXBASE® for information provided by the UK Teratology Information Service (UKTIS) on all aspects of the toxicity of drugs and chemicals in pregnancy.

Box 1.1. *TOXBASE®*

For up-to-date guidance on the management of acute toxicity, it is recommended that information be sought from the National Poisons Information Service (NPIS), specifically the NPIS 24-hour telephone service and the poisons information database TOXBASE®.

The database (http://www.toxbase.org) contains information on approximately 17,000 products, together with generic advice on the management of poisoning. It is available free of charge to registered NHS users and it is highly recommended that clinicians and departments be registered to be able to use these facilities. By using TOXBASE®, clinical staff can obtain key clinical information rapidly, including advice on potentially hazardous doses and appropriate management.

The NPIS 24-hour telephone helpline (in the UK 0844 892 0111 and Ireland NPIC (01) 809 2566) is available for discussion of more complex cases. When appropriate, senior medical staff can discuss their cases directly with an NPIS consultant clinical toxicologist.

Non-UK readers should consult their local or national guidelines.

Non-UK readers of this document should contact their local, regional or national poisons information service for up–to-date advice and guidance on the management of acute club drug intoxication and withdrawal.

NEPTUNE guidance is **time-limited** (provisionally to end 2017), not least because new compounds continue to emerge and the evidence is continuing to grow.

1.2. Novel Psychoactive Treatment UK Network (NEPTUNE): project aims and guidance development

1.2.1. Objectives of the NEPTUNE Project

This guidance has been developed by NEPTUNE (Novel Psychoactive Treatment UK Network), a project funded by the Health Foundation's* Shine Innovation Programme 2012† and led by Central and North West London NHS Foundation Trust.

The objectives of the NEPTUNE project were as follows:

- Convene a multidisciplinary group of UK experts in the treatment of harms resulting from the use of club drugs, including experts by experience (patients).‡
- Review the national and international evidence on club drugs, and most particularly the evidence on the harms and the management of harms linked to acute intoxication and acute poisoning, as well as those associated with long-term harmful use and/or dependence.
- Develop treatment guidance based on the best available research evidence. Where this is lacking, the guidance is based on the expert group's' clinical consensus and patient experience.
- Develop guidance specifically for the following clinical settings:
  (1) drug treatment services;
  (2) emergency departments;
  (3) general practice;
  (4) sexual health clinics.

The group convened comprises UK experts in the management of acute and chronic problems associated with club drugs. It is a collaboration between individuals from a number of different NHS and voluntary organisations, with observers from relevant government departments (for the full list see pp. ii–iii). The expert group includes psychiatrists, psycho-pharmacologists, psychologists, clinical and analytical toxicologists, emergency physicians, genitourinary medicine (GUM) physicians and HIV physicians, general practitioners, urologists, nurses, senior managers and experts in club drugs among lesbian, gay, bisexual and transgender (LGBT) populations.

1.2.2. Aims of the NEPTUNE clinical guidance

The aim of the guidance is to improve confidence and competence, and increase the skills of clinicians in the detection, assessment and management of the harms

* The Health Foundation is an independent charity working to improve the quality of health care in the UK. http://www.health.org.uk/

† http://www.health.org.uk/areas-of-work/programmes/shine-twelve/

‡ Henceforth referred to as 'expert group'.

associated with the use of club drugs, across all target settings. Specific areas addressed include:

- **Detection/identification**. Recognising the significant psychological, physical and social risks which can be associated with club drugs, and equipping professionals to be able to recognise problematic use, associated harms and dependence, and to be able to use screening tools where indicated.
- **Assessment**. Assessment of the problems related to the use of club drugs, including the assessment of both direct and indirect harms.
- **Management**. Clinical management of acute and chronic harms related to the use of club drugs- in the target clinical settings, based on the best available evidence, or on clinical consensus where evidence is lacking.
- **Harm reduction**. Interventions aimed at preventing morbidity and mortality among individuals presenting to clinical settings, including measures to reduce the harms of club drugs for individuals and communities and to help patients achieve and sustain recovery and well-being.

The underlying principles of good clinical practice in relation to the users of club drugs are applicable to all problematic psychoactive drug use and form the basis of national UK guidelines aimed at the drug treatment and recovery field. However, good assessment and management of the harms of club drugs (including NPS) must also take into account the particular challenges posed by these drugs and address them directly. These include challenges posed by:

- new drugs (rapidly changing profile and ever increasing numbers of substances, with poorly understood harms);
- new populations in treatment (including new patterns of drug use and contexts of harm);
- new harms (some club drugs are associated with harms not previously linked to illicit drug use, for example ketamine-related ulcerative cystitis).

NEPTUNE therefore aims to improve clinicians' knowledge of the specific issues relating to club drugs and to support evidence-based practice at local levels. It also aims to help improve clinicians' confidence in working with patients who use club drugs, by providing the following:

- 'technical' knowledge (what the drugs are and how they work).
- 'cultural' knowledge (who is using them, and how).
- 'clinical' knowledge (how to clinical manage both acute and chronic presentations).

1.3. Target audience for the guidance

1.3.1. Primary audience

This guidance is aimed primarily at a clinical audience. The target clinical settings have been chosen because they offer specialist treatment for acute or chronic problems (EDs and specialist drug services) or because they provide an untapped access to populations at risk of drug-related harms (sexual health clinics and general practice, which are potentially clinical areas with a high prevalence of patients using club drugs).

The stepped care approach used in this guidance document, as well as the phased and layer framework of drug treatment (see Chapter 2), takes into account the different roles and competencies of clinicians in each of the target settings in delivering interventions aimed at those who use club drugs.

1.3.2. Other audiences

The guidance is also a resource for commissioners and policy-makers in developing local and national services. It also provides patients and carers with information on what interventions should be available.

1.4. The process of developing the guidance: method for the literature review

A comprehensive review of the English language literature on the harms and the clinical management of a range of club drugs was carried out, using systematic methods.

Studies, including case reports, were identified using electronic searches of Medline, Medline Plus, the Cochrane Library, CINAHL, Current Content, Embase, PUBMED, PsychINFO, Google Scholar and the Science Citation Index. In addition, bibliographies of articles were screened for additional relevant studies.

Box 1.2. *Search terms included in combination with drug names*

Addiction; Adverse effects; Subjective effects; Craving; Chronic; Clinical features; Cognitive; Detoxification; Dependence; Harms; Ingestion; Intoxication; Pharmacology; Poisoning; Psychological interventions; Psychological treatment; Brief interventions; Drug management; Clinical features; Harms; Toxicity; Motivational; Chronic use; Withdrawal; Craving; Cue exposure; Detoxification; Dependence; Addiction; Managed care; Pharmacotherapy; Intoxication; Prevention; Health outcomes; Clinical outcomes; Recreational use; Toxicology; Prescribing; Relapse prevention; Relapse management; Motivational interviewing; CBT; Behavioural therapies; Cue exposure treatment; Community reinforcement approach; Motivational enhancement therapy; Relapse prevention; Relapse management; Psycho-sexual counselling; Care plan; Gay men; Men who have sex with men; LGBT; Clubbers; Party circuit; Drug use in clubs; Drug-facilitated sex; Injecting; Insufflation; Clinical; Guidelines; A&E; Substance misuse treatment; General practice; Sexual health; Urology; Dentistry; Ophthalmology; Pregnancy; HIV; Hepatitis C.

Search terms included the drugs names alone, or in combination with the terms listed in Box 1.2. Terms specific to one of the substances reviewed were also included where relevant (e.g. ulcerative cystitis for ketamine).

The outputs of searches were considered against sets of inclusion and exclusion criteria (see section 1.4.1). The citations produced by these searches were then screened via their abstract. Those considered relevant were identified and subjected to critical assessment by the core NEPTUNE team and other members of the NEPTUNE expert group.

The critical assessment of the evidence was based on the framework developed by the British Association for Psychopharmacology for the development of guidelines for the management of substance misuse.[1] This classifies the strength of evidence as follows:

- **Strong research evidence** (e.g. Cochrane reviews, meta-analyses, high-quality randomised controlled trials);
- **Research evidence** (e.g. controlled studies or semi-experimental studies);
- **Emerging research evidence** (e.g. descriptive or comparative studies, correlation studies, evaluations or surveys and non-analytic studies, for example case reports, case series);
- **Expert panel evidence/consensus;**
- **Expert by experience evidence** (service users/patients);
- **Lack of evidence** (no evidence, for or against);
- **Conflicting evidence.**

In order to assess the applicability and relevance of the international literature to a UK context, considerations of population, setting, intervention and outcomes have been taken into account for statements in the guidance.

It was clear from the onset of the literature review that the evidence base is relatively small. In particular, studies on the toxicity of NPS, and risks associated with long-term use and dependence liability, are few, partly because most NPS have limited or no medical use,[2] and partly because some of these substances have only recently emerged.

Overall, there is a lack of robust evidence, in particular from meta-analyses or high-quality randomised controlled trials, and even controlled and semi-experimental studies are few. The bulk of the research available provides what is referred to as **emerging research evidence**, as it is based principally on non-experimental descriptive studies, consisting mainly of case reports and series and a small number of prospective observational studies, retrospective cohort studies and analysis of patient records.

The literature review also identified clinical questions that were not addressed by the research evidence. Where evidence was lacking, consensus was sought from the multidisciplinary NEPTUNE expert group, based on a process of open discussion, with a view to producing guidance that is of practical use to clinicians.

This document therefore does not give definitive answers on the clinical management of club drugs and NPS, but broad guidance based on the current best available evidence and clinical consensus.

1.4.1. General inclusions and exclusions in the guidance

- The guidance focuses on acute and chronic harms linked to the use of club drugs, and their management.
- The guidance is aimed at the management of adults (18 years and older). The development of similar guidance for children and adolescents is recommended.
- The guidance does not address interventions in non-clinical or pre-hospital settings, such as nightclubs, schools and universities, or festivals, some of which are discussed elsewhere.[3]
- Issues specifically pertaining to prisons and corrective facilities have also been excluded, although much of the clinical guidance is equally applicable to clinical management within the prison service. The 2013–14 annual report of HM Inspectorate of Prisons mentions the increased availability of NPS, and most particularly synthetic cannabinoids, in prisons and the association of these drugs with debt and bullying, as well as their effects on health.[4]

1.4.2. Substances and drug groups covered by this guidance

Cocaine is the most commonly used substance in the UK that can be described as a club drug, despite some reduction in its use since its peak in 2008/09 in England and Wales. However, this document does not address the management of long-term harms and dependence of cocaine specifically. This is because substance misuse treatment professionals already have access to an extensive and robust body of evidence on the **long-term** harmful and dependent use of cocaine, and Cochrane reviews have been published. There is also good clinical experience in drug treatment services in the UK in the management of cocaine-related harms and evidence that people with primary cocaine problems are accessing treatment and recovery services (for more details see Chapter 2). This document does, however, address briefly **acute** cocaine intoxication, which is a significant clinical problem in the UK. Studies from the UK have shown under-recognition of acute cocaine toxicity in patients presenting with chest pain. There are aspects of acute cocaine toxicity that are different to the toxicity associated with other stimulants, in particular myocardial ischaemia/chest pain (related to vasospasm) and arrhythmias (related to ion channel effects). These are discussed briefly in Chapter 6.

Not all NPS meet the loose definition of a 'club drug' and some NPS have been excluded from this guidance document, such as the newly developed opioids receptor agonists and benzodiazepines that have recently been on sale on the internet.

Because of the potentially very large number of club drugs and NPS that can currently be bought on the illicit and 'legal' markets and those that will emerge in the future, it

is not possible to cover them all in any detail within the confines of this work. In order to address this issue, a two-pronged approach has been adopted:

First, the structure of the guidance provided by this document – and within which individual drugs are discussed – is based on the following broad classifications:

- predominantly depressant drugs;
- predominantly stimulant drugs;
- hallucinogens drugs;
- synthetic cannabinoids.

Although these classifications provide a useful framework for this guidance, it is important to note that they are not rigid categories. In reality, many club drugs have a combination of effects, for example stimulant and hallucinogenic effects.[5]

The second part of our approach was to focus in more detail on the drugs (as well as their derivatives and related compounds) most used in the UK and those that cause most harm.

Where a particular drug is not discussed in this document (either because it was infrequently used in the UK or because it was not developed at the time of writing), clinicians can refer to the broad groups to which it belongs and can extrapolate information on the management of its acute and chronic harms, while taking into account potential differences in potency, toxicity, half-life, length of effect and so forth.

1.5. An overview of club drugs

1.5.1. Old drugs, new drugs and 'legal highs'

'Club drugs' include a wide rage of substances. Some, such as ecstasy, are well established substances, that have been subject to legal control for many years. Others are new psychoactive substances (NPS), which are emerging at a fast pace on the drugs market, many supposedly as non-illicit alternatives to controlled drugs.[2] At the time of writing, many of these NPS were controlled, whilst others were sold as so-called 'legal highs'.

An increasing number of NPS can be found globally. The United Nations Office on Drugs and Crime has identified six main groups: synthetic cannabinoids, synthetic cathinones, ketamine, phenethylamines, piperazines and plant-based substances; there is also a seventh group, of miscellaneous substances – recently identified NPS which do not fit into the groups mentioned.[2]

The *World Drug Report 2014* indicated that the number of NPS on the global market more than doubled over the period 2009–13. By December 2013, the number of NPS reported to UNODC reached 348, up from 251 in July 2012 and 166 substances in 2009. This means that, now, the number of NPS exceeds the number of psychoactive

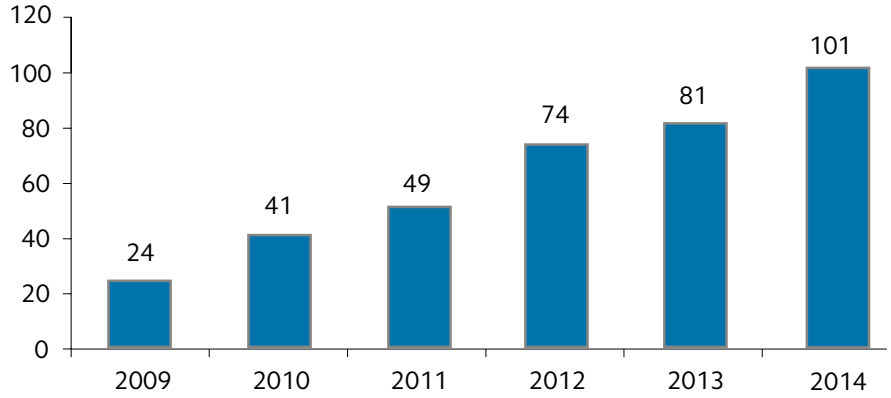

Figure 1.1. *Number of psychoactive substances with use reported for the first time within the European Union*

substances controlled at the international level (234 substances).[6] The overall increase over the period August 2012–December 2013 was mostly due to new synthetic cannabinoids (50% of newly identified psychoactive substances), followed by new phenethylamines (17%), other substances (14%) and new synthetic cathinones (8%).

The use of NPS is thus emerging as a truly global phenomenon. NPS are now found in most of Europe and North America, as well as Oceania, Asia and South America, and in a number of African countries. To some extent, however, NPS are a North American and European phenomenon, with the UK accounting for 23% of the European total of NPS users.[7]

The number of NPS is increasing at a fast pace in Europe, as shown in Figure 1.1.[8]

In recent years, these newly emerging 'legal highs' in Europe have been dominated by new synthetic cannabinoid receptor agonists, with phenethylamines, tryptamines and cathinones reflecting other popular illicit drugs. Of the 81 new psychoactive substances reported for the first time within the EU in 2013, 29 were synthetic cannabinoids, 14 phenethylamines, 7 synthetic cathinones, 7 arylalkylamines, 5 opioids, 2 benzodiazepines, 1 tryptamine, 1 aminoindane, 1 arylcyclohexylamine, 1 piperidines/ pyrrolinde, 1 piperazine, and 12 were substances that do not conform to any of these groups. Of particular concern are new synthetic opioids – such as AH-7921, MT-45, carfentanil and ocfentanil – reported as emerging in the past two years but which are already controlled under the Misuse of Drugs Act.[8] These are, however, outside the remit of this document, because they cannot be considered club drugs, as defined in section 1.1.

Most of these NPS are thought to be manufactured to mimic the effects of controlled drugs, usually in China or India, or in clandestine laboratories in Europe. There is no doubt that the producers of novel NPS and 'legal highs' are well aware of the legal framework surrounding illicit substances and are continuously replacing controlled compounds with an array of compounds which are modified to avoid legal control.

Given the very numerous possibilities for altering the structure of chemicals, the list of substances produced is likely to grow continuously.[2]

New substances are produced very quickly to replace those that are placed under legal control by various states. A well known example is from Germany, where a second generation of synthetic cannabinoid products (JWH-073) were available on the market just four weeks following the ban of JWH-018.[9] In the UK, and although JWH-018 continued to be found in 60% of 'spice' products after the ban, products containing JWH-073 increased from 6.5% to 70% of products tested.[10] Similarly, it was noted that online discussions on MDAI in drug user fora became more frequent after May 2010, following the UK ban on methcathinones the previous month. MDAI was then advertised as a 'legal' alternative to mephedrone.[11]

However, despite the fact that the manufacturers of so-called 'legal highs' often try to circumvent the law by developing compounds slightly different from those banned, there is evidence that some of these products sold online or in 'head shops' do contain classified compounds and are therefore illegal under UK law.[10] Reports of the Forensic Early Warning System (FEWS) confirm that this continues to be the case: products advertised as legal alternatives to illicit substances are not always legal.[12,13] In addition, the report showed that 81% of the approximately 2000 products that contained new psychoactive substances collected during 2012–13 were a mixture of two or three different active compounds.[12,13] Products with the same name brands also sometimes contained different mixtures of active compounds, even those from the same supplier.[12]

In 2013–14, 19.2% of NPS samples collected by FEWS contained controlled drugs. There a difference by setting, whereby a low proportion of controlled drugs was detected in NPS samples from headshops (4.3%) and the internet (3.0%), but a high proportion of controlled drugs was detected in NPS samples from festivals (88.1%). In addition, approximately 91% of the samples analysed that contained NPS were identified as mixtures of either two (61%) or three (30%) different active components; 1% of samples were identified as containing six different active components. Furthermore, products with the same brand name, such as 'Black Mamba', 'Critical Haze' and 'Sparklee', including those from the same suppliers, were observed to contain mixtures of different components.[13]

UK and other research has also shown that there is significant variation in the content of 'legal high' products bought over the internet.[14–19] One study found that six out of the seven products it analysed did not contain the advertised active ingredients but, rather, some controlled products.[19] Moreover, the actual components of products sold as 'legal highs' are subject to variation even between batches, and change over time and in different places. For example, 'Ivory Wave' was identified in 2009 as a mixture of MDPV and lidocaine,[20] but further toxicological analyses of other 'Ivory Wave' batches also revealed the presence of 2-DPMP[21] and D2PM.[22] It has also been reported that caffeine has been detected in legal high products and some products tested were shown to contain caffeine only.[14]

Therefore, although the term 'legal high' is used for a number of NPS, it is a confusing and unhelpful one. It has been argued that these substances are not 'legal' but are

instead 'not prohibited'. Their 'legal' status does not reflect their safety but rather the lack of regulation over their production, distribution and use.[23,24] Many are untested and have unknown psychological and toxicological effects.[25,26]

Moreover, not all NPS are 'novel'. 'New' does not always mean a new invention but could refer to substances that have recently been made available for recreational use. For example, mephedrone was reportedly first synthesised in 1929, but emerged as a recreational substance of misuse as late as 2007.[2] Other 'new' substances were synthesised and patented in the 1970s or earlier, but recently their chemistry has been modified slightly to produce psychoactive effects similar to those of well established illicit substances, as is discussed in the chapters below.

It is also important to note that new drugs may appear on the illicit market and then disappear, usually as a result of little demand. NPS may be popular at first and then fall in and out of favour, as users try them and move away from them; for example, pipradrols such as D2PM, desoxypipradrol and bromo-dragonfly are currently used less than previously.

There is some evidence that the appeal of some NPS is sometimes linked to the poor quality of more established illcit substances available on the black market. In particular, a reduction in the purity of ecstasy and cocaine was linked to an increased use of mephedrone in the UK[27] and 2C-B in Spain.[28]

1.5.2. New markets and user communication about drugs

Club drugs are sold through a variety of channels, including street-level drug dealers and through web sites; such outlets often sell controlled substances as well as 'legal highs' (see below for details). Some users will access a mixed economy; for example, there is anecdotal evidence from clinical practice that some GHB/GBL users will buy a small amount from street dealers as well as purchasing in bulk via the internet.

'Legal highs' are sold online, in 'head-shops' or sometimes alongside controlled substances on the illicit market. Anecdotal reports from the UK also suggest that some legal high products (such synthetic cannabinoid products) are being sold in a wide range of outlets,[29] including corner shops, pubs and petrol stations. Legal highs are marketed as 'plant food', 'bath salts', 'research chemicals', 'incense' or 'herbal highs' and are typically labelled as 'not for human consumption' in an apparent attempt to evade legal sanction.

One of the attractions of NPS to users is the inability of standard drug tests to identify them. There are currently no accurate field testing devices for most of the NPS, despite continued developments in the area of chemical standards, analytical capability and forensic detection of compounds.

The 'market' for club drugs and NPS appears to have gradually become more sophisticated. For example, a Spanish study of 2C-B has reported that whereas in 2006/07 the majority of 2C-B samples collected appeared to be in poorly elaborated forms such as powder or capsules, in 2008 and 2009 the most frequent form of presentation was tablets.[28]

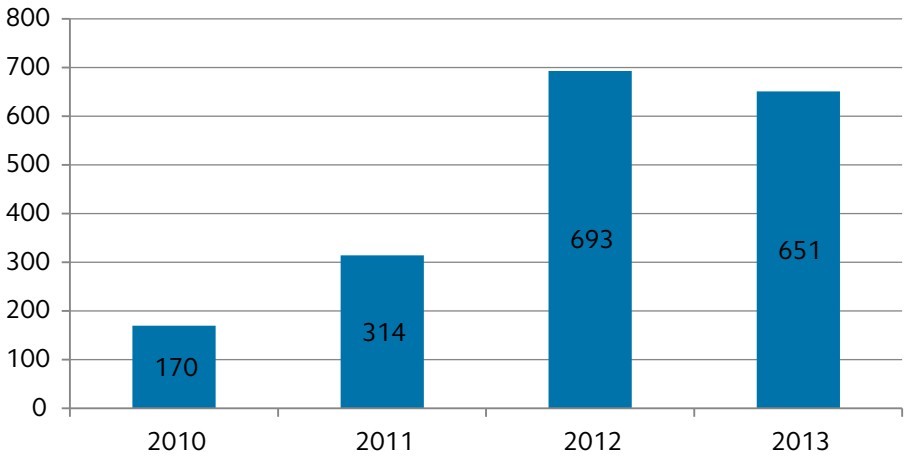

Figure 1.2. *Number of internet NPS shopping sites in Europe per year identified by the EMCDDA's targeted internet study (snapshot)*[8]

As compounds are controlled and substances banned, their new illegal status does not always deter use. Some drugs, like mephedrone, quickly made the cross-over in the UK from being a so-called 'legal high' to becoming a relatively commonly used Class B substance.[30] Most sales were then transferred to street dealers, with users reporting paying a higher price than they did before the substance was controlled, for what was perceived to be a lower-quality product.[31,32]

The rise in the use of club drugs and NPS coincided with the ability to purchase drugs online. Although mostly bought through street-level dealers, illicit substances are also sometimes bought on the internet (some with next-day delivery to consumers[8]), specifically from websites operating from outside the UK, or on the 'dark web' – that part of the internet which is not indexed by standard search engines and is accessible only through anonymising browsers such as Tor. A number of websites sell a wide variety of so-called 'legal high' products, as well as controlled substances, using this method.[6] Information about new psychoactive products is often now provided via 'alerts' in the form of text messages, instant messaging or emails ('email this product to a friend').[33,34]

There has been a steep rise in the number of online 'shops' selling both 'legal' and illegal products to European customers. The targeted internet (snapshot) study carried out by the European Monitoring Centre for Drugs and Drug Abuse (EMCDDA) looked at the rise in the number of internet NPS 'shops' over the period 2010–13.[35] The results are shown in Figure 1.2.[36]

The internet is also facilitating communication for people who use NPS and providing access to knowledge, expertise and logistics about these drugs. There are a number of sites and moderated discussion fora and blogs that are used to share information about newer compounds, feedback on the effects of drugs and harm reduction advice developed through experience.[36] User sites, such as Drugs Forum, Bluelight and Erowid, among others, have also provided researchers with some understanding of these drugs when scientific evidence was not available.

1.6. Club drug use in the UK

1.6.1. Overall drug use

Based on combined data from the Crime Survey of England and Wales (CSEW; formerly the British Crime Survey), with similar population data from Scotland and Northern Ireland for 2010/11, the UK Focal Point Report estimated that 35.6% of the adult population in the UK, between the ages of 16 and 59 years, had used drugs sometime in their lifetime.[37]

The most complete time series data available come from England and Wales through the CSEW. In 2013/14, approximately 1 in 11 (8.8%) adults aged 16–59 had taken an illicit drug in the last year. This proportion more than doubles when looking at those aged 16–24 years (18.9%).[38] Overall, data from the CSEW show that cannabis continued to be the most commonly used drug in 2013/14, with 6.6% of all adults between the ages of 16 and 59 years using it in the past year, followed by cocaine powder (2.4%) and ecstasy (1.6%).[38]

In the Scottish Crime and Justice Survey (SCJS) 2012/13,[39] 23% of respondents reported lifetime use of drugs, which was a statistically significant decrease from 2008/09, where 25.6% of adults reported drug use. Drug use in the last year also decreased, with 6.2% of adults reporting having used one or more illicit drugs in 2012/13, in comparison with 7.6% of adults in the 2008/09 SCJS.

1.6.2. Club drug and NPS use

As with drugs in general, subsequent CSEW data have consistently shown that adults between the ages of 16 and 24 years are more likely to use club drugs than adults in general. The data for 2013/14, for example, are shown in Table 1.1.[38]

Table 1.1. *Percentage of adults using drugs in the last year (CSEW, 2013/14)*

Drugs used in past year by age group, 2013/14	Adults aged 16–24 years	All adults aged 16–59 years
Ecstasy	3.9%	1.6%
Mephedrone	1.9%	0.6%
Ketamine	1.8%	0.6%
LSD	0.9%	0.3%
Magic mushrooms	0.8%	0.4%
Methamphetamine	0.1%	0.1%
Salvia	1.8%	0.5%
Nitrous oxide	7.6%	2.3%

The 2012/13 Scottish Crime and Justice Survey also showed variations, with men, and young people, most likely to have used any of five drugs from a group of new drugs (benzylpiperazine, GBL, synthetic cannabinoids, khat or *Salvia divinorum*) as well as mephedrone.[39]

Some club drugs and NPS can be injected. In England, the 2014 Public Health England (PHE) report on infections among people who inject drugs mentions a recent increase in the injecting of amphetamines and amphetamine-type substances, including mephedrone and methamphetamine. The injecting of these drugs is associated with high risks of infection and lower levels of intervention uptake.[40]

Among people presenting for treatment of their drug misuse in England and who have used mephedrone, methamphetamine, ketamine and GHB/GBL, the proportion of those who reported injecting doubled, to 10%, between 2011/12 and 2012/13.[40] In Wales, the proportion of those using needle and syringe exchanges and reporting injection of amphetamine and/or other amphetamine-type substances (ATS) as their main drugs increased from 7% in 2011/12 to 10% in 2013/14.[41] In Scotland, there is no evidence of an increase in presentations for treatment of people using amphetamines, ecstasy or mephedrone, and numbers remain small.[40]

1.6.3. Drug-using repertoires and poly-drug use

There are also are reports of indiscriminate use of substances by some, with users reporting taking unidentified synthetic white powders with no knowledge of their chemical content, as shown by a survey of participants in the night-time economy.[42] This was supported by the results of the Global Drug Survey, which found that 15% of all respondents and a fifth of those aged between 18 and 25 years had in the past 12 months used an 'unknown white powder'.*

Thus, the users of club drugs will typically use a wide repertoire of substances. The co-ingestion of more than one substance (simultaneous use), including alcohol, is also relatively common and increases the risk of adverse effects, as is discussed in greater detail in the chapters within Parts II to V of this document.

1.6.4. Club drug users and contexts of use

There is evidence that levels of drug use are higher among particular populations and that club drugs are a popular aspect of socialisation.[43] These include the following:

1.6.4.1. Clubbers and night-time economy

There is evidence that people who use the night-time economy, and dance clubs or nightclubs in particular, are more likely to use club drugs than the general population.[44,45] Data from the CSEW consistently show that the levels of drug use

* The Global Drug Survey is independent research organisation. See http://globaldrugsurvey.com/about. The results of a 2012 survey sponsored by the *Guardian* were reported in that newspaper: see http://www.guardian.co.uk/society/2012/mar/15/guardian-mixmag-drug-survey-drugs and http://www.guardian.co.uk/society/datablog/2012/mar/15/global-drug-survey-us-uk.

increase with frequency of visits to nightclubs and pubs. For example, the 2013/14 CSEW reported that 10.9% of respondents who had been to a nightclub four or more times in the last month were frequent users of drugs, in comparison with 2.3% of users who had not visited a nightclub in the past month. Similarly, 9.2% of adults who had visited a pub nine or more times in the last month had taken any drug in the last year, compared with 2.4% of those who had not visited a pub.[38]

Other targeted surveys have also shown variations by user of different types of venues in the night-time economy, for example with those attending nightclubs reporting significantly higher levels of drug use than bar/pub attenders.[44] Drug use is also higher in certain music or stylistic 'scenes', such as among club-goers attending dance events playing 'hard dance' music compared with the same venues when playing other genres of dance music.[44] There are reports of particularly high levels of lifetime use among 'clubbers' who attend electronic dance music clubs, ranging from 79% to 94%.[46,47] Clubbing and club drug use, as part of a socially active lifestyle, has been associated with elevated sexual health risks.[48]

1.6.4.2. Lesbian, gay, bisexual and transgender populations

There is UK and international evidence that levels of club drug use among LGBT people, and men who have sex with men (MSM) in particular, is higher than in the general population. The European Men-Who-Have-Sex-With-Men Internet Survey, carried out in 38 countries in 2013,[49] showed, for example, that UK has higher levels of the use of some drugs than do other parts of Europe.

Robust UK prevalence data on drug use among LGBT populations, and comparisons with the heterosexual population, are limited. The 2013/14 CSEW and its predecessor, the British Crime Survey (BCS), have provided data over a number of years, but these must be treated with caution because of the small numbers in the survey. In 2011/12 and 2013/14, respondents who identified themselves as lesbian, gay and bisexual (LGB) were approximately three times more likely to have reported taking any illicit substances in the last year in comparison with heterosexual respondents (28.4% versus 8.1%), with differences remaining when age-standardised data were analysed. LGB respondents were also much more more likely to report the use of stimulant drugs* (14.4% versus 2.9%). A higher level of use was reported by LGB respondents for most individual substances, including powder cocaine, ecstasy, hallucinogenic drugs, amphetamine, cannabis, tranquillisers, ketamine and amyl nitrite.[38]

There are increasing concerns over associations between club drug use and high-risk sexual behaviours among a minority of MSM. This includes concern over 'chemsex', a term used to describe sex between men that occurs under the influence of drugs immediately preceding and/or during the sexual session,[50] with methamphetamine, GHB/GBL and mephedrone the drugs most often used. A combination of factors, including high-risk sexual practices and injection, have been described as 'a perfect storm for transmission of both HIV and HCV, as well as a catalogue of ensuing mental health problems'.[51]

* The stimulant drugs surveyed were powder cocaine, crack cocaine, ecstasy, amphetamines and amyl nitrite.

1.6.4.3. 'Psychonauts'

'Psychonauts' is a term given to a group of people who explore their own psyche, especially by taking psychedelic or hallucinogenic substances. The emphasis of use is on seeking novelty and extremes of experience. Psychonauts may experiment with newly emerging psychoactive substances, including obscure hallucinogens, and may experiment with drug combinations or push boundaries in terms of dose, for example. The internet plays an important role and provides a platform for sharing experience and information.[52]

1.7. Overview of the effects and harms of club drugs

1.7.1. How drugs work

Drugs can be classified in various ways – according to chemical structure, pharmacological activity or psychological effects.[53,54] One approach is to consider a drug's primary effects along the dimensions of sedation–stimulation, although account needs to be taken of the fact that in some people sedatives can be disinhibiting in the early rising phase of drug entry into the brain, or at low doses, and so can mimic the effects of stimulants. For example, although GHB/GBL is a sedative, it has, at low doses, a stimulant effect.

A separate axis is in terms of alterations of perceptions and feelings. For example, MDMA, as well as being a moderate stimulant, is also an empathogen (empathy-enhancing), whereas magic mushrooms and LSD alter consciousness to cause novel phenomena such as hallucinations and a disordered sense of time and being (hallucinogens or psychedelics). Ketamine and related drugs are dissociative anaesthetics, producing a state of altered consciousness. Opioids dampen pain but also promote sleep and visions during it, and produce a profound sense of pleasure. Stimulants tend to activate a person.

The proximal mechanisms of most of these effects (as far as they are known) are shown in Table 1.2. Most NPS are designed to provide legal alternatives to controlled substances, and have harms similar to those associated with the controlled drugs they have been manufactured to mimic.

1.7.2. Toxicity and other harms

Club drugs and NPS are associated with a range of harms.[55] The harm associated with any drug of potential misuse may include: the physical harm to the individual user caused by the drug; the dependence-inducing potential of the drug; and the effects of drug use on families, communities and society.[56] All three aspects need to be considered when assessing the impact of a drug.

'Toxicity' generally refers to the extent to which a substance causes functional or anatomical damage to a living organism.[57,58] There are wide variations in the toxicity

Table 1.2. *The proximal mechanisms of drug effects*

Drug	Primary (proximal) target	Brain effects
Alcohol	Agonist at GABA and antagonist at glutamate receptors	Increases GABA Blocks NMDA glutamate receptors
Benzodiazepines	Agonists at benzodiazepine site on GABA-A receptor	Increase GABA
GHB	GHB and GABA-B receptor agonist	Mimics GABA Inhibits dopamine release
Ketamine	NMDA glutamate receptor antagonist	Blocks glutamate
Caffeine	Antagonist at adenosine A2 receptor	Reduces sedation Increases noradrenaline
Khat	Releases ephedrine, a dopamine releaser	Mild increase in noradrenaline and dopamine
Cannabis	Cannabis CB1 receptor agonist	Stimulates endo-cannabinoid signalling, leading to a change in cortical and memory functions
Cocaine	Blocks dopamine reuptake site	Greatly increases dopamine
Amphetamines (dexamphetamine and methyl)	Release dopamine and block reuptake	Greatly increase dopamine and noradrenaline
Nicotine	Agonist at (nicotinic) acetylcholine receptors	Slightly increases dopamine
MDMA	Blocks serotonin and dopamine reuptake	Increases serotonin and dopamine function
Mephedrone	Release dopamine and block reuptake	Increase dopamine, and serotonin
Hallucinogens	Agonists at serotonin 5-HT_{2A} receptors	Change across-cortex signalling
Heroin and other opioids	Agonists at endorphin receptors	Produce euphoria, reduce pain

Agonist = drug that activates or stimulates a receptor; Antagonist = drug that blocks a receptor.

of the various club drugs and NPS, including their single-dose lethal toxicity.[57] In addition, individuals vary greatly with respect to metabolism and psycho-physical vulnerability.

A number of other factors are also linked to acute toxicity:

- The co-use of more than one substance will increase the chances of acute toxicity, particularly when drugs with similar physiological effects are combined (e.g. sedatives such as GHB and alcohol or stimulants such as cocaine and amphetamine)
- The risk of overdose is increased by repeated administration of the drug.
- The safety ratio of drugs does not reflect the metabolic or functional tolerance that a user may have developed.
- Non-drug variables can alter toxic reactions significantly (e.g. the psychological effects of the environment, diet, stress, expectation etc.).[58]

- The mode of administration, with injecting not only exposing the user to the risk of bacterial infections but also increasing the risk of overdose and dependence.[55]
- Drug purity and adulterants can affect toxicity.

Club drugs and NPS pose a particular challenge to clinicians and may constitute a public health challenge, for the following reasons:[33]

- these substances are not approved for human consumption;
- they are possibly associated with a number of unknown adverse effects;
- insufficient information on them is available in peer-reviewed scientific journals;
- they appear in increasingly sophisticated (i.e. non-powder) forms and remain unregulated for long periods of time;
- they are often synthesised in underground laboratories by modifying the molecular structure of controlled drugs, raising concerns over the presence of contaminating agents;
- they are largely available online to everyone, 'just a click away';
- they are increasingly accepted as part of a 'trendy' lifestyle.

Whereas, all users of club drugs face the risk of acute toxicity, the harms caused by club drugs encompass a wide range of different patterns. Club drugs are associated with harmful use, defined by the World Health Organization (WHO) as a pattern of psychoactive substance use that is causing damage to health, which can be physical (e.g. ketamine can lead to bladder damage and ulcerative cystitis) or mental (e.g. psychosis associated with synthetic cannabinoids).[59] Some club drugs have also been shown to have a liability to produce dependence and some have been associated with a withdrawal syndrome, which can be severe, for example in the case of GHB/GBL.

1.7.3. Mortality related to the use of club drugs

Data on drug-related mortalities have been provided for a number of years by the National Programme for Substance Abuse Death (NPSAD). Deaths involving NPS (including 'legal highs') have increased in recent years,[60] although the rates remain much lower than deaths from heroin/morphine.

Overall, the limitations of data on drug-related mortality must be used with caution and as indicative, rather than robust.[61] The Office for National Statistics' report *Deaths Related to Drug Poisoning in England and Wales 2012* indicates a sharp increase in the number of deaths involving NPS, from 29 in 2011 to 52 in 2012.[62] This rose to 60 in 2013. There were 26 deaths in 2013 involving cathinones (including mephedrone). This was a rise of 44% from the 18 deaths in 2012, and was over four times greater than the 6 deaths in 2011.[63] Deaths in 2013 where other NPS were implicated include those listed in Table 1.3.

Table 1.3. *Number of deaths related to drug poisoning with a mention of a novel psychoactive substance, by specific substance, England and Wales, 2013*

Substance	Sole drug mentioned in coroner's report	Any drug mentioned in coroner's report
1-(benzofuran-6-yl)-propan-2-amine	0	2
2-(1H-indol-5-yl)-1-methylethylamine	0	1
4-fluoroephedrine	0	0
4-fluoromethcathinone	1	1
4-methylamphetamine	0	1
4-methylethcathinone	1	3
Alpha-methyltryptamine	4	7
BZP	0	1
Cathinone[a]	0	1
Desoxypipradrol	0	0
Fluoromethcathinone	0	0
Gamma-hydroxybutyrate (GHB)/ gamma-butyrolactone (GBL)	10	18
Khat	0	0
Legal high	0	0
Mephedrone	1	18
Methiopropamine	1	4
Methoxetamine	1	2
Methylenedioxypyrovalerone	1	2
Methylone	1	4
Synthetic cannabinoid	0	0
TFMPP	0	0
1-(benzofuran-5-yl)-propan-2-amine	0	3
1-(benzofuran-5-yl)-N-methylpropan-2-amine	0	1
APB	2	3
2-diphenylmethylpyrrolidine	0	1
4-Methoxymethcathinone	0	1
N-Methyl-3-phenyl-norbornan-2-amine	1	1
Fluoromethamphetamine	0	1
MDDA	0	1

[a] Where cathinone was found in the text of the coroner's report and no further derivative breakdown was available. This does not represent the total number of deaths relating to the group 'cathinones'.

Source: Deaths related to drug poisoning with a mention of NPS in the coroner's report, by specific substance, England and Wales, deaths registered in 2013.[63]

1.8. Response to club drug use

1.8.1. Policy response to club drug and NPS use

The question of how to respond to the challenges posed by the emergence of new drugs has now become a major concern within the EU and at the international level.[8] In the UK, the need to tackle the problematic use of NPS and club drugs and actions to do so featured prominently in the government's 2010 drug strategy[64] and the subsequent reviews of that strategy.[65] The issue of NPS was also addressed by devolved administrations in Scotland, Northern Ireland and in Wales, which supported the expansion of the WEDINOS (Welsh Emergency Doctor Illicit Novel Substances).

In December 2013, the Home Office convened an expert panel to look at NPS[66] and provide recommendations.[67] The government in its response endorsed the dissemination of effective practice and specifically highlighted the role of the NEPTUNE project in doing so.[68] NPS and club drugs continue to be a government priority.

To date, the government has banned more than 500 new drugs, created the Forensic Early Warning System to identify NPS in the UK and supported law enforcement action with the latest intelligence on new substances. It is also taking forward a comprehensive action plan to further enhance the response to prevention, treatment and information sharing regarding NPS, for example providing a toolkit for commissioners which gives a broad overview of the challenges and which provides them with resources and advice to inform a suitable local response. A guidance document has also been issued to informal educators of young people (e.g. youth workers), with basic information on NPS and which provides signposting information for further advice and support.

1.8.2. NPS and drug-related presentations to hospitals and treatment

Accurate data on emergency hospital admissions resulting from club drug use in the UK are difficult to obtain, for a variety of reasons, not least because ICD-10 codes do not include specific codes for NPS and because coding is generally based on clinical condition at presentation. In order to address this current paucity of reliable data, the European Drug Emergencies Network (Euro-Den) established in 2014 as a network of 16 sentinel centres in 10 EU and neighbouring countries. The project was set up to provide data on the clinical, demographic and geographical patterns of acute recreational use and NPS toxicity, and to act as a stimulus to ensure best practice in the management of acute toxicity from recreational drug and NPS in pre-hospital recreational settings.[69]

A useful indicator is provided by activity data of the NPIS, although it needs to be borne in mind that these do not record hospital admissions. The NPIS received 1561 telephone enquiries and 58,469 TOXBASE® accesses related to 61 drugs of misuse monitored by the NPIS during 2013/14. When adjusted for overall increases in all NPIS enquiries, telephone enquiries for these drugs of misuse increased by 24.9% and TOXBASE® accesses by 0.6% compared with 2012/13.[70]

Data are available on patient access to substance misuse recovery services. There is evidence that some individuals regularly using club drugs are developing on-going problems, including dependence. Data on club drug use among populations in treatment in England has been collected by the National Drug Treatment Monitoring System (NDTMS) for England since 2005/06.[71,72] A 'club drug user' was defined as a person citing any of the following five substances, as either a primary or an adjunctive drug: GHB/GBL, ketamine, ecstasy, methamphetamine or mephedrone. The number of clients presenting for drug treatment in England for a club drug reported by NDTMS increased from 2675 in 2011/12 to 3543 in 2013/14. Increases in numbers presenting to treatment were observed for all five substances: the most significant was an 82% increase in mephedrone presentations, from 900 in 2011/12, to 1641 in 2013/14. Numbers presenting to treatment citing methamphetamine use increased by 107%, from 116 in 2011/12 to 240 in 2013/14, but still made up just 0.3% of all presentations to drug treatment and recovery services.[73] The PHE report on drug treatment in England in 2012/13 suggested that recovery rates for the users of club drugs and NPS remained good.[72]

1.8.3. Principles underlying the assessment and management in target settings of the harms associated with the use of club drugs and NPS

1.8.3.1. Emergency departments

Emergency medicine physicians and other clinicians should seek advice on the diagnosis, treatment and care of patients who have been – or may have been – poisoned with a club drug, primarily from the National Poisons Information Service (NPIS) through its telephone service and TOXBASE® database. This will assist in ensuring optimal and up-to-date information on care for patients in cases of serious poisoning and, where toxicity is low, offering advice to minimise unnecessary hospital attendances and admissions.

The use of psychoactive substances in pregnancy can lead to multiple health and social harms to mother and child. The NPIS provides the UK Teratology Information Service (UKTIS), which is the national source of information and advice about exposures to drugs and chemicals during pregnancy. Information is provided to health professionals via a telephone information service and online through TOXBASE®, which holds the full pregnancy review documents produced by UKTIS on maternal exposures to drugs and chemicals. Other guidelines on the identification and management of substance misuse in pregnancy are available, including recent guidelines from the WHO.[74]

1.8.3.2. Sexual health services

The association between substance misuse and high-risk sexual behaviours is well established and there is evidence of a high prevalence of drug use among patients attending sexual health clinics. For example, one study of patients at a London sexual health clinic reported significantly higher rates of past month drug use, than in the general adult population in England and Wales. This was particularly so among

MSM.[75] Sexual health services may therefore provide opportunistic encounters to identify patterns of recreational drug use, explore motivations for use and implement strategies to reduce harms related to drug use.[75]

MSM and people who have alcohol and drug problems have also been identified as higher-risk groups for poor sexual health outcomes.[76,77] As a result, targeted work has been suggested. For example, the Royal College of Physicians and the British Association for Sexual Health and HIV recommend that sexual health settings distribute information on alcohol-related harms and facilitate brief alcohol interventions to reduce consumption and related sexual ill-health.[78,79]

NICE public health guidance (PH24)[80] identifies sexual health services as a specific setting where alcohol use should be assessed and interventions provided and/or referral made. Given the clear proven association (if not causation) between substance misuse and high risk sexual behaviour and consequent sexual ill health, along with some of the emerging harms associated with specific substances (e.g. ketamine bladder) there has been increasing recognition within the specialty for a need to identify those potentially at risk, and to provide either simple interventions or clear pathways into specialised services. Recent data[81] suggest there is a low level of screening for either alcohol and or substance misuse within sexual health services. However, screening for some risk behaviour is common (e.g. injecting drug use), as it forms part of the risk assessment for the acquisition of blood-borne viruses (BBV).

The British Association for Sexual Health and HIV (BASHH) provides recommendations on screening for alcohol and recreational drug use in several of its specialty guidance documents. The '2013 UK national guideline for consultations requiring sexual history taking'[82] recommends that all patients are asked about their alcohol intake and suggests that a recreational drug history is considered for specific at-risk groups, such as MSM and young people. The '2012 UK National Guidelines on safer sex advice'[83] highlighted the need to identify those who may be at risk of sexual ill health and thus may be good candidates for advice on safer sex and other brief interventions, including those individuals with a history of alcohol or substance misuse.

The BASHH statement on 'club' (recreational) drug use[84] identifies MSM, young people, students and 'clubbers' as possible target groups for screening, so as to identify potentially problematic use, and provides some proposed screening questions. It recommends that clinicians give simple safety advice and information on possible harm, including other sources of information, and that services have agreed referral pathways into appropriate local services.

The British HIV Association (BHIVA), in its *Standards of Care for People Living with HIV in 2013*,[79] recommends screening for drug and alcohol misuse within three months of diagnosis, and annually thereafter, and that services have appropriate referral pathways in place.

Currently, there is no systematic capture and reporting of alcohol and substance use by individuals accessing sexual health services in the UK. However, there are proposed changes to the national GUM clinical activity dataset (GUMCAD) which will include both alcohol and drug use data fields. If approved, this should, for the first time, permit some estimate of the scale of the problem within this patient group.

1.8.3.3. Substance misuse treatment services

Guidelines for substance misuse treatment in the UK in general is defined by the *Drug Misuse and Dependence: UK Guidelines on Clinical Management*[85] (a 2007 document that was due to be updated in 2015). These provide the standards and quality of care for the appropriate treatment of drug misusers, if the performance of any clinical area is to be assessed.

Guidelines for standards of care are also defined by range of relevant NICE clinical guidance and technology appraisals, although none currently focuses on club drugs and NPS. In order to deliver high-quality treatment, including for the users of club drugs and NPS, drug treatment services should be able to demonstrate their adherence to the NICE quality standards for drug use disorders (NICE Quality Standard 23)[86] and alcohol (NICE Quality Standard 11).[87] Such guidance should contribute to improving the effectiveness, safety and positive experience of care for people with substance misuse disorders. There should also be adherence to NICE psychological interventions guidelines on the management of drug misuse.[88] NICE Clinical Guidance 52, on opiate detoxification,[89] states that 'all interventions for people who misuse drugs should be delivered by staff who are competent in delivering the intervention and who receive appropriate supervision'.

To increase the prospects of recovery from drug misuse, PHE recommends that treatment needs to be dynamic, phased and layered.[90] Its publication *Medications in Recovery* suggests an approach to phasing and layering treatment which includes the following steps:[90]

- engagement and stabilisation;
- preparation for change;
- active change;
- completion.

1.8.4. Overview of the interventions for the screening, identification and management of drug harms in the target settings

The different target organisations (treatment settings) of the NEPTUNE guidance have different roles in the detection, identification and management of chronic harms and/or dependence resulting from the use of club drugs. This is determined by the competence of clinicians to deliver substance misuse treatment and particular pharmacological or psychosocial and recovery interventions.

Table 1.4 provides a summary of the role of each of the target settings and the aims of the interventions provided in terms of the screening, identification, assessment and management of the harms linked to the use of club drugs. Further information on the level of intervention needed is also presented in Chapter 2.

Table 1.4. *The role of particular settings and the aims of interventions provided*

	Detection	Assessment	Brief intervention	Complex intervention (acute)	Complex intervention (chronic)
Primary care	✓	✓	✓	✗	✗
Emergency department	✓	✓	✓	✓	✗
Sexual health	✓	✓	✓	✗	✗
Substance misuse treatment	✓	✓	✓	✗✓	✓

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