

The Novel Psychoactive Substances in the UK Project: empirical and conceptual review work to produce research recommendations

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Steve Parrott and Jim McCambridge*



***National Institute for
Health Research***

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Abstract

The Novel Psychoactive Substances in the UK Project: empirical and conceptual review work to produce research recommendations

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Background: Although illegal drug use has largely been declining in the UK over the past decade, this period has witnessed the emergence of a range of novel psychoactive substances (NPS) ('legal highs'). These are new, mostly synthetic, substances that mimic the effects of existing drugs). Despite there being many causes for concern in relation to NPS, there has been little prior study of the burden associated with their use in public health terms. Clarity is lacking on research priorities in this rapidly developing literature.

Objectives: To inform the development of public health intervention research on NPS by reviewing existing data on their use, associated problems and potential responses to such problems.

Design: A scoping review and narrative synthesis of selected bodies of evidence was undertaken to summarise and evaluate what is known about NPS use and the related harms of, and responses to, such use. Relevant literature was identified from electronic databases (covering January 2006 to June 2016 inclusive), Google (Google Inc., Mountain View, CA, USA), relevant websites and online drug forums and by contacting experts. Articles were included if they were primary studies, secondary studies involving the analysis and interpretation of primary research or discussion papers. A conceptual framework postulating an evidence-informed public health approach to NPS use in the UK was developed through a pragmatic literature review, the iterative development of concepts and finalisation in light of the results from the empirical review work. The process also involved feedback from various stakeholders. Research recommendations were developed from both strands of work.

Results: A total of 995 articles were included in the scoping review, the majority of which related to individual-level health-related adverse effects attributable to NPS use. The prevalence of lifetime NPS use varied widely between (e.g. with higher prevalence in young males) and within population subgroups. The most commonly reported adverse effects were psychiatric/other neurological, cardiovascular, renal and gastrointestinal manifestations, and there is limited evidence available on responses. In these and other respects, available evidence is at an early stage of development. Initial evidence challenges the view that NPS should be treated differently from other illicit drugs. The conceptual framework indicated that much of the evidence that would be useful to inform public health responses does not yet exist. We propose a systems-based prevention approach that develops existing responses, is multilevel and life course informed in character, and emphasises commonalities between NPS and other legal and illegal drug use. We make 20 recommendations for research, including nine key recommendations.

Limitations: Scoping reviews do not interrogate evidence in depth, and the disjunction between the scoping review and the conceptual framework findings is worthy of careful attention.

Conclusions: Key research recommendations build on those that have previously been made and offer more evidence-based justification and detail, as previous recommendations have not yet been acted on. The case for decision-making on commissioning new research based on these recommendations is both strong and urgent.

Future work: The validity of recommendations generated through this project could be enhanced via further work with research commissioners, policy-makers, researchers and the public.

Study registration: The systematic review element of this study is registered as PROSPERO CRD42016026415.

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List of abbreviations

A&E	accident and emergency	MDMA	3,4-methylenedioxyamphetamine (ecstasy)
ACMD	Advisory Council on the Misuse of Drugs	MDPV	methylenedioxypropylvalerone
AIPS	All Ireland Prevalence Survey	MSM	men who have sex with men
BZP	benzylpiperazine	NBOMe	<i>N</i> -methoxybenzyl
CSEW	Crime Survey for England and Wales	NEPTUNE	Novel Psychoactive Treatment: UK network
ED	emergency department	NPS	novel psychoactive substance
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction	PI	public involvement
EWS	early warning system	QALY	quality-adjusted life-year
GBL	gamma-butyrolactone	RCT	randomised controlled trial
GHB	gamma-hydroxybutyrate	SALSUS	Scottish Schools Adolescent Lifestyle and Substance Use Survey
HIV	human immunodeficiency virus	SCJS	Scottish Crime and Justice Survey
HSCIC	Health and Social Care Information Centre	TCDO	Temporary Class Drug Order

Plain English summary

What was the question?

Novel psychoactive substances (NPS) are new drugs, sometimes referred to as legal highs, that have recently received a lot of attention in the media and from governments across the world. We aimed to look at research on (1) what is known about who uses NPS, (2) what problems they experience and (3) what might be the best ways to reduce these problems. We also aimed to offer advice on what new research studies might be undertaken to better understand NPS in ways that help to improve the health of the public.

What did we do?

Before looking at any studies, we developed ideas about what research might be useful to help understand a new problem such as this. We then looked at what studies have already been undertaken on NPS. To advise on what new research was needed, we tried to find gaps between research that has already been done and what we thought still needed to be done. We also recorded and used what researchers in this area had previously recommended.

What did we find?

We found that there are many gaps in knowledge and that available research is at an early stage in understanding NPS. Reported side effects of using NPS include mental health, heart, liver and stomach problems. We made a number of recommendations on what new research we think should be done, and which of these research avenues we thought was most important.

What does this mean?

Much remains to be known about NPS. We suggest that there is no justified reason for investigating NPS in isolation from other illicit drugs. We have presented some options for what new research could be undertaken in the future. We hope that this will help experts on NPS to decide together what research would be most helpful to reduce harms for people who already use NPS, those who might be affected by NPS and those who might use NPS in the future, in the interests of better health across society as a whole.

Scientific summary

Background

The Advisory Council on the Misuse of Drugs (ACMD) defined novel psychoactive substances (NPS) as 'psychoactive drugs which are not prohibited by the United Nations Single Convention on Narcotic Drugs or by the Misuse of Drugs Act 1971, and which people in the UK are seeking for intoxicant use' [Advisory Council on Misuse of Drugs. *Consideration of the Novel Psychoactive Substances ('legal highs')*. London: ACMD; 2011]. There are a number of grounds for concern in relation to NPS use, including technological advances that outstrip legal controls, cheap availability through the internet as well as from traditional drug dealers, high levels of cultural acceptability of NPS use in the UK by international standards and a large degree of uncertainty about the identity of individual substances purchased online and on the streets. Even when a new substance is clearly and accurately identified, there may be very little information on its effects, the risks posed by its use and how these may be reduced. There are systems in place to monitor the emergence of new drugs nationally and internationally. The key UK policy development has been the implementation of the Psychoactive Substances Act (Great Britain. *Psychoactive Substances Act 2016*. London: The Stationery Office; 2016) in the spring of 2016. Although the research literature is developing rapidly, it is unclear how far the NPS phenomenon has been considered in explicitly public health terms and, therefore, the extent to which existing evidence is able to inform public health responses is also unclear.

Objectives

Three specific objectives of the Novel Psychoactive Substances in the UK (NPS-UK) project were to:

1. summarise and evaluate what is known about NPS use and related harms and responses
2. develop a dedicated conceptual framework for a public health approach to NPS use
3. make recommendations on key evidence gaps and priorities for future research.

Methods

The project comprised two main study components: a review of existing research (objective 1) and the development of a conceptual framework (objective 2). The conceptual framework was developed in part to assist with the narrative synthesis of the data from the empirical review. It was then used for the construction of a robust assessment of key evidence gaps and research priorities, and an articulation of the key issues facing public health intervention research (objective 3).

Evidence synthesis

The following electronic databases were searched between 1 January 2006 and 29 June 2016 inclusive: MEDLINE, EMBASE, PsycINFO and Science Citation Index. Searches for grey literature included a Google (Google Inc., Mountain View, CA, USA) search for 'novel psychoactive substances', 'new psychoactive substances' and 'legal highs'; hand searching of relevant UK and US websites; and contacting experts. Primary studies, secondary studies involving the analysis and interpretation of primary research, and discussion papers with data on NPS use, problems or responses that were published in English were included.

We conducted a scoping review of all relevant material to map the available evidence. We used these data to conduct an evidence gap analysis based on a set of a priori research questions. The literature as a whole was judged to be at such an early stage of development that the benefits of conducting detailed

risk-of-bias assessments were not justified. The evidence gap analysis informed decision-making on the selection of bodies of evidence for narrative synthesis. The four selected areas were those pragmatically judged to be the most promising for syntheses (e.g. in terms of UK relevance and sufficient depth of data) that would support the development of research recommendations.

Conceptual framework development

This work was done iteratively in two main stages. We began by examining the nature of contemporary evidence-informed public health and possible similarities between NPS and other complex multisectoral public health challenges, such as public mental health, climate change and obesity, as well as tobacco, alcohol and illicit drug use. We then developed a preliminary hypothetical public health approach to NPS. We identified possible research data needs to complete the first stage of this work. We then utilised this first stage research to interpret the data from the empirical review. Following the completion of the review work, we updated the conceptual framework in light of the empirical data in stage 2. Because of the early stage of development of the empirical literature, we made few substantive changes to the conceptual framework and exercised caution in using it as a basis for research recommendations.

Research recommendations and public involvement

Research recommendations were developed from two distinct data sources. First, research recommendations made by authors of primary studies in the existing literature selected for narrative synthesis were thematically coded. Second, we used the conceptual framework (developed prior to the review work and informed by wider public health sources of evidence) developed by the authors to identify what may be missing from this literature. Data from these two sources were then combined. Both earlier parts of the process and the research recommendations themselves were discussed in public engagement work involving policy-makers, researchers and NPS users and user carers as stakeholders to inform the study design and processes, interpret the findings and validate the study recommendations.

Results

Scoping review

A total of 995 studies met the inclusion criteria. We mapped, and made extensive use of, cross-tabulation to characterise the literature according to a set of analytic categories developed a priori. We also assessed evidence gaps in the literature according to a priori research questions to prioritise those research areas that should be synthesised in more detail. We found few data on social and other risk factors, population-level risk factors, harms associated with long-term NPS use, the provision and effectiveness of prevention interventions, and treatment outcomes for NPS users. We undertook more detailed narrative syntheses on surveys on the prevalence and patterns of NPS use in the UK, on UK qualitative studies on the patterns and harms associated with NPS use, on systematic reviews (largely comprising data on harms associated with NPS use) and on evaluations of policy responses to NPS use.

Narrative synthesis

UK survey data

We identified 29 studies. The most robust nationally representative data were for mephedrone (the Crime Survey for England and Wales and the Scottish Crime and Justice Survey have been conducting national surveys since 2010–11). Lifetime mephedrone use is uncommon in adults (approximately 1–2%) but is about two to three times more prevalent in men than in women and in younger adults than in older adults. Prevalence rates of recent mephedrone use are declining substantially. Nationally representative data on NPS use as a whole and on use of particular NPS other than mephedrone are less developed, and comparisons across years are not yet possible. Nationally representative surveys of school children have found a similarly low prevalence for mephedrone and other NPS use as a whole. Data on particular sentinel populations that are likely to be at greater risk of NPS use are growing, although they remain quite limited. The key contributions are the collation of existing UK survey data from multiple sources on

multiple substances, and drawing attention to the diversity of prevalence rates and issues in interpreting reported findings.

Systematic reviews

Systematic reviews ($n = 10$) mainly comprise summaries of clinical presentation data. Side effects of NPS were wide ranging, with psychiatric, cardiovascular, renal and gastrointestinal symptoms being the most commonly reported. Treatment of these effects appears mostly to involve observation and supportive care and in severe cases may require hospitalisation. We did not find population-level data on acute health harms with dedicated attention to prevalence and policy issues, or data on chronic health or social harms in a longitudinal context.

Qualitative studies of novel psychoactive substance use in the UK

Qualitative studies on NPS use in the UK ($n = 7$) are at an early stage of development. Existing studies have the potential to provide useful information on issues such as drug effects and reasons for, and patterns of, use. Qualitative studies may make useful contributions to behavioural epidemiological studies and to studies of drug market functioning and policy issues.

Responses to novel psychoactive substance use and problems/harms

Quantitative studies ($n = 17$) evaluated the effects of legislative prohibitions of NPS use or supply on a number of outcomes including access, use, health-care use and self-reported exposure and toxicity. Reductions in use, presentations or other outcomes were generally observed, although not always. Studies typically utilised simple counts of routinely collected data, particularly poison centre and hospital admissions data. Study designs were mainly before-and-after comparisons, without controls, which limits the basis for attribution of effects. Further examination of the utility of routinely collected NPS data in different settings is needed to assess sources of information bias and to evaluate pharmacovigilance and other data.

Conceptual framework

Stage 1

Our conceptual framework seeks to build on concepts and approaches developed for drug use in general, as well as on evidence-informed responses to other public health challenges, which may be viewed as having similar features. Many contemporary public health challenges (such as the health effects of climate change or obesity) are commonly conceptualised as requiring complex adaptive system changes that differ throughout the life course. NPS may also be regarded in this way.

We provide a conceptual map of key individual-level risks and harms attributable to NPS adapted from those developed for other forms of drug use (*Figure a*). Apart from acute effects, most forms of risk of harm accumulate over time with continuing use. Harms to individuals, whether they are health-specific or wider harms, are strongly shaped by environmental and contextual influences that dynamically interact with life-course stages. Intervention targets for prevention need to extend beyond those proximal to acts of drug use and include those within the social structural influences that shape individual risk. Other drug use, both licit and illicit, is expected to be implicated in the production of harm where other drugs are being used (it is rare that other drugs are not used).

Problems also manifest themselves at levels beyond the individual user, for example involving family members and local communities. Harms to society include the costs of health care, crime and law enforcement. Health impacts incurred by NPS users can be aggregated with measures of physical and/or mental health, or lost quality-adjusted life-years.

Stage 2

The empirical review findings indicated that the existing body of literature, although large, is at an early stage of development, and there are currently few data to inform directly what we hypothesised to be an

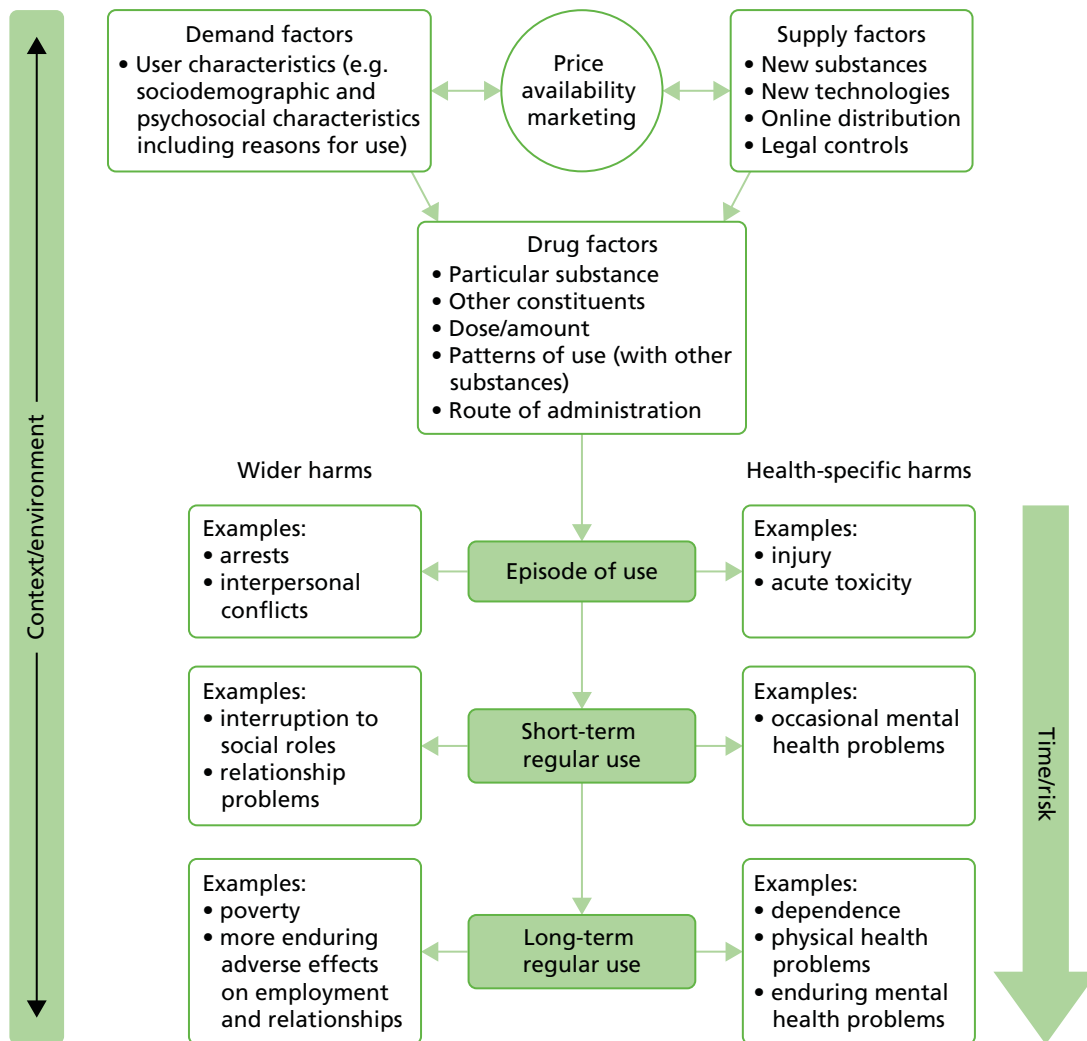


FIGURE a A model of risks and harms attributable to NPS use.

evidence-informed public health strategic response to NPS. The hypothesised need for research to inform public health responses has not yet been met. The conceptual framework itself was thus not significantly altered in stage 2, as we found no reason to make major changes. We took account of the hypothesised nature of our conceptual data in making research recommendations.

Public involvement

Public involvement activities had demonstrable value in validating our study design, findings and research recommendations. The project was successful in engaging with policy-makers and researchers at different stages of the research process. However, we were less successful with NPS user involvement, in part because the short-term nature of the project offered restricted scope for investment in building relationships with NPS users over time.

Conclusions

There are 20 research recommendations presented as the principal conclusions of this study, of which there are nine key recommendations as follows.

Pharmacology-related research

1. Evaluate the effectiveness and sustainability of the existing pharmacovigilance system for NPS and the effects of planned innovations.
2. Evaluate the pharmacological, toxicological and related scientific base needed to inform the pharmacovigilance and public health surveillance systems.

Epidemiology and related research

3. Evaluate the effectiveness and sustainability of the existing public health surveillance system for monitoring NPS markets and other new online drug trends. This evaluation should cover monitoring actions, both quantitative and qualitative research, and associated commissioning arrangements, and be cognisant of opportunities for innovations such as test-purchasing new brands online as they become available.
4. Develop the behavioural epidemiology and related science of patterns and correlates of NPS use and problems in the context of alcohol, tobacco and other drug involvements.
5. Use cohort study designs to better understand the determinants of NPS use and related physical health, mental health and psychosocial problems, and how patterns of involvement and consequences change over time.

Interventions

6. Develop the science of prevention of NPS and other drug use. This should include the evaluation of existing interventions and the development and evaluation of novel interventions addressing both proximal and distal determinants of NPS and related drug use, and how risks should be communicated to different groups.
7. Evaluate the public health impacts of legislative prohibitions of NPS use or supply, and other major policy initiatives.

Recommendations for research commissioners

8. Consider using the research recommendations presented here as a possible basis for conducting a formal research priority-setting exercise using consensus development methods (such as those developed by the James Lind Alliance).
9. Evaluate existing strategic provision for, and develop as necessary, a long-term planning system for research on NPS and other drug use.

Study registration

The systematic review element of this study is registered as PROSPERO CRD42016026415.

Funding

Funding for this study was provided by the Public Health Research programme of the National Institute for Health Research.

Chapter 1 Introduction and background

This report presents the findings from a National Institute for Health Research (NIHR) Public Health Research (PHR)-funded programme of work to inform the development of public health intervention research on novel psychoactive substances (NPS) through systematically reviewing existing data on their use in the UK and the problems associated with, and the potential responses to, such use.

This chapter provides the background and rationale for conducting this research and describes the research objectives. This chapter also provides content as it existed at the outset of this research (i.e. prior to the implementation of the Psychoactive Substances Act in 2016).¹ The remainder of the report is divided into the following chapters, which represent the phases of the study:

- *Chapter 2* – scoping review with a narrative synthesis of selected bodies of evidence on what is known about NPS use and the related harms of, and responses to, such use
- *Chapter 3* – what might an evidence-informed public health approach to NPS use in the UK look like? A conceptual framework
- *Chapter 4* – public involvement (PI)
- *Chapter 5* – research recommendations.

Background

Although illegal drug use has largely been declining in the UK over the past decade,² this period has witnessed the emergence of a range of new, mostly synthetic, substances that mimic many of the effects of 'traditional' drugs. These are known as 'legal highs', new psychoactive substances or NPS. The new/novel psychoactive substances description refers to the fact that use of the substance(s) in question has not been specifically prohibited. The Advisory Council on the Misuse of Drugs (ACMD), the expert body that advises the government on drug policy and practice issues, has defined NPS as 'psychoactive drugs which are not prohibited by the United Nations Single Convention on Narcotic Drugs or by the Misuse of Drugs Act 1971, and which people in the UK are seeking for intoxicant use'.³

Novel psychoactive substance use causes a number of grounds for concern. First, technological advances mean that supply sources with the capacity for continuous product innovations can be offered, leading to rapid increases in the numbers of different substances available, and, despite speeding up the legal processes in the UK for controlling these substances,⁴ the rapidity of the technological developments outstrips legal controls. Second, they are readily and cheaply available through the internet and 'headshop' outlets as well as from traditional drug dealers (the Psychoactive Substances Act implemented during 2016 has since prohibited headshop supply).^{1,5} Third, by international standards, there are very high levels of cultural acceptability of NPS use in the UK.⁶ Fourth, NPS are perceived to be safe or to pose little risk. Fifth, there are many uncertainties surrounding the identity of individual substances purchased online and on the streets. Even when a new substance is clearly and accurately identified, there may be very little information on its effects, the risks posed by its use and how these risks may be reduced.

Despite such causes for concern, there has been little consideration of the public health burden associated with NPS use, apart from investigations of acute problems presenting to health services and fatalities.⁷⁻¹⁰ In addition, although there has been valuable thinking about the implications for the regulation of drug use,^{5,11} dedicated attention to specifically public health responses has been limited.¹² This project seeks to address these gaps.

UK general population surveys report the past year prevalence of mephedrone use, which has attracted most concern, ranging from 1.1% to 1.8% among those aged ≥ 16 years,^{13,14} with prevalence largely stable in more recent years (up to the end of 2014 when these data were assembled).² However, among

those aged 16–24 years, past year use prevalence has been 3% or higher, which is similar to that of 3,4-methylenedioxymethamphetamine [MDMA (ecstasy)].^{13,14} The most recent national drug survey identified increases in the past year prevalence of nitrous oxide and salvia use, both in the 16–24 years age group and in all adults.² Among the former group, past year prevalence was 7.6%, which is approximately twice that of both ecstasy and powder cocaine.² Moreover, a number of deaths have been associated with mephedrone use, both before and after it became controlled.^{15,16}

The monitoring of the emergence of new drugs through early warning systems (EWSs) and of national policy responses in Europe is undertaken by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA).^{17,18} Very little work has been undertaken, however, on the problems associated with use. In addition, there has been scant research consideration of the nature of the need to develop interventions that target NPS, although initiatives such as the Novel Psychoactive Treatment: UK network (NEPTUNE) project work to improve clinical practice in the management of harms resulting from NPS use.¹⁹ This is despite the strong focus on developing the evidence base to support responses to NPS in the UK Drug Strategy.²⁰ These needs have also been emphasised for some years by the ACMD.³

Rationale

It is currently unclear how much dedicated targeting of the existing generation of NPS is needed, as the existing data suggest that NPS are rarely used by those who are not also involved in other forms of substance use.¹³ Even if the present generation of NPS is not very problematic, and it is very unclear whether or not this is the case, there is a need to develop the capacity for public health NPS responses to new substances that may become problematic in the future. The longer-term strategic need may be to develop the evidence base in such a way as to be able to identify and intervene early with some new drugs that appear likely to be particularly problematic (and, by implication, to identify new drugs that do not seem likely to be problematic), in order to alter the course of possible future epidemics.²¹

There is, therefore, a pressing need to review what is known about NPS use in the UK, and the extent and nature of problems associated with this use, and to consider potential public health responses. There have been no systematic reviews that evaluate what is currently known about NPS use in the UK. Moreover, given the continually changing nature of NPS use and the resulting uncertainty regarding the implications for public health and for the NHS, it is important that strategic research efforts are not confined to the current generation of NPS, but are capable of adapting to new drugs that should be expected to emerge in the coming years.

Research objectives

The overall aim of the NPS-UK project was to inform the development of public health intervention research on NPS use in the UK by systematically reviewing existing data on use, and the associated problems of, and the potential responses to, such use. The three specific objectives were as follows:

1. to summarise and evaluate what is known about NPS use, the related harms of, and responses to, such use by means of a review of peer-reviewed and grey literature
2. to develop a dedicated conceptual framework for a public health approach to NPS use that identifies the scope for interventions based on approaches developed for the use of other legal and illegal drugs, and the concerns of public health and prevention more broadly
3. to produce a statement of public health intervention research issues for NPS use in the UK that makes recommendations on key evidence gaps and priorities for future research.

The project comprised two main study components corresponding to the first two study objectives: (1) a systematic mapping of available evidence and a narrative synthesis of selected bodies of evidence (in relation to objective 1), and (2) the development of a dedicated conceptual framework (in relation to objective 2). We concluded that a full systematic review was inappropriate for the size and nature of the available literature within the scope of this project (see *Chapter 2*). Synergies between the two study components are a key feature of this project. The conceptual framework was elaborated in part to assist with the narrative synthesis of the data from the empirical review work. It was then also used for the construction of a robust assessment of key evidence gaps and research priorities and an articulation of the key issues facing public health intervention research in the form of a series of research recommendations (objective 3).

Chapter 2 Scoping review with a narrative synthesis of selected bodies of evidence on what is known about novel psychoactive substance use, related harms and responses

Background

Novel psychoactive substance use causes a number of grounds for concern, as elaborated in *Chapter 1*. These include technological advances that allow for rapid increases in the numbers of different substances available, in a way that outstrips the coping ability of the legal processes that control these substances,⁴ and easy accessibility via the internet.⁵ There has, however, been little consideration of the public health burden associated with NPS use,⁷⁻¹⁰ or of public health responses to NPS use.¹² It is unclear whether there is need for targeted responses to the existing generation of NPS, or the development of the capacity of public health NPS responses to new substances that may become problematic in the future. To be able to address this evidence gap, there is need to review what is known about NPS use and the extent and nature of problems associated with this use, and to consider potential effective public health responses.

Aim

This scoping review and narrative synthesis aimed to summarise and evaluate what is known about NPS use and related problems/harms and responses in the international peer-reviewed and grey literature. The core purpose of undertaking this study was to inform the development of public health intervention research in the UK.

Research questions

The broad-ranging nature of this review posed significant challenges to the development of detailed research questions that could be answered in relation to the overarching research aim. We thus developed an initial set of research questions a priori that we hypothesised would be useful to the development of public health intervention research. These questions were organised into three preliminary concepts of use, problems and responses. In addition, a small number of more methodological questions were identified. It was intended from the outset that the research questions for this study would be iteratively developed along with the corresponding content of the conceptual framework (see *Chapter 3*). The framework would be used to shape the interpretation of the data included in this study and to guide decision-making about more advanced targets for study. The initial research questions were identified as follows.

Novel psychoactive substance use

1. What are the prevalence and patterns of NPS use in the UK general population and do they differ in particular subgroups of the population?
2. How do existing patterns of both legal and illegal drug use and social and other risk factors influence NPS use?
3. Which other population-level risk factors influence NPS use?

Novel psychoactive substance-related problems/harms

4. Which acute intoxication problems are associated with NPS use?
5. What problems are associated with long-term regular NPS use?
6. In addition to intoxication, long-term regular use and dependence problems, are there other types of NPS-specific problems or other problems associated with NPS use?

Responses

7. Are there dedicated primary or secondary prevention interventions in the UK, and, if so, what is known about their outcomes?
8. Which generic interventions (early in life and early in drug-using careers) target NPS?
9. How extensively does current generic UK drug prevention practice cover NPS?
10. How good are treatment outcomes for NPS?
11. What promising approaches are currently available, or can be made available, in the UK for intervening with NPS use?
12. What are the population-level or social structural factors limiting the effects of individual-level interventions?

Methodological questions

13. What is the nature of the current EWS provision?
14. Are there sentinel populations capable of being monitored to provide early warnings of new trends?
15. What are the issues raised by uncertainties about the identities of substances being used?

In each case, we first endeavoured to examine whether or not data were available to answer these questions, and if the data did not exist or were judged insufficient, we considered the extent to which this constituted an important evidence gap, with an assessment of importance shaped by the conceptual framework detailed in *Chapter 3*.

Review methods

The review was registered with the international prospective register of systematic reviews (PROSPERO registration number CRD42016026415).²² Given that we decided not to conduct a systematic review, we did not use PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guidelines,²³ as many of the criteria were not applicable to our work. Instead, we have endeavoured to provide a detailed and transparent account of the review methods and results that we judged appropriate for this evidence synthesis work.

Literature searches

Relevant literature was identified through performing a range of searches, including electronic database searches, Google (Google Inc., Mountain View, CA, USA) searches, hand searches of websites relating to the UK, identifying relevant online drug forums and contacting experts. Details of these searches are described below.

Electronic database searches

The following electronic databases were searched via the Ovid platform for articles published between 1 January 2006 and 16 November 2015 inclusive: MEDLINE, EMBASE, PsycINFO and Science Citation Index (see *Appendix 1* for the search strategies used in each database). The database searches were updated on 29 June 2016. The search strategies also included trade or brand names of a number of NPS products. These names were selected by perusing the websites of three popular NPS headshops (i.e. globalweekends.co.uk, www.iceheadshop.co.uk and www.legalhighsworld.co.uk) and selecting those that appeared in all three for inclusion (see *Appendix 2*).

Google search for grey literature

A Google search was conducted using the following key phrases: 'novel psychoactive substances', 'new psychoactive substances' and 'legal highs'. The file type was restricted to portable document format (PDF), and the searches were conducted on 17 March 2016.

Hand search of websites relating to the UK and USA

Websites of the following institutions and organisations were hand searched on 13 May 2016 to identify national and international surveys, monitoring systems and EWSs: www.gov.uk (which includes the Department of Health, the Home Office and Public Health England), NHS Evidence, the Office for National Statistics, the National Drug Treatment Monitoring System, the EMCDDA, the Scottish Government, the National Assembly for Wales, Public Health Wales, Welsh Emerging Drugs and Identification of Novel Substances, Information Services Division Scotland, the Department of Health Northern Ireland, the Centres for Disease Control and Prevention, the National Institute on Drug Abuse, and the Substance Abuse and Mental Health Services Administration.

Search for relevant online drug forums

Relevant online drug forums were identified from published literature as well as by contacting experts in the field.

Contacting experts

Calls for information were sent to Public Health England and forwarded to the NPS Clinical Network Working Group and NEPTUNE. Nineteen researchers were also contacted for any unpublished relevant literature or literature not identified by the searches.

Inclusion/exclusion criteria

Type of article

Articles were included if they were primary studies (i.e. involving the collection of original primary data through directly measuring the outcome of interest within the relevant population), secondary studies involving the analysis and interpretation of primary research, or discussion papers. Commentaries and letters were included only if they presented new primary or secondary data. Non-English-language publications were excluded.

Condition or domain being studied or discussed

Articles were included if they related to NPS use, problems and responses.

Participants/population

Articles were included if they reported on humans. No other limits were set on the population.

Response(s), exposure(s)

The exposure of interest was NPS use, and we were interested in any associated problems. Any intervention or response aimed at addressing NPS use and related problems was eligible and we were particularly interested in population-level data.

Comparator(s)/control

Not applicable.

Context

There were no restrictions on context or location.

Primary outcomes

The primary outcomes were the prevalence of NPS use, prevalence of problems associated with NPS use and responses to NPS use.

Secondary outcomes

None.

Article selection

The screening of titles and abstracts and the selection of articles from retrieved potentially relevant full manuscripts were conducted by two reviewers (NM and NDM) using the selection criteria described above. The reviewers independently classified the articles as 'include', 'unclear' or 'exclude', with discrepancies being resolved by discussion or referral to a third reviewer (JM). Full manuscripts that did not fulfil all of the criteria were excluded, with reasons for their exclusion documented.

Data extraction

Data extraction was performed using EPPI-Reviewer 4 software (EPPI-Centre, Social Science Research Unit, Institute of Education, University of London, London, UK). The data extraction form was designed by two researchers (NM and NDM), piloted on a small selection of articles and adjusted as necessary. The following data were extracted:

- include/exclude decision, with reasons for exclusion where applicable
- general characteristics for included studies – author, year, location, setting, study design, publication type
- population characteristics – age, sex, ethnicity, sample size, NPS use status
- NPS type – principal focus (use, problems, responses)
- research recommendations in the case of reviews, systematic reviews, qualitative studies, surveys and articles on responses.

Data from each article were extracted by one researcher and checked by another, with discrepancies being resolved by consensus or recourse to a third researcher if necessary. Where necessary, authors were contacted for missing or unclear data.

Definitions

This section focuses on key definitions of categories used in this study.

Principal focus

The following definitions were used for use, problems and responses:

- use – any use of a NPS
- problems – any acute or chronic health-specific, social or wider harm attributable to NPS use, experienced by the user or others
- responses – any intervention at policy, health or other service, or clinical levels, aimed at addressing NPS use and/or related problems.

Study designs

For study designs, a distinction had to be made between generic literature reviews and systematic reviews. To be included as a systematic review, a paper had to meet the following criteria:

- search of at least two electronic databases, or one electronic database and reference checking of included studies or some other source of obtaining further studies
- explicitly stated inclusion/exclusion criteria
- list of included studies
- risk-of-bias assessment of included studies conducted by authors or sufficiently reported study characteristics of included studies that would enable others to make judgements on the risk of bias of individual studies
- narrative or quantitative synthesis of data from included studies.

Any review that did not meet these criteria was classified as a literature review.

Risk-of-bias (quality) assessment

No risk-of-bias assessment was conducted.

Strategy for data synthesis

The framework for data synthesis was the conceptual framework specifically designed for use in data analysis and interpretation for the current scoping review and narrative synthesis, to which the research questions listed above contribute. Data synthesis was undertaken in three stages: (1) evidence mapping, (2) identification of evidence gaps and (3) a narrative synthesis of selected research areas.

Evidence map

For reviews addressing complex topic areas, evidence mapping is a well-established tool by which to explore relevant literature before progressing to more advanced research design decision-making.²⁴ The extracted data were utilised by one researcher to map the literature according to the principal focus (use, problems/harms or responses), NPS type, study design, region, setting, year of publication and publication type. This was checked by another researcher. The aim of the map was to provide a comprehensive but concise descriptive map of the nature and breadth of research on NPS, and to identify obvious research gaps.

The evidence map also included the analysis of the following subgroups:

- number of records by year of publication and principal focus (use, problems/harms, responses), NPS type, study design and publication type
- number of studies by geographic region
- percentage of records by NPS type and publication type, study design, geographic region and setting.

Identification and evaluation of evidence gaps

After the mapping, the research questions listed above were then used to identify and evaluate evidence gaps, and to make decisions about narrative syntheses. In addition, the conceptual framework (see *Chapter 3*) guided our evaluation of what was missing from the literature.

This process, based on the evidence map, facilitated discussions about categories of evidence where it was feasible to conduct narrative syntheses (in consultation with the project steering group). We initially considered whether or not it would be possible to restrict the inclusion criteria to a small number of narrowly focused research questions for the purposes of conducting a full systematic review (i.e. including a detailed risk-of-bias assessment).

However, in discussion with the project steering group, we concluded that, given the early stage of development for all areas of the literature, this would not be the best use of the time and resources of the project. Therefore, we developed broader inclusion criteria that enabled us to conduct narrative syntheses where there was judged to be a sufficient evidence base.

The steering group supported this decision. We were also necessarily pragmatic in our decision-making, addressing questions of primary relevance to the UK as the data allowed, in ways that were manageable within the time and resources allocated to the project, and bearing in mind the large volume of literature included in the scoping review and the short duration of the project (14 months).

Narrative synthesis

In addition to the evidence map and evidence gap analysis, a narrative descriptive synthesis was conducted for the following categories of articles and data:

- systematic reviews
- UK survey data on NPS use
- UK-based qualitative studies
- articles on responses, including policy evaluation studies and studies of individual-level interventions.

Changes to the review protocol

This review was originally designed as a systematic review of what is known about NPS use, related problems and responses from a public health perspective (PROSPERO registration number CRD42016026415).²² However, after the identification of 995 eligible studies and the mapping of these, it was decided that all areas represented by this literature that were not already adequately covered by systematic reviews were not sufficiently mature in terms of study numbers and quality to warrant a full systematic review. A decision was then made on this basis to conduct narrative syntheses in the areas indicated above, in addition to updating the evidence map up to the end of June 2016 (with a view to complete the project at the end of October 2016). This decision was influenced by the time available for this project and was discussed and approved by the project steering group committee as the best way to proceed.

Results

Evidence map

Literature searches

A total of 13,772 records were identified through electronic databases searches. A further 3260 were obtained through other sources, including contacting key researchers and policy experts (Figure 1). Of the 19 key researchers contacted, six responded, with four providing further records of published literature and one stating that the full results of one study had not yet been published. Policy experts provided four

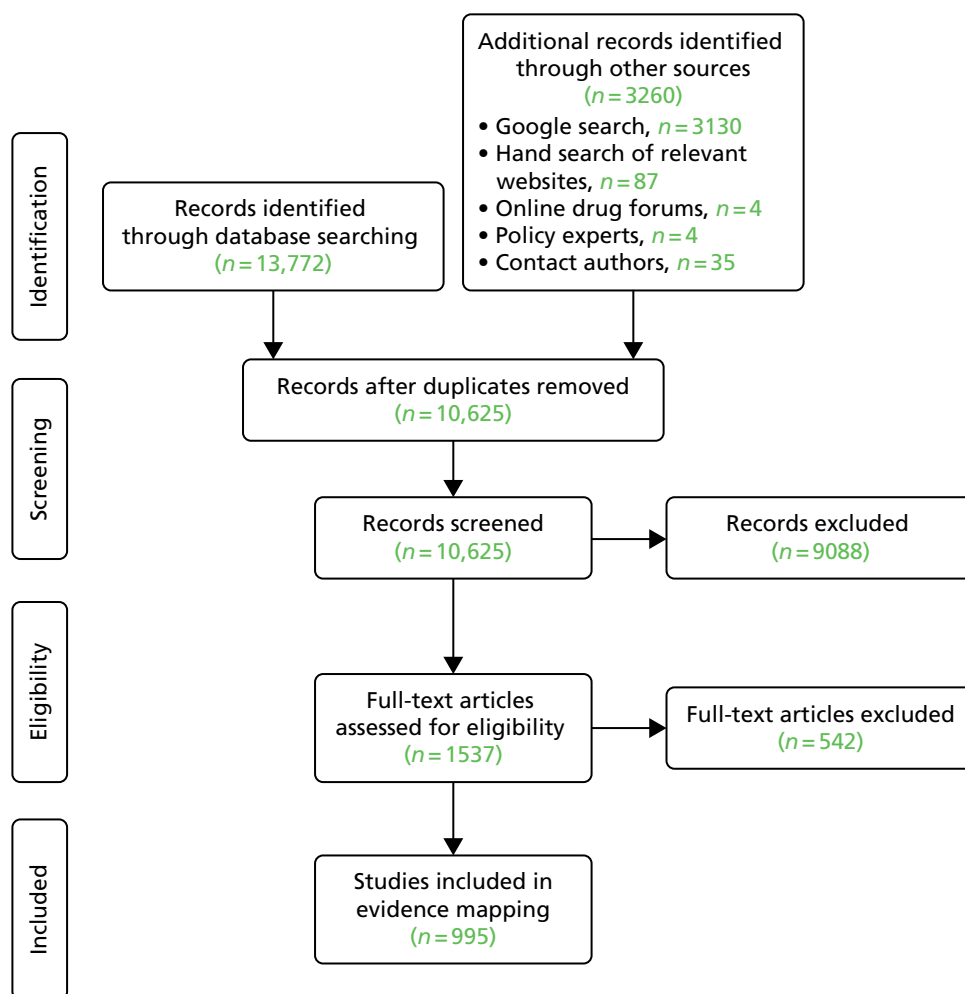


FIGURE 1 Flow of articles for the evidence mapping.

further records. A total of 995 articles were eligible for inclusion in the review after removing duplicates and screening titles, abstracts and, where necessary, full texts.^{3,5,7,10,11,15,16,25–1008}

Of the 542 records excluded after reviewing the full texts, the main reasons for exclusion were not being specific to NPS (e.g. recreational drug use, club drug use, substance use/abuse, psychoactive substance use without presenting data on NPS use separately) ($n = 211$); being on drugs that are not included as NPS in the review [e.g. specific to illicit drug use, alcohol, tobacco, ketamine, khat, gamma-hydroxybutyrate (GHB) or gamma-butyrolactone (GBL)] ($n = 107$); being on the detection, identification and quantification of NPS, including methods validation ($n = 69$); being comments, editorials or letters to an editor within new primary or secondary data ($n = 65$); or being in a language other than English ($n = 56$). Most of the remaining 34 records were either Acts, regulations or drug schedules, or descriptions of surveillance and pharmacovigilance systems.

Characteristics of included articles

General characteristics of the 995 included articles in terms of the principal focus, setting, NPS type, study design and publication type are briefly summarised in *Table 1*. The majority of articles reported on problems or harms attributable to the use of NPS. Many of the articles focused on multiple issues, as represented in *Figure 2*. Synthetic cannabinoids and synthetic cathinones were the NPS that were most reported on, with case report/series being the most popular study design, followed by non-systematic literature reviews. Most articles reported on general hospital settings, followed by specialist settings. Within hospital settings, most articles were for emergency departments (EDs) ($n = 236$ reports), while within specialist settings, most articles were for poison centres ($n = 65$ reports). A total of 252 of the included reports were not specific to a particular setting.

TABLE 1 General characteristics of included articles

Characteristics	Distribution (n)
Principal focus	
Use	385
Problems/harms	773
Responses	148
NPS type	
All NPS	259
Synthetic cannabinoids	310
Synthetic cathinones	271
Phenethylamines	69
Piperazines	29
Other	114
Setting	
Specialist settings (addiction treatment, psychiatric treatment, forensic and rehabilitation, poison centres, needle exchanges, other similar settings)	134
General hospital (inpatient, A&E/ED, outpatient settings)	294
Primary care setting	3
Educational setting (school, higher educational institutions such as university/college)	32
Criminal justice	9

continued

TABLE 1 General characteristics of included articles (*continued*)

Characteristics	Distribution (<i>n</i>)
Police	27
Defence forces (Air Force, Army, Navy)	9
Community setting	64
Home	27
Club/disco/dance scene	14
Internet	59
Data registry	13
EWSs	9
Research setting	22
Other	21
Not applicable	252
Not reported	24
Study design	
Systematic review	10
Literature review	243
RCT	13
Survey	130
Laboratory sample analysis	58
Secondary quantitative data analysis	99
Prospective cohort studies	6
Case-control	1
Qualitative study	47
Case series/reports	367
Other	64
Publication type	
Peer-reviewed journal article	654
Peer-reviewed report	1
Non-peer-reviewed article/report	119
Conference abstracts	205
Book	4
Dissertation	1
Online discussion forum	4
A&E, accident and emergency; ED, emergency department; RCT, randomised controlled trial.	

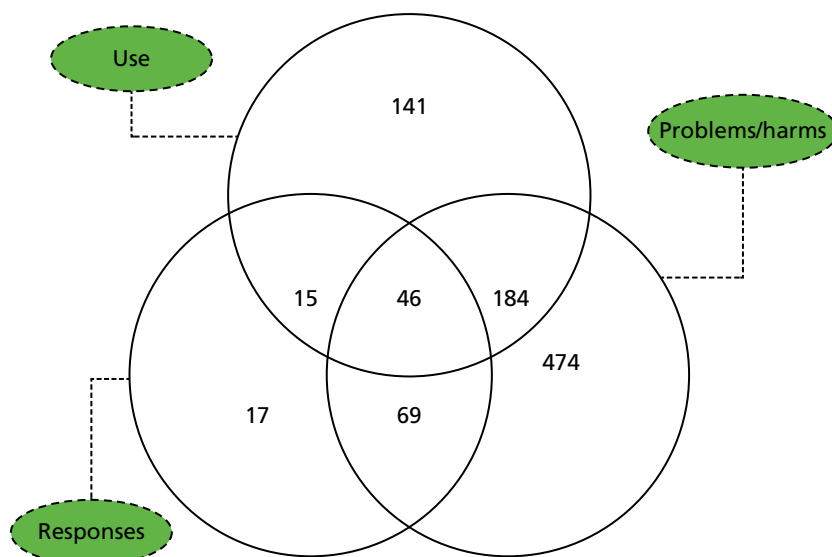


FIGURE 2 Principal focus.

Most of the categories above are not mutually exclusive. For example, some articles use multiple study designs. Another example is presented in *Figure 2* for principal focus.

Principal focus

The majority of reports were on problems/harms to individual NPS users. It is, however, important to note that many articles had more than one focus, as demonstrated in *Figure 2*.

Use

Of the 385 reports on NPS use, 117 presented survey data. The remaining 268 articles presenting NPS use data were case reports/series ($n = 20$); laboratory sample analyses ($n = 39$); qualitative studies ($n = 39$); randomised controlled trials (RCTs) ($n = 1$); reviews ($n = 124$); secondary qualitative data analyses ($n = 49$); systematic reviews ($n = 1$); prospective cohort studies ($n = 2$),^{215,976} or other designs ($n = 21$).

The 117 NPS use articles based on survey data comprise 13 national surveys and 104 surveys of subpopulations or convenience samples. Of the 13 national surveys, seven were conducted among adults, of which three were conducted in the UK, two in the USA, and one each in Canada and New Zealand. Two were conducted among young people (one covering Europe and the other covering Poland), and four were in schools (two in the UK, and one each in the USA and Romania). In terms of NPS type, of the 117 surveys presenting NPS use data, 54 provided data on all NPS, 28 provided data on synthetic cathinones, 25 provided data on synthetic cannabinoids, 4 provided data on piperazines, 1 provided data on phenethylamines and 19 provided data on other NPS.

UK survey data are presented in detail below (see *UK survey data*).

Problems

The 773 articles on problems attributable to NPS comprised at least 566 primary studies or secondary quantitative data analysis and 211 evidence syntheses; among these, four included both a primary study and evidence synthesis (*Table 2*).

Of the 10 systematic reviews, one was on all NPS, five were on synthetic cannabinoids, two were on synthetic cathinones and two were on phenethylamines. More details of these 10 systematic reviews are provided within the narrative synthesis results section (see *Systematic reviews*).

TABLE 2 Study design of reports on problems/harms attributable to NPS

Study design	Frequency
Primary studies and secondary quantitative data analyses (N = 566)	
RCTs	12
Surveys	44
Prospective cohort studies	4
Case-control	1
Secondary quantitative data analyses	78
Laboratory analysis	27
Qualitative studies	33
Case reports/series	367
Evidence syntheses (N = 211)	
Systematic reviews	10
Reviews	201

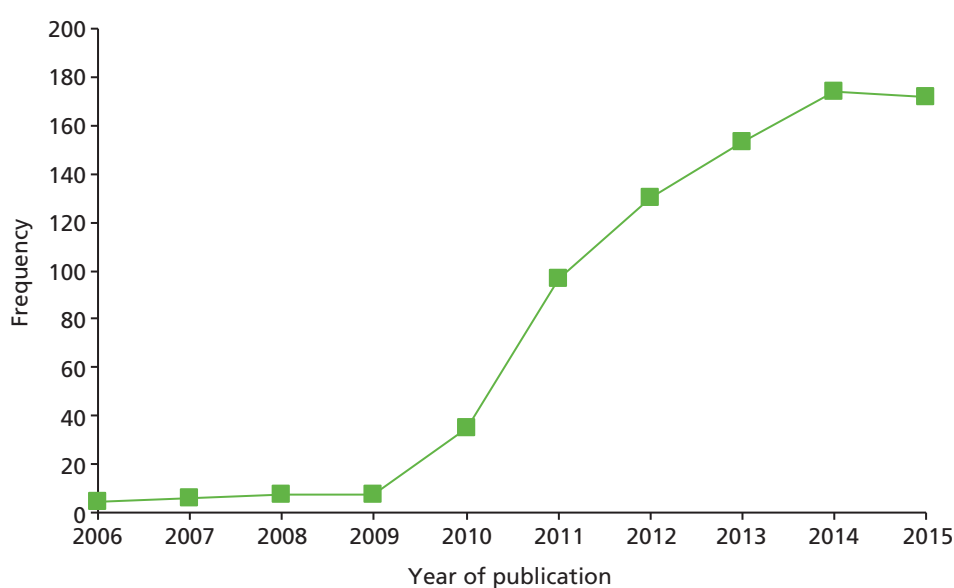
Responses

Of the 148 reports on responses to NPS use, 17 were quantitative policy evaluation reports mainly evaluating legislative policy responses utilising before-and-after comparisons. Six reports were qualitative studies of legislative policy responses, 84 were policy discussion papers, 34 reports were on the clinical management of NPS users, 13 were on interventions to increase awareness and understanding of NPS among clinicians and members of the public and 5 were on harm reduction. Two reports were quantitative surveys of opinions on policy responses and another two classified under 'other' were on forensic science and research responses.

The quantitative policy evaluation studies are presented in more detail below (see *Responses to novel psychoactive substance use and problems/harms*).

Year of publication

The number of records by year of publication is shown in *Figure 3*.

**FIGURE 3** Number of records by year of publication for 2006–15.

There has been a year-on-year increase in the number of publications on NPS between 2009 and 2014. Although there is a slight dip in 2015, this may reflect the fact that, at the time of searching, not all studies published in 2015 had yet been added to the bibliographic databases. Therefore, we cannot yet confirm whether or not this trend continued into 2015. This general trend is also observed for principal focus (Figure 4), for NPS type, except for synthetic cathinones and piperazines (Figure 5), and for peer-reviewed journal articles and non-peer-reviewed journal articles and reports (Figure 6). Our search also identified 198 records from 2016 and nine records that did not have a publication date.

There were 85 records on use, 143 on problems/harms and 26 on responses also identified from 2016, and six records on use, eight on problems/harms and two on responses that did not have a publication year.

Of the records identified for 2016 (up to 29 June 2016), 71 were for synthetic cannabinoids, 34 were for synthetic cathinones, 6 each were for phenethylamines and piperazines, 24 were for other NPS and 72 were on all NPS. Of the nine records with no publication year, one was on synthetic cathinones, one was on other NPS and seven were on all NPS types.

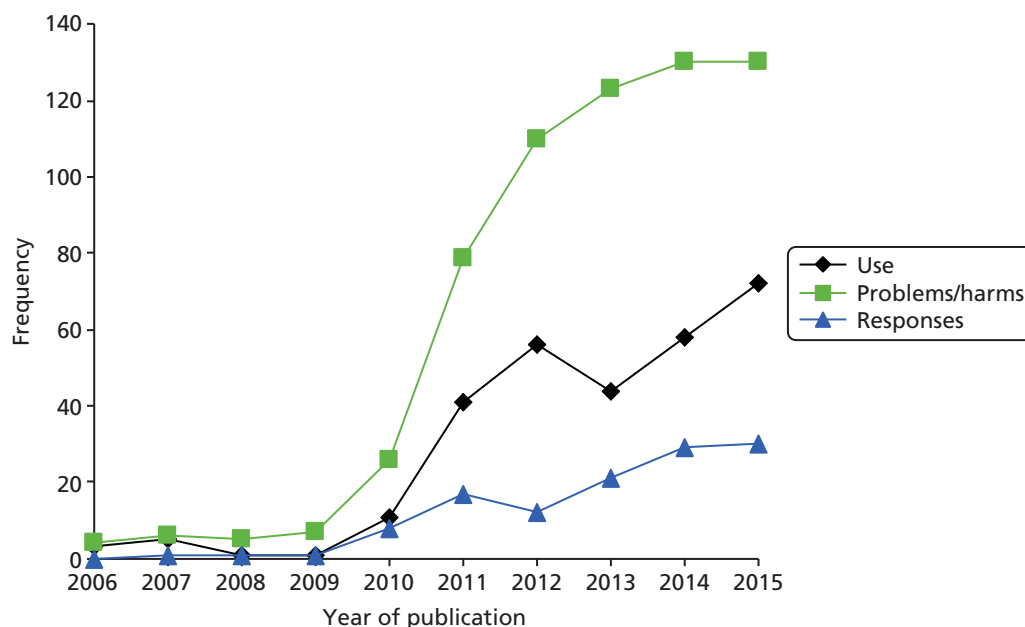


FIGURE 4 Number of records by year of publication and principal focus for 2006–15.

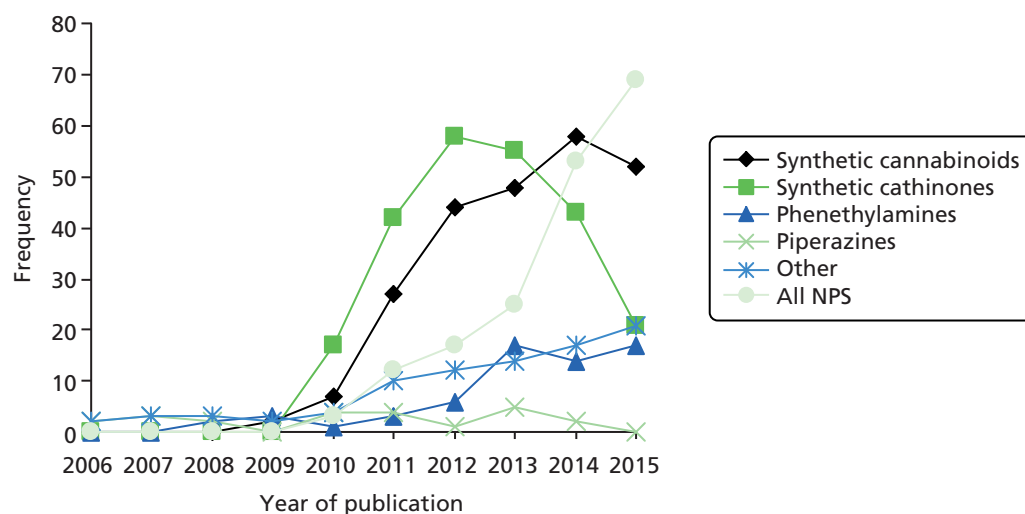


FIGURE 5 Number of records by year of publication and NPS type for 2006–15.

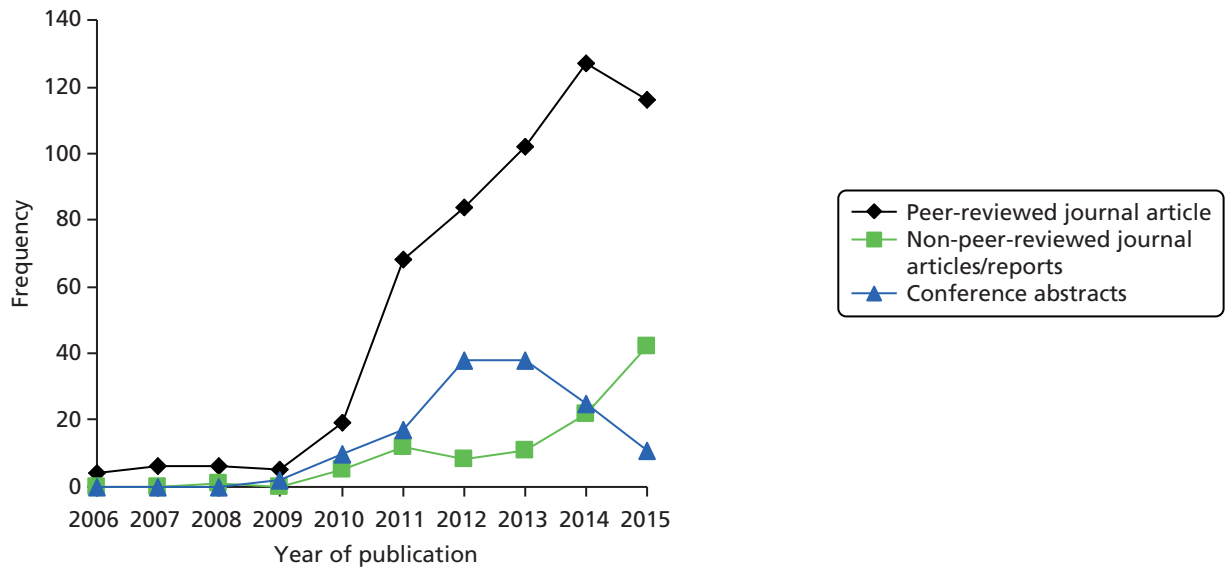


FIGURE 6 Number of records by year of publication and publication type for 2006–15.

For 2016, 114 peer-reviewed journal articles, 13 non-peer-reviewed journal articles/reports and 63 conference abstracts were identified. Peer-reviewed reports, books, dissertations and online discussion forums have not been included in the graph as the numbers are too low.

Figure 7 shows the number of records by year of publication and study design. The general trend for case reports/series, reviews, systematic reviews, surveys and qualitative studies was an increase up to 2013/14 and then a decrease. However, there is a general increase in the number of qualitative studies, RCTs and other research designs. The nine records with no publication year include qualitative studies (two records),

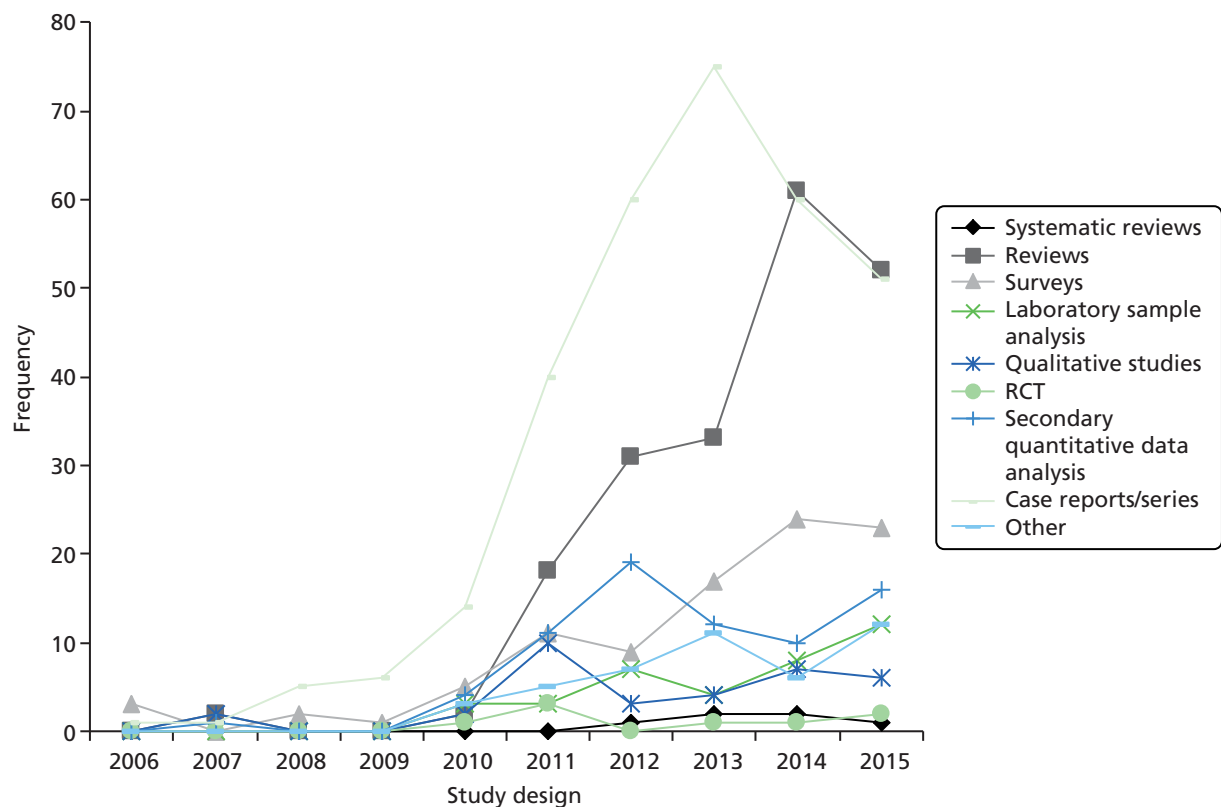


FIGURE 7 Number of records by year of publication and study design for 2006–15.

reviews (two records), a survey, a case report and four records in the 'other' category. There was also a prospective cohort study for both 2013 and 2015, and a case-control study in 2015. Of the identified 2016 records, 2 were systematic reviews, 40 were reviews, 34 were surveys, 53 were case reports/series, 20 were laboratory sample analyses, 12 were qualitative studies, 5 were RCTs, 26 were secondary qualitative data analyses and 4 were prospective cohort studies. A total of 15 fell into the 'other' category and there were no case-control studies identified for 2016.

Geographical location

Table 3 shows the number of articles included by geographic region where the study was conducted. A total of 19 of the 185 articles reporting on the UK also reported on at least one other country in Europe (this figure is also included in the 200 under the 'Rest of Europe' category but excluded from the 'Multiregional' category). The 'not applicable' category comprises reviews and systematic reviews that are international in nature, summarising data from different regions.

Novel psychoactive substance type

The figures below show percentage of records by NPS type and study design (Figure 8), region (Figure 9), setting (Figure 10) and publication type (Figure 11).

For most NPS types, the majority of studies were case reports/series, reviews or surveys. Prospective cohort and case-control studies are not represented here because of very low numbers.

The majority of studies on synthetic cannabinoids, synthetic cathinones and phenethylamines were conducted in North America, whereas the majority of studies on piperazines were conducted in Australia/New Zealand. Articles that looked at NPS in general were mostly from the UK and the rest of Europe.

The majority of studies on synthetic cannabinoids, synthetic cathinones and phenethylamines were conducted in general hospital settings. However, the majority of studies on piperazines were either conducted in research settings or not specific to any setting.

Most articles were peer-reviewed journal articles for each NPS category.

TABLE 3 Number of studies by geographic region

Region	Distribution (n)
UK	185
Rest of Europe	200
North America	294
Australia/New Zealand	58
Africa	0
Asia	29
Middle East	7
Multiregional	22
Not applicable	216

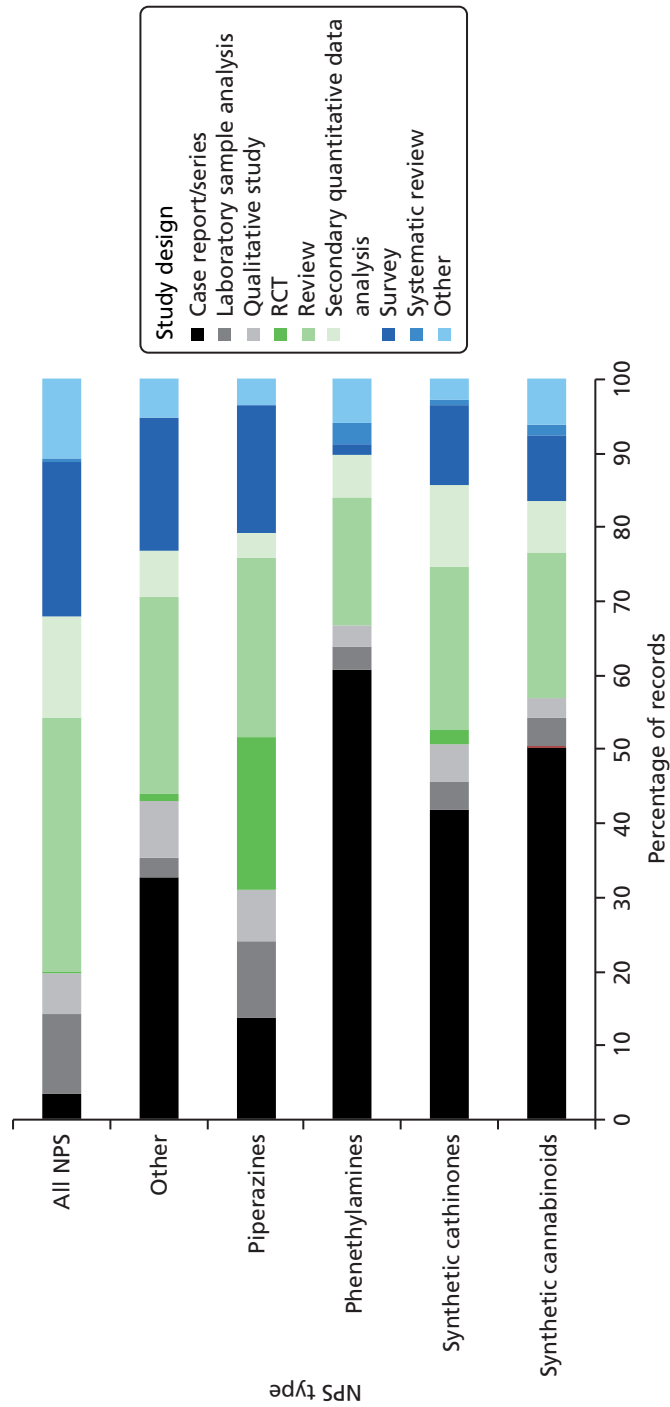


FIGURE 8 Percentage of records by NPS type and study design.

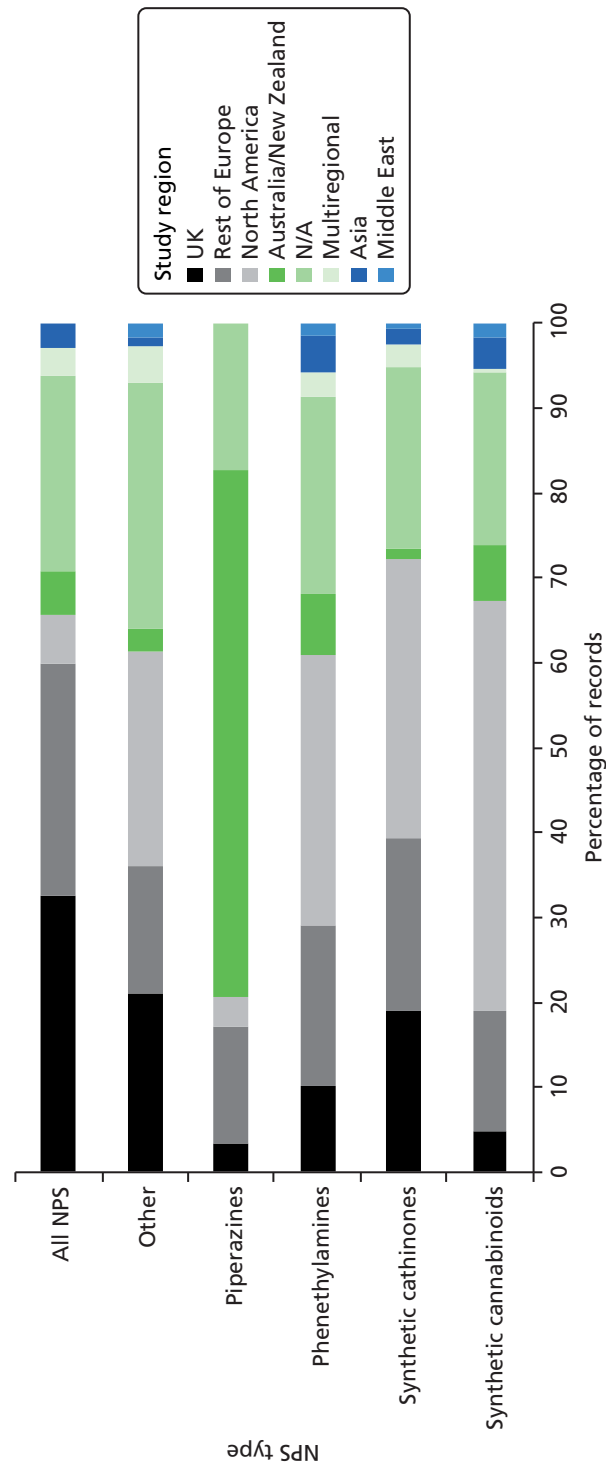


FIGURE 9 Percentage of records by NPS type and study region.

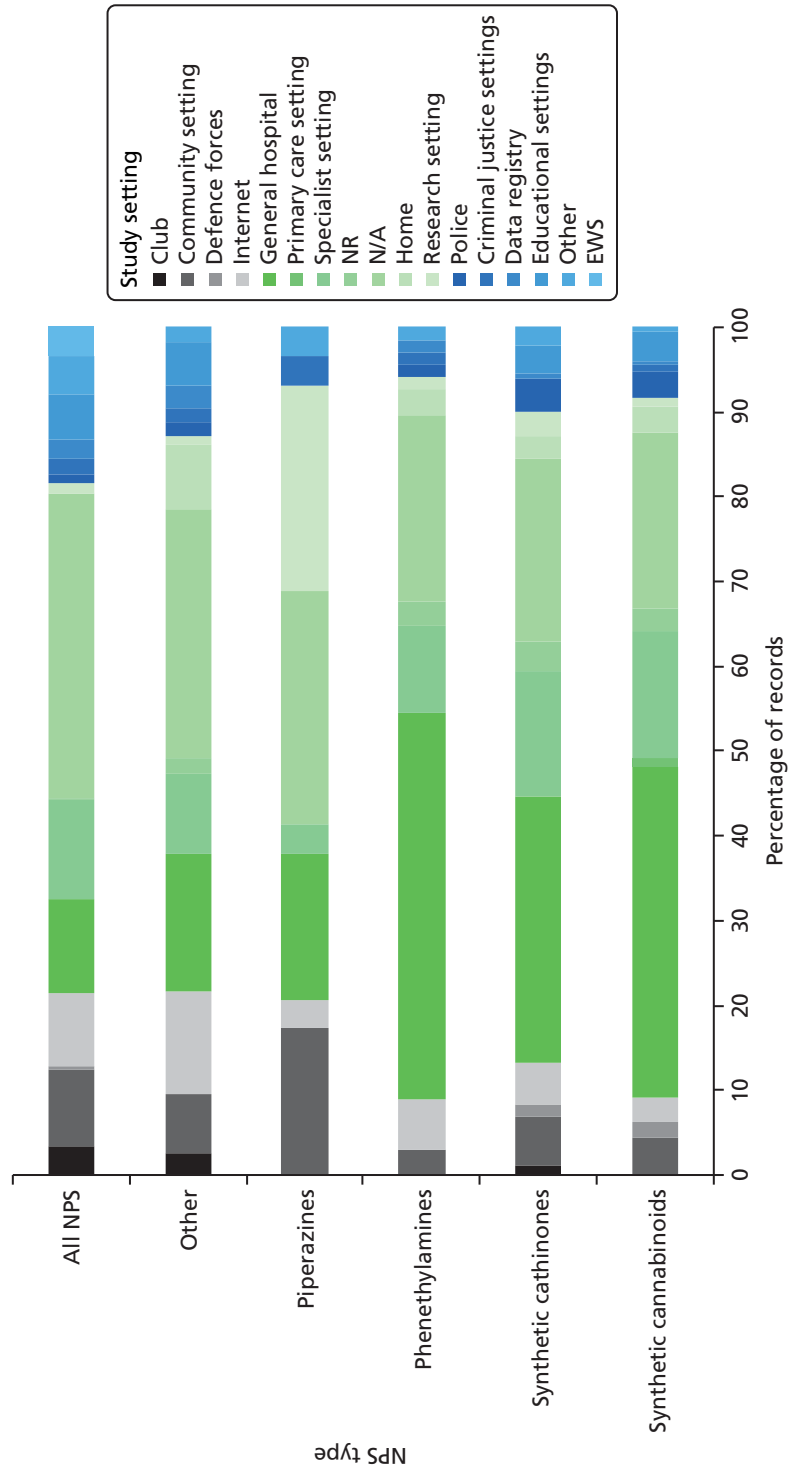


FIGURE 10 Percentage of records by NPS type and study setting. N/A, not applicable; NR, not reported.

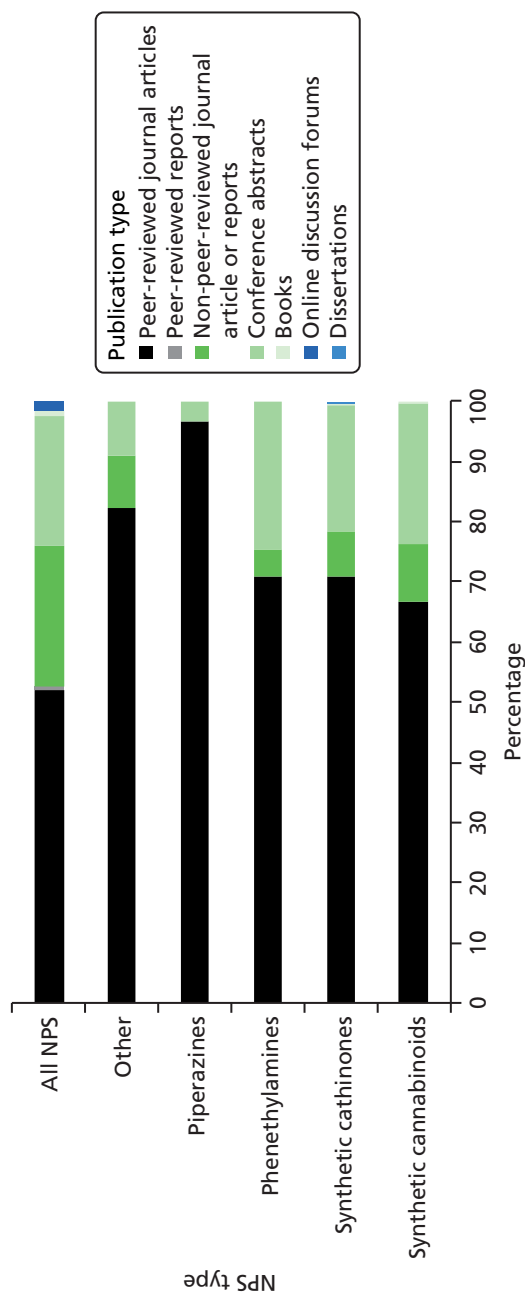


FIGURE 11 The percentage of records by publication type for each NPS category.

Study design

Figure 12 summarises the percentage of records by publication type for each study design category.

Most types of study designs were published as peer-reviewed journal articles. There were also three peer-reviewed articles and three conference abstracts on prospective cohort studies, one peer-reviewed article for a case-control study, four online drug forums and one dissertation that conducted secondary quantitative data analyses.

Summary of the evidence mapping

We identified a very large number of relevant reports ($n = 995$). However, despite the large volume of literature in this area, large gaps in the evidence base still remain, presumably owing to its recent development. It is, therefore, challenging to both summarise this literature and prioritise areas of the evidence base that require more detailed evidence synthesis.

In order to structure this summary and make decisions about further synthesis, we return to the a priori research questions on NPS use, NPS-related problems/harms and responses introduced at the beginning of this chapter. We briefly summarise the data available in relation to each initial question as the basis for an assessment of whether or not there were sufficient data to conduct more detailed syntheses.

Novel psychoactive substance use

1. What are the prevalence and patterns of NPS use in the UK general population and do they differ in particular subgroups of the population?

We identified studies on prevalence and patterns of NPS use in the UK (see *Table 4*). These comprised nationally representative surveys in adults [such as the Crime Survey for England and Wales (CSEW)⁹⁶³ and the Scottish Crime and Justice Survey (SCJS)¹⁰⁰⁹] and school children (such as the *Smoking, Drinking, and Drug Use Among Young People in England in 2014* survey⁹²⁵) which indicate that NPS use is relatively rare at the population level (between 1% and 2%). Population prevalence rates for mephedrone use are declining; however, it is not yet possible to assess trends over time for NPS use as a whole. Surveys in targeted subgroups thought to be more likely to engage in NPS use have been conducted. Most data relate to attendees of gay-friendly nightclubs, where a similar pattern of a decline in mephedrone use has been identified. Therefore, the prevalence and patterns of NPS use in the UK is a promising area of research, which suggests that a more detailed synthesis of these data will be informative.

2. How do existing patterns of both legal and illegal drug use and social and other risk factors influence NPS use?

There is limited preliminary evidence, as this research question does not appear to have been investigated in a dedicated manner. It would be challenging to provide even basic information on this subject. Therefore, there does not appear to be sufficient data available to conduct a more detailed synthesis.

3. Which other population-level risk factors influence NPS use?

There are nationally representative survey data suggesting that males rather than females and younger adults rather than adults as a whole are more likely to engage in NPS use. However, we identified very few data on other population-level risk factors that influence NPS use. Given the limited exploration of these risk factors, we concluded that there were insufficient data to conduct further evidence syntheses. However, we decided that data on age and sex should be considered in the context of the national survey data on prevalence (see *Narrative synthesis*).

Novel psychoactive substance-related problems/harms

1. Which acute intoxication problems are associated with NPS use?

There were a large number of case reports and case series on intoxication problems associated with NPS [e.g. attending accident and emergency (A&E) services after NPS use]. However, there were little or no population-level data other than registries of drug-related deaths. These data have begun to be

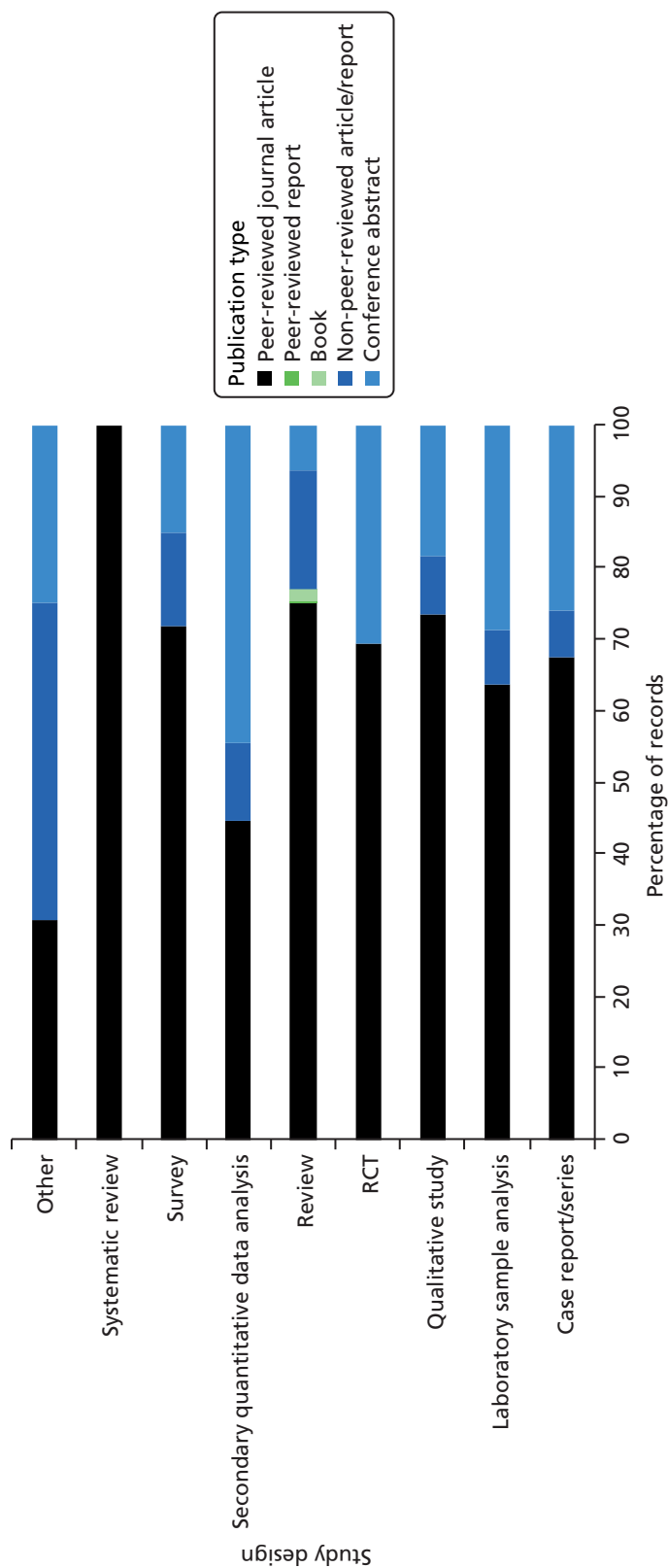


FIGURE 12 The percentage of records by publication type for each study design category.

synthesised and we identified 10 published systematic reviews (see *Table 5*). Given the size of the literature and the limited quality of the primary studies, the priority for synthesis appears to be summarising the findings of systematic reviews in this area, including an assessment of the extent to which this large volume of literature on case reports and registry data has been covered by these reviews.

2. What problems are associated with long-term regular NPS use?

We identified very limited epidemiological data on problems associated with regular NPS use (such as symptoms of dependence, physical health problems and enduring mental health problems). However, this has begun to be explored in qualitative studies in NPS using populations. We identified seven qualitative studies in nine papers and, therefore, we synthesise these studies in more detail in subsequent sections of the report.

3. In addition to intoxication, long-term regular use and dependence problems, are there other types of NPS-specific problems or other problems associated with NPS use?

Social and health harms associated with NPS use other than the types described above do not appear to have been investigated. Therefore, we concluded that it would be premature to conduct further syntheses, and, indeed, it may be better to pursue such questions in future research in the first instance in relation to specific NPS drugs or drug types rather than for NPS as a whole.

Responses

1. Are there dedicated primary or secondary prevention interventions in the UK and, if so, what is known about their outcomes?

We did not identify evidence on primary or secondary prevention interventions in the UK; therefore, further syntheses are not currently possible.

2. Which generic interventions (early in life and early in drug-using careers) target NPS?

We did identify some treatment audit data that show the proportions of people who use NPS receiving drug treatment services. However, no specific data exist on the content of these interventions and, therefore, there are very limited opportunities to conduct further syntheses.

3. How extensively does current generic UK drug prevention practice cover NPS?

We did not find any data to inform a response to this question; therefore, no further evidence synthesis was conducted. Although there are policies such as the Psychoactive Substances Act 2016¹ and publicly available educational resources such as Talk to Frank (see www.talktofrank.com) that incorporate NPS, there were no data available for inclusion.

4. How good are treatment outcomes for NPS?

We did not find any studies to inform a response to this question; therefore, no further synthesis was conducted.

5. What promising approaches are currently available, or can be made available, in the UK for intervening with NPS use?

Although limited, there are data on NPS responses that indicate the need for further exploration.

For example, key policy responses at present in many countries around the world involve the prohibition of NPS possession or supply. We have identified studies that have begun to evaluate the effectiveness of such responses, which we shall therefore further examine in the narrative synthesis (see *Table 6*).

6. What are the population-level or social structural factors limiting the effects of individual-level interventions?

We did not find any data to inform a response to this question. Therefore, we did not conduct further evidence syntheses.

There were also three methodological questions as follows:

1. What is the nature of the current EWS provision?
2. Are there sentinel populations capable of being monitored to provide early warnings of new trends?
3. What are the issues raised by uncertainties about the identities of substances being used?

We did identify some data that were relevant to all three questions, although this related to the substantive areas such as descriptions of EWSs, sentinel population studies and detection, identification and quantification of substances (including waste water analysis, use of the world wide web and validation of analytical methods). Such topics are already covered elsewhere in the evidence mapping, and as the studies are not methodological in nature, it would be impractical to identify methodological issues across the literature as a whole. We therefore have no basis for any further methodological syntheses within this study.

Interim conclusions

We have identified a number of areas of the NPS evidence base in which there has been very limited research. For example, there are very limited data on epidemiological studies of the long-term harms of NPS, outcomes associated with current UK prevention provision for NPS use, and outcomes associated with the effectiveness of psychosocial interventions for NPS use.

We identified UK prevalence data on NPS use both at a general population level and in potential sentinel populations. Initial scoping suggests that this is an area that requires more detailed synthesis to assess current findings and future research needs. Similarly, given the importance of legislation and other policy initiatives on NPS use, synthesising studies evaluating the effectiveness of these types of responses should be useful. There is also a need to explore further the qualitative studies that we identified on long-term harms and other subjects to inform future research. Finally, there is a relatively large body of literature on harms and problems associated with NPS use, although this mainly consists of case reports and case series. In addition, we identified systematic reviews of harms and problems that seek to synthesise some of this literature. We judged that a detailed synthesis of the primary literature may be useful, although a review of existing systematic reviews should be considered before any synthesis of the primary literature. Therefore, we made a pragmatic decision to summarise these reviews, judging this to be of greater priority given the size and scope of our project.

Narrative synthesis

As indicated in earlier sections, the narrative synthesis focuses on UK survey data, which include general population surveys as well as particular targeted subgroup studies, data from the 10 identified systematic reviews, qualitative studies of NPS use in the UK, and responses to NPS use and problems/harms.

UK survey data

We identified 29 studies assessing the prevalence of NPS use in the UK (*Table 4*). These surveys varied in focus, with some examining NPS prevalence in general populations (including some nationally representative surveys of adults and school children in the UK).^{904,915,925,960,963,1009} Others focused on specific sentinel populations, such as attendees of nightclubs, people attending mental health services, homeless populations and prisoners.^{159,170,184,192,455,491,509,516,517,570,704,741,842,843,874,876,931,943} Finally, other surveys particularly targeted NPS users to investigate patterns of use.^{15,538,820,884,918,959,1001}

Nationally representative prevalence studies

Adults

Data on adults' NPS use are available from nationally representative surveys conducted by government agencies. The most extensive data are on mephedrone use; these have been collected annually since 2010/11 (questions on lifetime use of mephedrone were included from 2012/13) in the CSEW⁹⁶³ and the SCJS.¹⁰⁰⁹ Data on mephedrone use are also available from the All Ireland Prevalence Survey (AIPS) collected in 2010/11 and 2014/15.⁹⁰⁴

TABLE 4 Summary study characteristics of surveys of NPS use in the UK

Author	Population	Drug	Sampling	Participant characteristics
Nationally representative				
Department of Health, Northern Ireland (2015) ⁹⁰⁴	General population	NPS	Nationally representative sample of Ireland	N = 2535 Reflective of the general population
European Commission (2014) ⁹¹⁵	European youth (15- to 24-year-olds)	NPS	Nationally representative samples for Member States	N = 13,128 (UK: n = 501) Reflective of the general population
Health and Social Care Information Centre (2015) ⁹²⁵	11- to 15-year-olds	NPS	Nationally representative sample of schools in England	N = 6173 Reflective of the general population
NHS National Services Scotland (2014) ⁹⁶⁰	13- and 15-year-olds	NPS	Nationally representative sample of schools in Scotland	N = 33,685 Reflective of the general population
Office for National Statistics (2015) ⁹⁶³	General population	NPS	Nationally representative sample of England and Wales (CSEW ⁹⁶³)	N = 35,000 Reflective of the general population
Robertson (2016) ¹⁰⁰⁹	General population	NPS	Nationally representative sample of Scotland (SCJS)	N = 12,035 Reflective of the general population
Community sample: not nationally representative				
Corazza <i>et al.</i> (2014) ¹⁷⁰	Pupils and students	NPS	Online (the Study Room forum)	N = 446 Sex: 50% male Mean age: 19 years (range 13–30 years)
Dargan <i>et al.</i> (2010) ¹⁸⁴	Pupils and students	Mephedrone	Tayside area	N = 1006 Sex: 50% male Mean age school children: 14 years Mean age university students: 21 years
Penney <i>et al.</i> (2016) ⁵⁷⁰	School children (15- to 18-year-olds)	NPS	Greater London	N = 533 Sex: 55% male Age: range 15–18 years Ethnicity: 14% white, 26% black, 9% mixed ethnicity, 23% Asian, 28% other
Mounsey <i>et al.</i> (2016) ⁵¹⁷	School children (15- to 18-year-olds)	NPS	Greater London (four private schools and four state schools)	N = 917 Sex: not reported Age range: 15–18 years

TABLE 4 Summary study characteristics of surveys of NPS use in the UK (continued)

Author	Population	Drug	Sampling	Participant characteristics
Sentinel populations/subgroups				
Baker (2015) ⁸⁷⁶	Prisoners	Synthetic cannabinoids	Prison in Rochester	N = 101 Sex: 100% male Mean age: 32 years (range 18–59 years) Ethnicity: 72% white, 12% black, 6% Asian, 6% mixed ethnicity, 4% other Offences for which convicted: 30% violent offences, 21% robbery, 26% drugs, 5% motoring related, 9% acquisitive, 9% other
Homeless Link (2016) ⁹³¹	Homeless people	NPS	Clients of day centres for homeless people	N = 56 Sex: 59% male Mean age: 29 years
Chung <i>et al.</i> (2014) ¹⁵⁹	HIV-positive MSM	NPS	HIV outpatient clinic	N = 223 Sex: 100% male Sexuality: 100% MSM
Daskalopoulou <i>et al.</i> (2014) ¹⁹²	HIV-positive MSM	Mephedrone	HIV outpatient clinic	N = 2248 Sex: 100% male Median age: 46 years Ethnicity: 89% white Sexuality: 100% MSM
Thurtle <i>et al.</i> (2016) ⁷⁴¹	Attendees of sexual health clinics	NPS	Two clinics in London	N = 1472 Sex: 53% male Mean age: 30 years
Lovett <i>et al.</i> (2014) ⁴⁵⁵	Attendees of gay-friendly nightclubs	Mephedrone, methiopropamine	Gay-friendly nightclubs	N = 397 Sex: 89% Mean age: 30 years
Measham <i>et al.</i> (2011); ⁴⁹¹ Moore <i>et al.</i> (2013) ⁵⁰⁹	Attendees of gay-friendly nightclubs	NPS, mephedrone	Gay-friendly nightclub (2010)	N = 308 Sex/gender: 82% male, 17% female, 1% transgender Mean age: 30 years Ethnicity: 75% white, 10% black, 10% mixed race, 4% Asian, 1% other Sexuality: 70% homosexual, 9% bisexual, 17% heterosexual, 4% other

continued

TABLE 4 Summary study characteristics of surveys of NPS use in the UK (*continued*)

Author	Population	Drug	Sampling	Participant characteristics
Measham <i>et al.</i> (2012) ⁸⁴³	Attendees of nightclubs	NPS	Nightclubs in Lancashire	<i>N</i> = 343 Sex: 48% male Mean age: 23 years (range 17–55 years) Ethnicity: 96% white
Wood <i>et al.</i> (2012), ⁸⁴³ Wood <i>et al.</i> (2012) ⁸⁴²	Attendees of nightclubs	NPS, mephedrone	Gay-friendly nightclubs in London (2011)	<i>N</i> = 315 Sex/gender: 82% male, 15% female, 1% transgender, 2% other Mean age: 30 years
Roche and Huke (2016) ⁸⁷⁴	Psychiatric populations	NPS	Eating disorders outpatients	<i>N</i> = 72 No further data on study characteristics reported
Moore and Lesser (2015) ⁵¹⁶	Psychiatric populations	NPS	Acute mental health services in Devon	<i>N</i> = 100 No further data on study characteristics reported
Stanley <i>et al.</i> (2016) ⁷⁰⁴	Psychiatric populations	NPS	General adult psychiatric wards in a Scottish city	<i>N</i> = 388 Sex: 49% male Mean age: 36 years (NPS users), 43 years (non-NPS users) Ethnicity: not reported
Winstock <i>et al.</i> (2011) ⁸²⁰	NPS users	Mephedrone	Recruited through dance music and clubbing website	<i>N</i> = 947 Sex: 60% male Mean age: 24 years
Winstock <i>et al.</i> (2011) ¹⁵	NPS users	Mephedrone	Recruited through involvement in the dance music scene (subsample of Winstock <i>et al.</i> ⁸²⁰)	<i>N</i> = 100 Sex: 77% male Mean age: 25 years
Winstock <i>et al.</i> (2016) ¹⁰⁰¹	Polydrug users	Methoxetamine	Online survey of UK-based polydrug users	<i>N</i> = 5367 Sex: 82% male Mean age: 25 years Ethnicity: 91% white, 9% other Sexuality: 78% heterosexual, 9% homosexual, 7% bisexual, 6% other
Fletcher <i>et al.</i> (2014) ⁹¹⁸	NPS users	NPS	Tayside area	<i>N</i> = 687 Sex: ratio of female to male participants was approximately 5 : 2 Age: most respondents were 20–64 years

TABLE 4 Summary study characteristics of surveys of NPS use in the UK (*continued*)

Author	Population	Drug	Sampling	Participant characteristics
O'Brien <i>et al.</i> (2015) ⁵³⁸	NPS users	NPS	Online survey	N = 183 Sex: 78% male Age: majority of participants aged 16–29 years
NHS Lothian Substance Misuse Directorate (2015) ⁹⁵⁹	NPS users	NPS	Opportunistic sampling by outreach workers	N = 100 Sex: 77% male Age range: 21–59 years Approximately half of participants were homeless, 76% had been in prison and almost all were unemployed
Brookman (2014) ⁸⁸⁴	Various at-risk groups	Mephedrone	Agencies in South Wales: criminal justice and charities working with offenders, drug users or those with broad range of needs	N = 67 Sex: 73% male Age range: 15–55 years – 12% < 18 years; 48% aged 18–29 years; 40% > 30 years

HIV, human immunodeficiency virus; MSM, men who have sex with men.

Data on generic NPS use from nationally representative surveys are more limited. The CSEW⁹⁶³ and the AIPS⁹⁰⁴ began collecting data on generic NPS use only in 2014/15. The SCJS has been collecting data on generic NPS use since 2010/11.¹⁰⁰⁹ However, comparisons of prevalence over time are difficult because specific substances included in this category have changed. Of particular note, the 2014/15 SCJS no longer categorised mephedrone as a 'new drug', which has a substantial impact on prevalence estimates of NPS use.¹⁰⁰⁹ However, the advantage is that this is comparable to the CSEW⁹⁶³ and AIPS, thereby making comparisons across surveys possible in 2014/15 and potentially in the future. The European Commission⁹¹⁵ also conducted a nationally representative survey of NPS use in Member States, including the UK.

Mephedrone use The lifetime prevalence of mephedrone use for all adults (aged ≥ 16 years) has remained relatively constant in the past 3–5 years of surveys. Estimates were similar in the CSEW⁹⁶³ and the AIPS,⁹⁰⁴ with 2% of the population using mephedrone, compared with 1% in the SCJS.¹⁰⁰⁹ Past year prevalence declined in both the CSEW⁹⁶³ (2010/11: 1.3% to 2014/15: 0.5%) and the SCJS (2010/11: 0.7% to 2014/15: 0.3%);¹⁰⁰⁹ we could not find data to assess this on the AIPS.

Estimates for younger adults (aged 16–24 years) were two to three times higher than for all adults. Mephedrone lifetime use was 5–6% across years (2012/13, 2013/14, 2014/15) in the CSEW,⁹⁶³ and 4% in the SCJS (2012/13)¹⁰⁰⁹ and AIPS (2010/11).⁹⁰⁴ Past year use declined from 4.4% in 2010/11 to 1.9% in 2014/15 in the CSEW;⁹⁶³ we could not assess whether there was a similar decline in SCJS¹⁰⁰⁹ or AIPS.⁹⁰⁴ Together, these data suggest that the peak incidence of mephedrone has passed.

Generic NPS use As discussed above, comparisons across surveys are not possible nor are comparisons across years in the SCJS; therefore, we focus only on the 2014/15 data.

For all adults, the prevalence of lifetime NPS use (excluding mephedrone) was 2% in the AIPS and SCJS¹⁰⁰⁹ and slightly higher (3%) in the CSEW.⁹⁶³ NPS use was approximately two to three times higher in younger

adults, at 4% (SCJS: 16–24 years),¹⁰⁰⁹ 6% (CSEW: 16–24 years)⁹⁶³ and 7% (AIPS: 15–34 years).⁹⁰⁴ The UK prevalence estimate of lifetime NPS use from the European Commission (2014) survey⁹¹⁵ was higher (10%) than the other UK national surveys and higher than the average prevalence across European countries (8%).

All three UK national surveys found that men were approximately two to three times more likely than women to engage in NPS use. However, the European Commission⁹¹⁵ did not find that NPS use differed by sex.

Young people (aged 11–15 years)

NPS use A Health and Social Care Information Centre (HSCIC; now NHS Digital) survey in England of 11- to 15-year-olds found that lifetime prevalence of NPS use was 2.5%.⁹²⁵ This was similar to the Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS), which found a prevalence of 2%.⁹⁶⁰ Both surveys found that older children were more likely to use NPS. In England, NPS prevalence was 0.5% for 11-year-olds but 5% for 15-year-olds.⁹²⁵ In Scotland, 1% of 13-year-olds and 4% of 15-year-olds reported NPS use.⁹⁶⁰ NPS use was slightly higher for boys than for girls in the SALSUS (2% boys and 1% girls)⁹⁶⁰ but there was no evidence of sex differences in the HSCIC survey.⁹²⁵

Mephedrone and other individual NPS Mephedrone use was low in both the HSCIC survey (0.5%)⁹²⁵ and SALSUS (1%).⁹⁶⁰ In England, the prevalence remained relatively constant across the years 2012–14.⁹²⁵ In Scotland, there was a reduction from 2% in 2010 to 1% in 2013.⁹⁶⁰

The SALSUS provided more data on individual NPS.⁹⁶⁰ Prevalence of synthetic cannabinoids increased from 1% in 2010 to 2% in 2013. Salvia use was recorded for the first time in that survey in 2013, with a 1% reported prevalence.

Subpopulation studies

School children and university students

Four additional studies^{170,184,517,570} were identified that conducted surveys of schools or university students. However, like all studies included in this section, these surveys are not designed to provide nationally representative samples of this population.

NPS use Prevalence estimates differed substantially between studies. Corazza *et al.*¹⁷⁰ conducted an online survey using the Study Room website (see www.thestudentroom.co.uk). Participants' ages ranged from 13 to 30 years, with a mean of 19 years. They reported the highest lifetime prevalence estimate (31%) of NPS use for any subpopulation in this group of website users. This was much higher than national surveys looking at a similar age group, for which lifetime prevalence of NPS use ranged from 4% to 10%. Corazza *et al.*¹⁷⁰ found that the most commonly reported NPS used were mephedrone (41%), salvia (20%) and synthetic cannabinoids (11%). Mounsey *et al.*,⁵¹⁷ in a questionnaire survey of the schools population of eight schools (four private and four state schools) of 15- to 18-year-olds in Greater London, found a lifetime prevalence rate of 8% for NPS use. In contrast, Penney *et al.*⁵⁷⁰ had a much lower estimate (1.1%) of NPS use in a similar study in three schools in London (see above for national prevalence data among 11- to 15-year-olds).^{925,960}

Mephedrone and other individual NPS use Estimates of mephedrone use differed widely in subpopulation surveys. The highest estimate (20%) was found by Dargan *et al.*¹⁸⁴ in a survey of schools, colleges and universities in Tayside. Corazza *et al.*¹⁷⁰ also found a relatively high rate of 13% for mephedrone use. This contrasted with the Penney *et al.*⁵⁷⁰ survey of school children, which reported a much lower prevalence (0.5%). All data reported here refer to lifetime prevalence.

Data on other individual NPS were limited. Corazza *et al.*¹⁷⁰ reported prevalence rates of 6% for salvia and 3% for synthetic cannabinoid use. Penney *et al.*⁵⁷⁰ provided prevalence data on synthetic cannabinoids (0.7%) and methoxetamine (0.2%).

Attendees of nightclubs

Surveys were conducted by the same research team in gay-friendly nightclubs in south-east London in 2010, 2011, 2012 and 2013. Lifetime use of mephedrone was high: 54% in 2011⁴⁹¹ and up to 72% in 2013.⁴⁵⁵ However, past month use and use on the night of survey declined steeply in these surveys: past month use was 41% and use that night was 21% in 2010.⁴⁹¹ In 2011, this increased to 53% for past month use and 41% for use that night.⁸⁴² However, in 2013, past month use had declined to only 6%.⁴⁵⁵ Other NPS use was much less frequent across all years of the surveys including 5,6-methylenedioxy-2-aminoindane (MDAI), benzylpiperazine (BZP), methiopropamine and methoxetamine.

Measham *et al.*⁹⁴³ also conducted surveys of drug use in 10 nightclubs in Lancashire (2010/11), which did not focus on gay-friendly clubs. Prevalence of NPS use was much lower, with a lifetime reported use of mephedrone of 13%, a past year use of 7% and a past month use of 2%. The lifetime prevalence of 'Bubble' use was 18%, past year use was 11% and past month use was 3%. Methoxetamine use in the past 12 months was only 3%, but this was before it had been banned, which may impact on future use.

Cybernauts

O'Brien *et al.*⁵³⁸ conducted an online survey of 'cybernauts' ($n = 183$). Frequency of NPS use was high, with 32% of participants reporting using in the past week. Participants identified themselves as knowledgeable consumers, who used the internet to accumulate information about NPS and who also shared their own experiences and informed fellow users of potential harms.

Psychiatric populations

Two eating disorders clinics in Leeds and London were surveyed for NPS use based on case notes.⁸⁷⁴ A total of 22% reported lifetime use (14% ketamine and 13% mephedrone). NPS use was higher in people with binge-purge behaviours and a history of self-harm.

Stanley *et al.*⁷⁰⁴ in a larger retrospective case notes review ($n = 388$) of adult inpatients in general psychiatric wards, found the same prevalence rate (22%) of lifetime NPS use. NPS use was thought to contribute to psychiatric symptoms in 59% of these participants. NPS users were more likely to be younger, to be male and to have a forensic history than non-NPS users.

Moore and Lesser⁵¹⁶ also conducted a retrospective review of case notes of 100 patients presenting to acute mental health services in Devon. They found an overall prevalence rate of 8% for lifetime NPS use, with higher rates of use in inpatients (12%) than those seen by the crisis team (4%). In seven out of eight NPS users in the sample, it was judged that their use was associated with their clinical presentation.

Attendees of sexually transmitted infection clinics

Chung *et al.*¹⁵⁹ conducted a retrospective case review of 431 sexually transmitted infection screens in 223 human immunodeficiency virus (HIV)-positive men who have sex with men (MSM). Prevalence was high, with 24% reporting lifetime mephedrone use. However, a larger study ($n = 2248$) of HIV-positive MSM attending 10 HIV clinics¹⁹² found a much lower prevalence estimate for mephedrone use (7%).

Thurtle *et al.*⁷⁴¹ surveyed attendees of two sexual health clinics in central London ($n = 1626$), 44% of whom were MSM. Regular monthly use was relatively low (1.6%) in the total sample and lower in 16- to 24-year-olds (0.3%). Prevalence for other NPS, such as ivory wave, spice, naphyrone and methylone, was even lower.

Prisoners

Baker⁸⁷⁶ conducted a non-randomly sampled survey in a prison in Rochester. Questionnaires were provided in classrooms and activity areas within prison, as well as to prisoners employed as cleaners. A total of 66% reported that it was fairly easy or very easy to buy spice, but the figure was higher for those who reported using spice (88%). A total of 43% reported any use of synthetic cannabinoids ('spice'), 39% reported use in prison, 22% reported being a current user of spice. Of those using spice in prison, 21% said that they would still use spice outside, 39% said that they would use an alternative drug and 23% reported that they would not have used anything. The most frequently given reasons for using spice were making time pass quicker (37%), relaxation (22%) and it not being detected in mandatory drug testing (22%). Most (71%) did not think that spice was safer because it was legal outside prison. Most also thought that spice was more dangerous than cannabis (56%), and 13% thought that spice was as safe as cannabis. A total of 57% of those who used spice viewed it as fairly or very addictive.

Homeless populations

Homeless Link⁹³¹ conducted a small survey among homeless clients ($n = 56$) of four day centres in Manchester. Lifetime prevalence was strikingly high in this study (80%) and the majority of those who reported using NPS did so on a daily basis (66%). A further 14% engaged in NPS use 5 or 6 days a week. Most NPS users also used a variety of other substances, most commonly crack cocaine and cannabis. In terms of the most commonly consumed individual NPS, most users simply reported 'any' or 'all', followed by a range of different synthetic cannabinoids (such as Pandora's box, hipster and spice). Most used at least three types of NPS (84%).

The most common reasons given for use were convenient and easy access (38%), legality of substances (31%), substitute for other substances (e.g. alcohol or illegal drugs, 26%) and cheaper than other substances (21%). NPS use was reported to have a negative impact on their relationships (27%), physical health (27%) and homelessness (21%). A total of 57% reported having a drug problem, 3% reported that they were in recovery and the rest did not think that they had a drug problem.

Targeted studies of novel psychoactive substance users

General novel psychoactive substance use

All studies described here do not employ random or other formal sampling methods. Fletcher *et al.*⁹¹⁸ conducted a survey in Tayside recruiting 120 people who had used NPS (as well as those who knew of people who had used NPS and those who had not used NPS).

Over half of those who reported lifetime NPS use had last used more than 1 year previously and were thus no longer users. In addition, 10% had used in the past week, 20% had used in the past month, and 20% had used between 6 months and 1 year ago. Mephedrone was the most common drug reported. NPS were most commonly used as tablets or powder, and were snorted or smoked. A NPS was most commonly first tried between the ages of 16 and 19 years. A total of 19% reported that a NPS was the first drug that they had ever taken. Cannabis was much more commonly reported as the first drug taken (51%), and cocaine rather than a NPS being the first drug taken was slightly less common (14%). Of those who ceased using NPS, 91% found it either easy or very easy to stop. Most commonly, cessation was due to side effects of NPS.

Mephedrone

Winstock *et al.*⁸²⁰ examined data on 947 (41%) people in the UK who reported lifetime mephedrone use as part of a larger online survey of club drug use. Reported mephedrone use was much higher in the larger online survey than lifetime methylone (11%) and methylenedioxypropylvalerone (MDPV) (2%) use. Among participants who had reported lifetime mephedrone use, 94% reported use in the past year and 80% reported use in the past month. The most common route of administration was snorting (66%). Those who snorted mephedrone rated it as more addictive than cocaine and as carrying more risk.

Winstock *et al.*¹⁵ conducted a more detailed telephone survey of 100 participants of this sample of mephedrone users. Use of other drugs with mephedrone was very common. Participants reported high lifetime prevalence rates for ecstasy (96%) and cocaine use (92%). In a typical mephedrone session, 82% drank alcohol, 36% used cannabis, 35% used ketamine, 26% used cocaine and 23% used ecstasy. Possible stimulant dependence (three or more dependence symptoms) was reported in 30% of participants.

Brookman⁸⁸⁴ investigated violence and other harms in mephedrone users ($n = 67$). She provided questionnaires designed for young people and adults to 14 agencies across South Wales (including criminal justice organisations and charitable agencies working with offenders or drug users). A total of 46% used mephedrone on a daily basis, 15% used it every other day, 19% used mephedrone once a week, 6% used it every other week and 13% used it once a month. Almost two-thirds (63%) snorted the drug, 56% injected it and 45% injected it orally. Just over 80% used mephedrone with another drug, most commonly alcohol ($n = 29$), cannabis ($n = 23$) or heroin ($n = 19$). Diazepam was most frequently used to reduce the effects of comedown ($n = 37$), followed by cannabis ($n = 7$). Violence was fairly frequent, with 42% reporting becoming violent when using mephedrone. Females were more likely (50%) than males (40%) to report becoming violent as a result of mephedrone use.

Methoxetamine

Winstock *et al.*¹⁰⁰¹ reported on a subsample ($n = 326$) of past year users of methoxetamine from a larger online survey (Global Drug Survey) of 7700 UK-based polydrug users (other material from this survey is reported only as news items in mass media and thus is not eligible for inclusion, as there were no reports of study findings available). This comprised 4% of the overall survey population. A total of 25% of past month methoxetamine users reported use on 4 or 5 days of that month. Motivations for use of methoxetamine rather than ketamine were that it was easier to get hold of, that it was less damaging to their kidneys or bladder or that users preferred the effects. A total of 89% reported first use via the intranasal route.

Injecting drug users

A harm-reduction service in Lothian conducted a survey of their NPS-using clients ($n = 100$).⁹⁵⁹ The majority of participants were existing injectors (92%), and the most common reported reason for using NPS was that their friends were taking them (approximately 70%). Of those injecting NPS, the majority injected multiple times a day. The most commonly used NPS were ethylphenidate, synthetic analogues of methamphetamine (e.g. methiopropamine) and mephedrone. Heroin (73%), methadone (49%) and benzodiazepines (51%) were also commonly used in this sample. Twenty per cent reported sharing needles, and approximately half shared injecting equipment. A total of 22% of participants had stopped using NPS. The most common reason was the physical or mental health impact, with 54% receiving medical treatment as a result of NPS use.

Summary

The most robust nationally representative data on NPS use are for mephedrone, for which CSEW and SCJS have been conducting national surveys since 2010/11. However, we acknowledge that there are a number of limitations to the data on mephedrone use and NPS use in general. For example, although participants may report using a substance (such as mephedrone), the names of NPS are used interchangeably, with a number of other types of drug going by the same name. Therefore, there is inherent uncertainty in the reported use of a particular NPS.

Lifetime mephedrone use is relatively uncommon in adults as a whole (approximately 1–2%) but is about two to three times more prevalent in men than in women and in young adults than in older adults. It appears that prevalence rates of recent mephedrone use are declining substantially; for example, the CSEW found a halving of prevalence from 2010/11 to 2014/15 in both adult and young adult samples. Nationally representative data on NPS use as a whole and on the use of particular NPS other than mephedrone are much less developed, and comparisons across years are not yet possible. Considerable uncertainties about basic data therefore persist in terms of monitoring this issue.

Surveys of school children have also found low prevalence for mephedrone use and NPS use as a whole. Prevalence rates are higher in older children than in younger children and higher in boys than in girls. Other surveys focusing on a small number of schools in a particular area of the UK differ widely and it is impossible to conclude whether observed variations reflect the particular characteristics of the schools studied, differences in prevalence among particular subgroups of school children or methodological issues.

Data on particular sentinel populations likely to be at greater risk of NPS are growing, although they remain limited. At present, there are some data on attendees of gay-friendly nightclubs for whom trends in mephedrone use can be assessed. However, the main limitations of such studies regard their generalisability across the UK and the possible impacts on levels of problems. NPS use has also been examined in a variety of other potential sentinel populations such as broader populations of nightclub attendees, prisoners, homeless people and psychiatric populations. However, at present, the small number of studies for each population limits the conclusions that can be drawn.

There are also a small number of surveys examining in more detail patterns of NPS use. However, further work is needed to draw firmer conclusions and to enable such work to contribute substantially to decision-making.

Systematic reviews

The 10 included systematic reviews^{118,127,137,286,293,409,502,561,710,714} (see *Chapter 2, Methods, Definitions*) are summarised in *Table 5* by NPS type. The majority address clinical problems/harms attributable to NPS, with one also including data on clinical management. One was on all NPS, five were on synthetic cannabinoids, two were on synthetic cathinones and two were on phenethylamines.

All novel psychoactive substances

Gray *et al.*²⁸⁶ focused on mental and physical health effects and fatalities attributable to NPS use among adults with a diagnosis of severe mental illness. Fourteen studies representing a total of 648 individuals (19 individuals from 12 case studies, 608 from one questionnaire study and 21 from one qualitative study) were included. Participants were mostly males aged between 20 and 35 years. The most commonly reported effects of NPS were psychotic symptoms (in some cases they were different in form and content from the patients' usual symptoms) and significant changes relating to behaviour, including agitation, aggression and violence. Patients' vital signs, such as blood pressure, pulse rate and temperature, were also reported to be commonly affected. Gray *et al.*²⁸⁶ reported one death from the case reports.

Synthetic cannabinoids

User groups

Castaneto *et al.*¹³⁷ included nine surveys on synthetic cannabinoid use. One study was a world-wide online survey and another was an online survey of online drug forum users. The rest were single-country surveys of self-selected individuals (five in the USA, including two among military personnel and one among high school students; one in Australia; and one in the UK). They reported that the majority of synthetic cannabinoid users are young adults who perceive synthetic cannabinoid to be safer than non-cannabinoid illicit drugs and a favourable cannabis alternative that elicits a cannabis-like 'high' while avoiding detection by standard drug screens. Most synthetic cannabinoid smokers are men aged between 13 and 59 years, many of whom have a history of polydrug use (e.g. cannabis, alcohol and nicotine).

Side effects

Brewer and Collins¹¹⁸ summarised 24 case reports (settings and study regions were not specified in the report) with > 550 cases included. Varied presentations of psychological and physiological manifestations were reported, including vague symptoms, such as glassy/red eyes, mild diarrhoea, abdominal pain, loss of motivation, insomnia or difficulty concentrating, and more distinct signs, such as agitation, anxiety, nausea and vomiting, hallucinations, paranoia and profound tachycardia.

TABLE 5 Systematic reviews

Study	Principal focus	Population	NPS type	Types of included studies
Brewer and Collins (2014) ¹¹⁸	Problems/harms: clinical manifestations	Adolescents and adults: age range 12–67 years	Synthetic cannabinoids	Case reports
Busardo <i>et al.</i> (2015) ¹²⁷	Problems/harms: fatalities	Cases with analytically confirmed presence of mephedrone	Synthetic cathinone: mephedrone	Case reports
Castaneto <i>et al.</i> (2014) ¹³⁷	Use Problems/harms: clinical manifestations	Not specified	Synthetic cannabinoids	Wide ranging including surveys, case reports, series and retrospective case reviews
Gray <i>et al.</i> (2016) ²⁸⁶	Problems/harms: mental and physical health effects and fatalities	Adults (aged 18 years or over) with a diagnosis of SMI and a history of NPS use	All NPS	Case reports/series, qualitative interviews, explorative questionnaire study
Gunderson <i>et al.</i> (2012) ²⁹³	Problems/harms: clinical manifestations	Not specified	Synthetic cannabinoids	Case reports; semistructured interviews; toxicology laboratory studies
Kyriakou <i>et al.</i> (2015) ⁴⁰⁹	Problems/harms: clinical manifestations and fatalities	Not specified	Phenethylamines: NBOMe	Not specified
Miotto <i>et al.</i> (2013) ⁵⁰²	Problems/harms: physical and neuropsychiatric adverse effects; withdrawal	Not specified	Synthetic cathinones: bath salts	Retrospective studies, toxicology data, chemical analyses studies and case reports
Papanti <i>et al.</i> (2013) ⁵⁶¹	Problems/harms: clinical manifestations (psychosis)	Psychiatric treatment patients; A&E patients; general public calls to toxicology/poison centres	Synthetic cannabinoids	Retrospective toxicology surveys; case reports/series; human laboratory studies; interviews/surveys with synthetic cannabinoids users
Suzuki <i>et al.</i> (2015) ⁷¹⁴	Problems/harms: clinical manifestations and fatalities	Not specified	Phenethylamines: NBOMe	Case reports
Tait <i>et al.</i> (2016) ⁷¹⁰	Problems/harms: adverse events Responses: clinical management (associated treatment of adverse events)	Hospital presentations and poison centre data	Synthetic cannabinoids	Case series (≥ 10 cases) Case reports (≤ 10 cases)

NBOMe, *N*-methoxybenzyl; SMI, serious mental illness.

Gunderson *et al.*²⁹³ reported on nine studies (five case reports of toxicity, three human toxicology studies evaluating synthetic cannabinoid detection in serum and urine samples, and one semistructured interview qualitative study among inpatients on a forensic and rehabilitative psychiatric unit) with a total of 28 cases. They reported side effects including an alteration in mood or perception, conjunctival injection, xerostomia, increased pulse, hypertension, hyperventilation, diaphoresis, numbness and tingling, nausea, vomiting, tremors, muscle twitching and seizures, as well as more severe adverse effects including acute anxiety and psychotic reactions, particularly in those with an underlying biologic vulnerability.

Papanti *et al.*⁵⁶¹ reported on 41 studies with > 2200 individuals with an average age of 23 years and a male-to-female ratio of more than 3 : 1. The studies included retrospective toxicology surveys ($n = 9$), case reports/case series ($n = 25$), human laboratory studies assessing potential acute toxicological effects ($n = 4$) and interviews/surveys focusing on self-reported harms/unwanted effects identified in users ($n = 3$). Eleven studies were carried out in psychiatric treatment settings, five in consultation/liaison psychiatry settings following presentation to A&E departments, two in substance abuse services and one in a forensic setting. Furthermore, 15 studies were carried out in A&E settings, whereas nine included retrospective toxicology/poison centres' studies analysing calls concerning a suspected exposure. Reported adverse effects included florid/acute transient psychosis (six studies), persistent psychotic disorder (four studies) and relapse/worsening of a pre-existing psychosis (four studies). Two studies based on exposure calls reported psychotic disturbances in 9.4–11% of the cases, and two studies involving emergency department (ED) patients with analytical confirmation of synthetic cannabinoid recorded psychotic disturbances in 19–41% of cases. Other psychopathological issues reported in association with synthetic cannabinoid intake included paranoid thoughts/combateness/irritability (nine studies), altered perceptions/mental status (six studies), thought disorganisation (four studies), confusion (three studies), agitation/anxiety/panic attacks/restlessness (nine studies), and depression/suicidal thoughts (three studies).

Tait *et al.*⁷¹⁰ reported on 106 papers, letters and conference abstracts representing > 4000 cases. They also included \approx 1900 cases from the USA National Poison Data System for 9 months in 2010 in their report. They reported a prototypical ED presentation of a young male (59–100%) with tachycardia (37–77%), agitation (16–41%) and nausea (13–94%). The most frequent cardiovascular symptom was tachycardia, with some cases presenting with chest pain, more severe outcomes including perimesencephalic subarachnoid haemorrhage, middle cerebral artery occlusion, myocardial infarction in adolescent males and cardiac arrest. Acute kidney injury was reported in 29 cases in total, all of which required hospitalisation. Generalised tonic-clonic seizures were reported in 4% of poison centre synthetic cannabinoid reports, 14% of ED synthetic cannabinoid presentations and 15% of paediatric (0–19 years) poison centre synthetic cannabinoid reports. Gastrointestinal side effects included nausea and vomiting (13–94% of presentations) and abdominal pain, which was relieved by hot showers; these effects are similar to the hyperemesis syndromes seen with cannabis abuse. Psychiatric presentation features such as agitation, panic attacks, paranoia and hallucinations were also reported. More severe cases included the onset of psychosis (10 cases reported) in many cases with concurrent use of other substances. These cases required hospitalisation and symptoms persisted for up to 5 months and potentially included affective, suicidal or psychotic symptoms, significant self-injury, catatonic features and Capgras delusion. Synthetic cannabinoids were reported to potentially worsen existing psychosis attributable to other causes. Withdrawal symptoms were also reported in two cases. The treatment of adverse effects was reported to be mostly observation and supportive care (intravenous fluids, benzodiazepines, oxygen) with discharge within 8 hours.

Castaneto *et al.*¹³⁷ reported acute synthetic cannabinoid intoxication that could lead to ED presentation and hospitalisation and that required supportive care, benzodiazepines and fluids. Although most such patients were released within 24 hours of admission, severe adverse effects such as cardiotoxicity, acute kidney injury and psychosis resulted in hospitalisation for as long as 2 weeks. Some chronic synthetic cannabinoid users experienced withdrawal symptoms when they stopped drug intake.

Fatalities

Castaneto *et al.*¹³⁷ reported that deaths directly linked to synthetic cannabinoid use were quite rare (only four fatalities identified). Tait *et al.*⁷¹⁰ reported at least 26 synthetic cannabinoid deaths: 22 (maximum 27) in the USA, three in Europe and one in Japan.

Synthetic cathinones

Side effects

The systematic review by Miotto *et al.*⁵⁰² included 29 case reports and 11 surveys (the settings and study regions were not clearly identified in the report). They reported the following physical adverse effects: cerebral oedema, diaphoresis, hyper-reflexia, hypertension, hyperthermia, jaw tension, muscle spasms, mydriasis, myocardial infarction, respiratory distress, seizures, tachycardia, palpitations, chest pain, tremors, nausea, headaches, infections, sweating with a distinct acidic odour and negative comedowns symptomatology. A number of neuropsychiatric adverse effects were also reported, including aggression, agitation, combative behaviour, dysphoria, hallucinations, insomnia, paranoia, anxiety, psychosis and suicidal thoughts. Withdrawal has also been reported among bath salt binge users and is described as similar to, or more intense than, withdrawal from other stimulants.⁵⁰² Surveyed mephedrone users identify withdrawal symptoms similar to the *Diagnostic and Statistical Manual of Mental Disorders* criteria for stimulant withdrawal.⁵⁰²

Fatalities

The review by Busardo *et al.*¹²⁷ of fatalities attributable to mephedrone use included 10 case reports representing 18 fatal cases with analytically confirmed mephedrone in biological samples taken from the deceased. Of these fatalities, 14 were male, 2 were female and the sex was unknown in 2 cases; the average age was 28 years (range 17–55 years). Death was attributed to mephedrone intoxication in nine cases (range of post-mortem blood mephedrone concentration 1.33–22 mg/l). Six deaths were due to multiple drug toxicity involving mephedrone (range of post-mortem blood mephedrone concentration 0.04–1.3 mg/l). Three deaths were attributed to other causes to which mephedrone could have contributed (i.e. vehicular collision; severe self-inflicted injury; adverse effects of this drug, with cardiac fibrosis and atherosclerotic coronary artery disease as a contributing factor).

Phenethylamines

Side effects

Kyriakou *et al.*⁴⁰⁹ included 14 case reports in total, of which nine reported 17 cases of intoxication (including one case of attempted suicide) attributable to *N*-methoxybenzyl (NBOMe). Only one of these studies had a clearly identified study region/country, namely the UK. Clinical manifestations of intoxication included serotonergic and sympathomimetic symptoms.

The review by Suzuki *et al.*⁷¹⁴ included 10 case reports, representing 20 individual patients [85% male, average age of 20.3 years (range 15–31 years)]. The most common adverse effects included agitation (85%), tachycardia (85%), hypertension (65%), dilated pupils (55%), delirium (40%), hallucinations (40%), seizures (40%), tachypnea (25%) and fever (25%). The most common laboratory abnormalities were elevated creatine kinase levels (45%), leucocytosis (25%), hyperglycaemia (20%), transaminitis (15%) and elevated creatinine levels (10%), which were identified in only three (15%) cases. Seven cases were discharged after a short period (< 15 hours) of observation, whereas eight (40%) required admission to an intensive care unit. One (5%) required surgery for a self-inflicted stab wound.

Fatalities

From the 14 case reports in the review by Kyriakou *et al.*,⁴⁰⁹ four reported on five deaths. Suzuki *et al.*⁷¹⁴ reported three fatalities.

Summary

The literature categorised here as systematic reviews mainly comprises summaries of clinical presentation data. Reported side effects of NPS are wide ranging and include psychological and physiological manifestations, with psychiatric and other neurological manifestations, and cardiovascular, renal and gastrointestinal manifestations being the most commonly reported. Treatment of these effects appears mostly to involve observation and supportive care, although in severe cases may involve hospitalisation.

An important limitation to the current data is the difficulty of recording hospital admissions that are due to NPS because of a lack of relevant or specific *International Classification of Diseases*, Tenth Edition codes by which to identify these.¹⁰¹⁰ Further methodological development is needed to improve the monitoring of harms associated with NPS. There are no previous systematic reviews that are concerned with acute health harms in a population context, including dedicated attention to use prevalence and policy issues, or to chronic health or social harms in a longitudinal context.

Qualitative studies of novel psychoactive substance in the UK

We identified seven qualitative studies (reported in nine papers).^{183,483,538,544,876,881,884,940,1011}

Effects of particular novel psychoactive substances

Mephedrone

Two studies (reported in four papers) focused on the effects and side effects of mephedrone.^{483,544,884,940} Participants were recruited through personal contacts of the researchers and through internet forums. The findings from O'Neill⁵⁴⁴ combine data from McElrath and Van Hout⁹⁴⁰ and McElrath and O'Neill;⁴⁸³ therefore, the focus will be on the O'Neill⁵⁴⁴ paper for this study. The author interviewed two samples of mephedrone users in Northern Ireland (study 1 $n = 23$ and study 2 $n = 45$) with a similar age range (19–51 years and 19–49 years, respectively). Study 2 had a higher proportion of males (62%) than study 1 (48%). Brookman⁸⁸⁴ interviewed a sample of 12 mephedrone users in Wales with a mean age of 28 years, 75% of whom were male.

Both studies^{544,884} reported similar findings in terms of subjective effects, such as positive feelings (e.g. euphoria and well-being), and physical side effects (e.g. damage to the nose from snorting, unpleasant 'come downs'). Brookman was particularly interested in the effects of mephedrone on crime and violence and, therefore, reported more data on this subject.⁸⁸⁴ Just over half of participants had engaged in acquisitive crime to fund their use and described mephedrone as highly addictive. Violence was also commonly reported; for some this was associated with the 'buzz' phase, for others violence was more likely to be a result of the 'come down' phase or to be associated with acquisitive crime needed to fund the drug habit.

Salvia

Dalgarno¹⁸³ conducted e-mail interviews with 10 salvia users recruited from internet forums, 70% of whom were male and who ranged in age from 23 to 38 years. Experiences varied widely; some participants reported no or limited effects of salvia. There are various potential explanations for the unpredictable effects of salvia, including its short half-life. Others reported more unpredictable effects: sometimes users experienced pleasant hallucinogenic effects, although not every time they used salvia. Two participants reported some similarities to ketamine, although the effects were less predictable.

Subgroups

Chemsex

One study⁸⁸¹ conducted interviews of 30 gay men in London, of whom most (27/30) used mephedrone, typically in combination with GHB/GBL. Their mean age was 36 years and just under half (13/30) were HIV positive. Frequency of use during sex differed among participants; some used chemsex drugs only infrequently with a regular partner, and some used them only with casual partners. Others engaged in chemsex on almost a daily basis and this had a substantial negative effect on their relationships.

Most commonly, chemsex involved group sexual activity and a majority of participants engaged in more adventurous sexual activity (e.g. ano-brachial intercourse and being anally receptive to multiple men in quick succession) than when they were not using drugs. However, it is unclear whether or not this led to a greater risk of health harm. Although one-third reported injecting drugs, all reported the use of clean needles and using safe injection practices.

The most commonly reported harm was risk of overdose, particularly in relation to GHB/GBL use. Many reported dissatisfaction with chemsex in that it led to sexual selfishness. Other social harms were the effect on employment (missing work owing to withdrawal effects and a lack of career development associated with apathy and depression).

Prisoners

There was one small study of prisoners (four males in a young offenders' prison) that focused on 'spice' (a synthetic cannabinoid) use.⁸⁷⁶ All four had tried spice first in prison, after having used illegal drugs outside prison. The main reasons reported for use were it not being detected in mandatory drug testing and that it made time go quicker. The most common side effects were paranoia, a racing heart and blackouts. All participants reported perceptions of addictiveness of this drug and that high prices in prison had led to debt.

Macro factors influencing novel psychoactive substance use

O'Brien *et al.*⁵³⁸ conducted a qualitative analysis based on online interactions with NPS users ($n = 9$) and their responses to open-ended questions ($n = 93$) on an internet forum. NPS users were critical of drug policy, particularly the Temporary Class Drug Orders (TCDOs) that were being employed at that time.

O'Neill⁵⁴⁴ conducted two qualitative studies of mephedrone users ($n = 23$) and recreational drug users ($n = 45$) in Northern Ireland. Of these samples, five mephedrone users reported lower levels of drug purity and continued availability after legislation prohibiting mephedrone use and supply.

Wallis¹⁰¹¹ conducted interviews with retailers and early innovators in NPS use, and also with enforcement professionals, policy-makers and EWS representatives (sample size not reported). Participants expected that the supply of NPS was unlikely to be affected by the most recent UK legislation (Psychoactive Substances Act 2016¹) designed to prohibit all NPS. They thought that such legislation would be unlikely to affect access through the internet or the fast courier system. Participants also noted a more professional approach to marketing NPS than for traditional illegal drugs, including a focus on attractive packaging and branding, with long-term demand for particular NPS depending on competition with existing drugs in terms of price and effects.

Internet forums were considered an important channel through which to communicate information on new drugs, and retailers reported monitoring forums to determine which drugs to stock in their store. Mass media reports were also thought to influence NPS use, with spikes in the use of particular NPS receiving attention in the mass media, even when reported negatively as dangerous drugs.

Summary

Qualitative studies on NPS use in the UK are at an early stage of development. Existing studies show some potential to provide useful information on issues such as drug effects and reasons for, and patterns of, use. Such data may inform targets for behavioural epidemiological studies. Qualitative studies more generally may also make useful contributions to the study of drug market functioning and policy issues.

Responses to novel psychoactive substance use and problems/harms

This section summarises data from quantitative policy evaluation studies by country. Seven of these studies were conducted in the UK,^{7,186,592,818,839,1004,1012} five were conducted in the USA,^{590,613,628,776,1012} two were conducted in New Zealand^{162,976} and one each was conducted in Australia,¹¹⁹ Finland⁹⁵⁰ and the Republic of Ireland.⁹⁷⁸ The study characteristics including country, intervention/response, study setting, publication type, NPS type and study design are summarised in *Table 6*. There was also one study for which the country was not specified. Sixteen of these studies were on legislative control and one was on a multipronged approach that included surveillance and reporting, in addition to law enforcement and legislative changes.⁷⁷⁶

TABLE 6 Characteristics of and results from quantitative policy evaluation studies

Study country	Setting and publication type	Intervention	NPS type	Study design
Brown <i>et al.</i> (2014), ¹¹⁹ Australia	Poisons Centre; conference abstract	9 June 2013: legislation and enforcement by state and federal governments to restrict the sale of synthetic cannabinoids	Cannabinoids	Before-and-after comparison through retrospective review of Poisons Information Centre Data (5 months prior to and 5 months after ban)
Christie and MacFarlane (2016), ¹⁶² New Zealand	Addiction treatment setting; letter to editor	May 2014: ban of NPS under the Psychoactive Substances Act ¹⁰¹³	Cannabinoids	Before-and-after comparisons (12 months before and 12 months after)
Dargan <i>et al.</i> (2011), ¹⁸⁶ UK	Community setting; peer-reviewed journal article	December 2009: the classification of synthetic cannabinoid receptor agonist constituents of spice was Class B in the UK	Cannabinoids	Before-and-after comparison using product purchased from legal high websites
Kriikku <i>et al.</i> (2015), ⁹⁵⁰ Finland	Police custody: driving under the influence of drugs; toxicology unit: autopsy cases; peer-reviewed journal article	Ban of MDPV in June 2010	Cathinone: MDPV	Before-and-after comparison
Loeffler and Craig (2013), ¹⁰¹² USA and UK	Poison centre; letter to editor	The 21 October 2011 temporary federal ban on a number of bath salt compounds in the USA April 2010: mephedrone ban in the UK April 2012: ban on methoxetamine in the UK	Cathinones: bath salts; mephedrone; methoxetamine	Before-and-after comparison using data from national poison control centres
Pettie <i>et al.</i> (2016), ⁵⁹² UK	General hospital inpatient setting; conference abstract	10 April 2015: control of methylphenidate-based NPS by the UK government under the Misuse of Drugs Act 1971 (Temporary Class Drug) Order ¹⁰¹⁴	Methylphenidate-based NPS	Before-and-after comparison using hospital admissions data
Plumb <i>et al.</i> (2012), ⁵⁹⁰ USA	Poison centre; conference abstract	A state law making spice illegal	Cannabinoids	A retrospective chart review: before-and-after comparison
Reuter (2016), ⁶¹³ USA	Setting: not applicable; PhD thesis	2011: legislation criminalising the possession of ingredients used in the production of synthetic drugs	Cathinones: bath salts	Before-and-after comparison
Ryan and Arnold (2012), ⁶²⁸ USA	Poison centre; conference abstract	Control of six cathinones under Schedule I in Louisiana on 6 January 2011	Cathinones	Before-and-after comparison through secondary analysis of the National Poison Data System (December 2010 – month prior; and February 2011– month after ban)

TABLE 6 Characteristics of and results from quantitative policy evaluation studies (continued)

Study country	Setting and publication type	Intervention	NPS type	Study design
Sheridan <i>et al.</i> (2013), ⁹⁷⁶ New Zealand	Internet; peer-reviewed journal article	Prohibition of BZP-containing party pills and related substances from 1 April 2008 (provided for a 6-month amnesty period in which possession of small quantities for personal use was permitted)	Piperazines: BZP and related substances	Before-and-after comparison through an internet-based survey among adults aged 18–30 years
Smyth <i>et al.</i> (2015), ⁹⁷⁸ Republic of Ireland	Specialist alcohol treatment service: Youth Drug and Alcohol service; peer-reviewed journal article	2010: legislative changes in Ireland – adding > 100 NPS to the Misuse of Drugs Act ¹⁰¹⁵ and restrictions on the sale of psychoactive substances ¹⁰¹⁵	All NPS	Before-and-after comparisons (before: 6 months prior to 10 May 2010; after: 6 months after 10 May 2011) using data from the National Drug Treatment Report System
Wahl and Theobald (2013), ⁷⁷⁶ USA	Poison centre; conference abstract	A multipronged approach of surveillance, reporting, law enforcement partnership and legislative changes	All NPS	Before-and-after comparison with national averages
Winstock <i>et al.</i> (2010), ⁸¹⁸ UK	Internet survey; letter to editor	April 2010: classification of mephedrone and similar compounds as Class B substances in the UK under the Misuse of Drugs Act ¹⁰¹⁴	Cathinone: mephedrone	Before-and-after comparison: findings from an online survey conducted in June 2010 compared with those from one in November 2009, and another telephone survey in 2010 before the legislation
Wood <i>et al.</i> (2011), ⁸³⁹ UK	ED; conference abstract	Control of cathinones under the UK Misuse of Drugs Act 1971 on 16 April 2010 ¹⁰¹⁴	Cathinones: mephedrone	Before-and-after comparison through secondary analysis of ED data (8 months each side)
Wood <i>et al.</i> (2011), ⁷ UK	ED; peer-reviewed journal article	Control of cathinones under the UK Misuse of Drugs Act 1971 on 16 April 2010 ¹⁰¹⁴	Cathinones: mephedrone	Before-and-after comparison through secondary analysis of ED data (12 months each side)
Wood <i>et al.</i> (2013), ¹⁰⁰⁴ UK	Nightclubs (gay-friendly); conference abstract	Control of methoxetamine under the Temporary Class Drug Order (TCDO) legislation in March 2012	Methoxetamine	Before-and-after survey comparison (July 2011 and July 2012)

PhD, Doctor of Philosophy.

UK

Dargan *et al.*¹⁸⁶ evaluated the impact of the December 2009 classification of synthetic cannabinoid constituents of spice as Class B on the components in 'spice' products. They purchased 16 and 20 spice products from online sources before and after the classification, respectively. They found that classified synthetic cannabinoid receptor agonists continued to be supplied over the internet to UK users. The proportion of spice products that were purchased online containing at least one classified synthetic cannabinoid fell to 85% of all pre-classification sources. Furthermore, new synthetic cannabinoid receptor agonists not covered by the legislation appeared after legislative controls.

In April 2010, cathinones such as mephedrone and similar compounds were classified as Class B substances under the UK Misuse of Drugs Act, 1971. In their online survey of 150 mephedrone users, Winstock *et al.*⁸¹⁸ found a decrease in the number who continued to use mephedrone after classification. There were also changes in access to, and sources of, mephedrone, with a 40% increase in purchases from dealers and a significant increase in the mean price per gram of mephedrone from £10 to £16. Loeffler *et al.*¹⁰¹² reported a decrease in the number of poison control centre contacts regarding mephedrone. Wood *et al.*⁸³⁹ reported a reduction in the levels of presentations to the ED with toxicity associated with self-reported mephedrone use, from 57 in the 8 months before the reclassification to 47 in the 8 months after. In another study, the level of presentations fell significantly in the first 6 months following reclassification to a steady level of three to five presentations every 2 months in months 7–12 following reclassification.⁷

Loeffler *et al.*¹⁰¹² reported a decrease in the number of poison control centre contacts regarding methoxetamine after its ban in the UK in April 2012. However, Wood *et al.*¹⁰⁰⁴ reported a significant increase in lifetime, past year and past month use of methoxetamine from 2011 to 2012 among ED attendees (lifetime 2011: 6.1% vs. 2012: 21.0%, $p < 0.001$; last year 2011: 4.8% vs. 2012: 19.2%, $p < 0.001$; last month 2011: 1.9% vs. 2012 10.1%, $p < 0.0001$) after its control under the TCDO legislation in March 2012. Data were collected via two non-randomly sampled surveys, with 315 respondents in July 2011 and 330 respondents in July 2012, respectively.

A study by Pettie *et al.*⁵⁹² evaluated the impact of the 10 April 2015 control of methylphenidate-based NPS by the UK government under the Misuse of Drugs Act 1971 TCDO. They found 290 drug-related admissions in the 6 months before and 263 in the 6 months after control for all substances. Admissions associated with NPS decreased from 192 (66% of total admissions) pre-control to 135 (52%) post control. Methylphenidate NPS-related admissions reduced significantly from 88 pre-control to eight post-control. However, synthetic cannabinoid admissions increased from 22 patients before to 60 patients after the legislation, as stimulant NPS admissions (methiopropamine and cathinones) increased from 12 to 27. Hospital admissions associated with opioid (heroin, dihydrocodeine, methadone) toxicity increased from 83 (29%) to 109 (41%) after control. Benzodiazepine admissions also increased from 17 to 37 cases in the 2 months before and after legislation.

USA

In their study evaluating the impact of the October 2011 temporary federal ban on a number of bath salts (synthetic cathinones) in the USA, Loeffler *et al.*¹⁰¹² found that the ban resulted in a decrease in the number of poison centre contacts regarding mephedrone and bath salt compounds. Reuter⁶¹³ examined the 2011 legislation criminalising the possession of ingredients used in the production of synthetic drugs using Arizona poison control data and found that bath salt use decreased following criminalisation. Control of six cathinones under Schedule I in Louisiana on 6 January 2011 was reported to have resulted in a 94.5% decrease in the number of synthetic cathinone calls to the Louisiana Poison Centre from 110 to 6.⁶²⁸

A conference abstract by Wahl and Theobald⁷⁷⁶ reported that a state-based multipronged approach of surveillance, reporting, law enforcement partnership and legislative changes for all NPS resulted in a decrease in cathinone derivative exposure from 11% higher to 59% below the national average during a 25-month surveillance period. Exposure to cannabinoids also decreased from 30% higher to 78% lower than the national average during the same period.

Plumb *et al.*⁵⁹⁰ reported on a state law making spice illegal which resulted in significant decrease in the rates of synthetic cannabinoid exposures reported to the poison centre from 16 months before to 13 months after the legislation.

New Zealand

On 1 April 2008, BZP-containing party pills and related substances were prohibited in New Zealand. The prohibition provided for a 6-month amnesty period in which possession of small quantities for personal use was permitted. A study by Sheridan *et al.*⁹⁷⁶ examined longitudinally the effect of prohibition on use in

273 participants. They found that, overall, the use of BZP party pills significantly decreased over time. However, both time points of the survey were after the ban (the first survey included retrospective questions for use 6 months previously). Christie and MacFarlane¹⁶² reported a reduction in presentations for clinical management of synthetic cannabinoid effects in an addiction treatment setting from 47 in the 12 months before the May 2014 ban of NPS under the Psychoactive Substances Act, to 24 in the following 12 months.

Australia

In Australia, Brown *et al.*¹¹⁹ reported a reduction in the number of synthetic cannabinoid cases reported to the poison information centre from 70 in the 5 months prior to June 2013 legislation and enforcement by state and federal governments to restrict their sale to 20 cases in the 5 months following.

Finland

Kriikku *et al.*⁹⁵⁰ reported that the number of MDPV-related driving under the influence of drugs and autopsy cases decreased markedly after its ban in June 2010.

Republic of Ireland

In 2010, legislative changes in the Republic of Ireland resulted in > 100 NPS being added onto the Misuse of Drugs Act, and restrictions on the sale of psychoactive substances. Smyth *et al.*⁹⁷⁸ conducted a before-and-after comparison (before: 6 months prior 10 May 2010; after: 6 months prior 10 May 2011) using data from the National Drug Treatment Report System. They reported a range of reductions in presenting substance use with the exception of NPS oral pills. Lifetime rates of use were similar between the two periods.

Summary of findings

Most studies presented here evaluated the effects of legislative prohibitions of NPS use or supply on a wide range of outcomes including access, use, health-care utilisation and self-reported exposure and toxicity. Positive outcomes are generally observed, although studies typically utilised simple counts of routinely collected data, particularly poison centre and hospital admissions data. The study designs were mainly before-and-after comparisons without any controls, which makes the attribution of effects difficult. There is a need to examine the utility of routinely collected NPS data in different settings and sources of information bias, and to evaluate pharmacovigilance and other data. This will allow more rigorous study designs capable of assessing major policy changes.

Conclusions

Main findings

The main finding is that the literature on NPS use, problems and responses is currently at a very early stage of development in terms of being capable of informing public health decision-making. Nationally representative surveys on prevalence are available for the UK. However, the most comprehensive data are on mephedrone, with data on NPS use as a whole, and on particular NPS other than mephedrone being much less developed, and comparisons across years are not yet possible. Data on reasons for, and patterns of, use are largely limited to a small number of qualitative studies.

For problems or harms attributable to NPS use, we identified a large number of case reports/case series of acute intoxication, toxicity, emergency presentation or similar data. There were also 10 systematic reviews of this literature, which mostly reported psychiatric and other neurological manifestations and cardiovascular, renal and gastrointestinal adverse effects, the treatment of which was mostly observation and supportive care. There are also limited data on subjective adverse effects of NPS use from few qualitative studies. Literature on acute health harms in a population context is also limited, as is literature on adverse effects attributable to long-term regular NPS use and chronic health or social harms in a longitudinal context.

We identified studies evaluating the effectiveness of regulation or prohibition of NPS possession or supply. Seventeen of these studies were quantitative evaluation studies, 16 of which evaluated the effects of legislative prohibitions of NPS use or supply, and one of which evaluated a multicomponent intervention comprising surveillance, reporting, law enforcement partnership and legislative changes. Overall, the studies reported generally favourable effects on a number of outcome including access, use, health-care utilisation and self-reported exposure and toxicity. However, most outcomes were simple counts of routinely collected data (poison centre/hospital admissions data) and all studies were before-and-after comparisons without any controls, which makes rigorous attribution of changes to intervention effects challenging.

Strengths and limitations of the study

Strengths

This study utilised a multistaged, multipronged analytical approach, as summarised in *Figure 13*. This involved the development of a conceptual framework hypothesising an evidence-informed public health approach to NPS use in the UK (see *Chapter 3*) and systematic review work that comprised a scoping review evidence mapping stage, evidence gap analysis in relation to a priori research questions and a narrative presentation/synthesis of four selected bodies of literature. Two researchers independently selected articles and extracted data in order to minimise selection bias and errors in data extraction. The findings of the scoping review were interpreted in light of the conceptual framework. Together, these strands of conceptual and empirical research were used as the basis of a set of research recommendations. Although the review and conceptual framework findings were quite distinct, the analytical approach afforded high-level integration of findings, with the main observation being that the existing literature does not resemble what we think may be needed for an evidence-informed public health strategic approach, and there is a reasonable level of support for our view in the research recommendations made in the existing studies themselves. In addition to what is presented in *Figure 13*, the findings of the review work, conceptual framework and the draft research recommendations derived from these were shared and

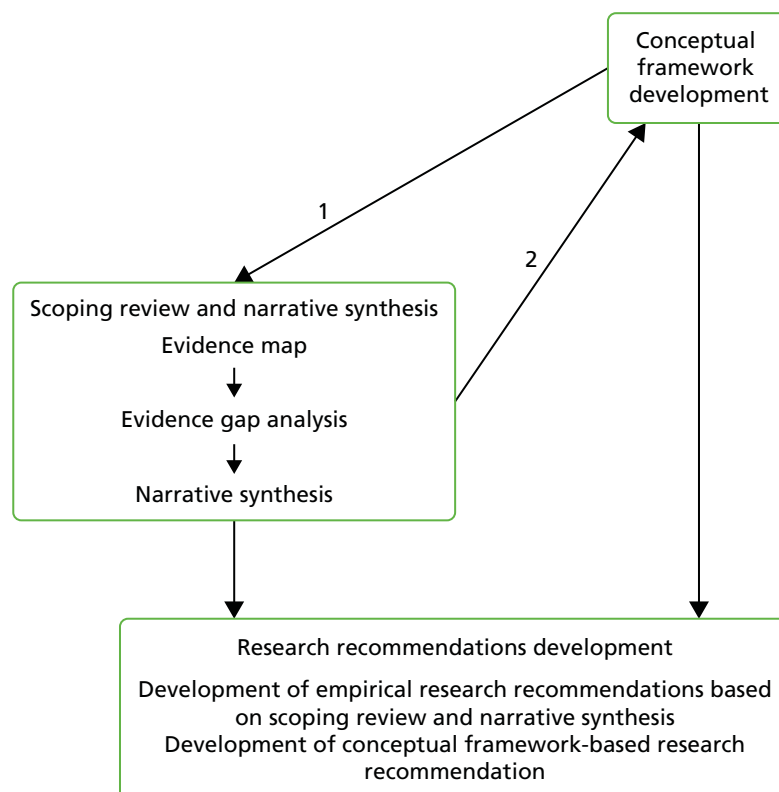


FIGURE 13 Overarching analytical approach. 1 = Interpretation of scoping review and narrative synthesis findings in light of conceptual framework; 2 = planned revision of conceptual framework in light of the systematic review findings.

discussed with one NPS user, five user carers (who attended a group discussion at a face-to-face user carer forum), four policy-makers and five researchers (who constituted the project steering group; see *Chapter 4*). The feedback from these three groups was utilised to refine and finalise the research recommendations (see *Chapter 5*). It is intended that this analytical approach, and the transparency with which it is presented, has enhanced the validity and rigour of the research recommendations drawn from this work, as well as their relevance to the UK context.

Limitations

A risk-of-bias assessment was not conducted because of the large number of articles identified. In addition to the size of this body of literature, however, the areas covered by this review that were not already covered by systematic reviews were judged not to have adequate study numbers and/or study quality and/or study findings sufficient to warrant a systematic review. In most cases the study designs were such that it is difficult to establish the nature of relationships between NPS use and problems/harms, or responses to NPS use and outcomes. This was also a pragmatic decision, made while mindful of time pressures and in light of the need to undertake this work quickly in order for it to be as useful as possible.

Possible implications for research recommendations

There are a number of evidence gaps identified in the scoping review and narrative synthesis. First, there are a number of areas in which literature is scarce (a priori research questions 2, 3, 5–10 and 12). Second, even in those areas in which some literature was identified, at a high level of generality, existing studies are not sufficiently well advanced to be able to meaningfully inform public health approaches to NPS use. For example, there is need for epidemiological research on acute health harms (i.e. undertaken in a population-at-risk context), as well as on chronic health and other health and social harms attributable to regular NPS use. There is an obvious need for more rigorous study designs capable of assessing major policy changes. In addition, there is a need to examine the utility of routinely collected NPS data in different settings, as well as pharmacovigilance data, including sources of information bias.

Chapter 3 What might an evidence-informed public health approach to novel psychoactive substance use in the UK look like? A conceptual framework

Background

There has been increasing international concern about the use of NPS, also known as 'legal highs'.¹⁰¹⁶ NPS can be defined as narcotic or psychotropic drugs that are not currently controlled under the United Nations drug control conventions.^{982,1017–1019} The principal drug types currently identified in the UK are presented in *Table 7*. The number of new substances reported annually to the European Union EWS increased seven-fold between 2008 and 2013.⁹⁰⁹ Some NPS may be structurally similar to other known drugs, whereas others may be quite different. Nonetheless, many NPS have been previously synthesised and are, therefore, newly available, popular or 'rediscovered' rather than newly created as such.^{979,982} It is thus appropriate to question the precise meaning of the term, and the value of such a category.

Novel psychoactive substances have posed challenging problems for policy-makers. They have become widely available through the internet at a low cost, and their legal status may promote connotations of safety before their possession is made illegal.^{910,1017} Technological developments and the globalisation of trade and communications have facilitated major innovations in drug production and supply.¹² Refinements can be made to the design of synthetic mood-altering drugs rapidly, in response to consumer demand, and such drugs can be produced and shipped on an industrial scale. The United Nations Office on Drugs and Crime has accordingly declared that 'the international drug control system is floundering'.⁹⁸² For the UK, the most obvious demand to date has been among existing drug users who have extended their repertoires,

TABLE 7 Main NPS types

NPS type	Description	Example(s)
Synthetic cannabinoid	Chemicals that are often similar in molecular structure to THC, the main psychoactive component in cannabis. The term may also describe chemicals with different structures but similar effects. Effects: similar to cannabis	'spice gold'
Synthetic cathinones	Related to cathinone, a monamine alkaloid and a key stimulant in khat. The most common synthetic cathinone used as an NPS is mephedrone. Effects: stimulant similar to amphetamine, cocaine and MDMA	'm-cat' (mephedrone), 'mexe' (mexedrone)
Phentylamines	Broader class of stimulants and hallucinogens, including mescaline, amphetamine and MDMA. NPS used include benzodifurans and the 2C series. Effects: stimulant, hallucinogenic and/or empathogenic	'Bromo-Dragonfly', 'FLY'
Piperazines	Class of synthetic chemicals within a piperazine functional group. NPS include BZP (used extensively in New Zealand in the early 2000s as a legal and reliable alternative to MDMA) and mCPP. Effects: euphoric, similar to MDMA	'party pills', 'smileys'

mCPP, meta-chlorophenylpiperazine; THC, Δ^9 -tetrahydrocannabinol.

Sources: EMCDDA and UNODC.

Note

Definitions of NPS vary and GHB and ketamine are sometimes included. They are excluded here because they are extensively legally controlled and are not recently synthesised.

rather than the recruitment of new populations.¹⁰²⁰ Nonetheless, the UK Government's ACMD has identified this phenomenon as having 'changed the face of the drug scene remarkably and with rapidity'.¹⁰²¹

Concerns about the future is prominent in discussions of NPS, including possible epidemics of dangerous drugs, as well the health harms consequent on long-term use of less-risky drugs.^{982,1017,1018} It is widely perceived that the most strongly evidenced public health approaches to psychoactive substances in general (controlling affordability through pricing and other demand reduction strategies, and regulating supply and other dimensions of availability such as cultural acceptability for tobacco, alcohol and illicit drugs) are inapplicable to NPS, leaving little capacity for evidence-based responses.^{1022–1026} For these reasons, we undertook a conceptual exercise that sought to elaborate what an evidence-informed public health approach to NPS use in the UK might look like.

Methods

This work was done iteratively in two main stages. We began with discussions about the nature of the phenomenon, as reflected in the preceding text. This process informed pragmatic decisions about literature that might be helpful to consult, and we chose to consider the evidence bases on tobacco, alcohol and illicit drug use, and developments in drug policies. We discussed the nature of contemporary public health and possible similarities between NPS and other complex multisectoral and public health challenges, particularly in how they were conceptualised and strategically approached. We then developed a preliminary version of a hypothetical public health approach to NPS based on the literature examined and on our interpretation of possible relevance. From this, we identified possible research data needs to complete the first stage of this work. We then utilised this stage 1 version to interpret the data from the review.

The review findings indicated that the existing literature, although large, is at an early stage of development, and there are currently meagre data to inform directly what we hypothesised to be an evidence-informed public health strategic response to NPS. The conceptual framework itself was thus not significantly altered in stage 2. The main changes related to the *Discussion* section, where we substantially revised our interpretation of the possible implications of the framework given the review data.

Results

The changing context of developments in drug policies

Legal prohibition of drug possession has been the cornerstone of the societal response to illicit drugs for a century.¹⁰²⁷ Although a public health approach to drugs is often counterpoised to that of law enforcement, this can be regarded as a false dichotomy, as the illegality of drugs can in certain circumstances raise prices and restrict availability (both generally effective approaches for addictive behaviours), and reduce use and associated harms.¹⁰²⁴ In addition, treatments such as opioid substitution treatment can reduce crime.¹⁰²⁴ While initially introducing TCDOs to rapidly bring individual NPS under legal control, the UK government has decided to follow Ireland by making all psychoactive substances illegal to produce and supply, without prohibiting possession or considering potential harm.⁷⁰⁵

Decriminalisation of drug use and other recent global policy innovations, including the quasi-legalisation of cannabis production and supply in some US states and in Uruguay,^{1028,1029} provide another context for thinking about NPS. Data are beginning to emerge on the effects of these policy changes,¹⁰³⁰ although rigorous evaluation studies are needed. The use of drugs remains a controversial and difficult issue for society, although seemingly not as difficult as it once was.^{1031–1035} The goals of drug policy are now less contested, as there is greater recognition of the limitations of sole reliance on prohibition, and more willingness to address tobacco, alcohol and drugs together.¹⁰³⁵ Use reduction is now more widely accepted as a vehicle for harm reduction, reducing problems among users, and those directly and indirectly affected by drug use, as well as reducing the overall societal burden.^{1026,1033}

Contemporary evidence-informed public health

The history of public health has been strongly influenced by the growth of scientific knowledge, the rise of the welfare state and an increased focus on lifestyle risk factors in recent decades.^{1036–1038} The evidence required to inform any public health approach is to some extent determined by how public health itself is defined. Contemporary definitions highlight the improvement of population health and wellbeing.^{1039,1040} The underpinning rationale for strategic public health approaches that move the entire population distribution of risk in a more healthy direction was based on data showing that a large number of people at lower risk can often result in greater health burden than a smaller group at higher risk (the prevention paradox).^{1041,1042} In addition, individual or group behaviour is usually socially influenced and thus contextually dependent, so modifying population factors underlying the risk distribution may be more effective than seeking to encourage high-risk individuals to act against social norms, both for those at high risk and for the rest of the population.^{1041,1042}

Many contemporary public health challenges have been conceptualised as requiring complex adaptive system changes.^{1036,1038} Mehta *et al.*¹⁰⁴³ provide a useful example of how contemporary thinking on public mental health can draw on well-established ideas, such as the biopsychosocial model of health, and about levels of prevention in addressing such complex challenges. Complex challenges often require that careful attention is given to future risks, which are somewhat unpredictable in scale and are likely to impact differently on different groups,¹⁰⁴⁴ rather than to current harms. For example, frameworks for responding to the health impacts of climate change highlight the importance of building the evidence-base through surveillance of morbidity, mortality and health system indicators, and modelling trend data for future risks including contextual factors impacting on risk of harm.^{1045,1046}

The social ecological framework offers one way of thinking about complex public health issues.¹⁰⁴⁷ This also encourages multilevel conceptualisations of problems and invites multilevel strategic responses.¹⁰⁴⁸ For example, risk behaviours and intervention targets can be understood as being shaped by interactions between the micro- (e.g. family, school, neighbourhood), meso- (interactions between the different micro-systems), exo- (systems that impact on the micro-system such as worksite policies) and macro- (cultural values, norms and laws) levels.¹⁰⁴⁹

Obesity is another example of a socially structured public health challenge where risk differs substantially between groups in a given population, which may also be facing a malnutrition problem.¹⁰⁵⁰ Relevant unhealthy behaviours cluster, particularly among more socioeconomically deprived populations. The World Health Organization Commission on childhood obesity uses a multilevel social-ecological approach to identify the need for interventions targeted at contextual factors such as political (e.g. fiscal policy), built (e.g. urban planning and design), social (e.g. norms in different groups) and family (e.g. parental knowledge, norms, behaviour) environments. In addition, they recommended a life-course approach, arguing that the key contextual risk factors that impact on obesity differ through the life course.¹⁰⁵¹ Targets for prevention thus need to be conceptualised at environmental levels, and in long-term individual developmental perspectives.

Towards a hypothetical prevention systems approach to novel psychoactive substances

We make a number of assumptions here, which we shall revisit to interrogate their validity. We hypothesise that the challenges posed by NPS have many of the features of the complex problems previously discussed. Hypotheses on NPS can also take advantage of the conceptual frameworks already developed for other drugs.^{1022,1026} Figure 14 provides a conceptual map of key individual-level risks and harms attributable to NPS adapted from those developed for other forms of drug use, and incorporating an overarching biopsychosocial perspective. Apart from the acute effects, most forms of harm develop over time. Beyond potency and toxicity, harms to individuals, whether they are health-specific or wider harms, will be strongly shaped by environmental and contextual influences dynamically interacting with life-course stages. Prevention therefore has the potential to interrupt the evolution of harm over time, and this is insufficiently recognised.¹⁰⁵² Intervention targets for prevention extend far away from those that are proximal to acts of drug use, as attention is warranted to social structural influences that shape individual

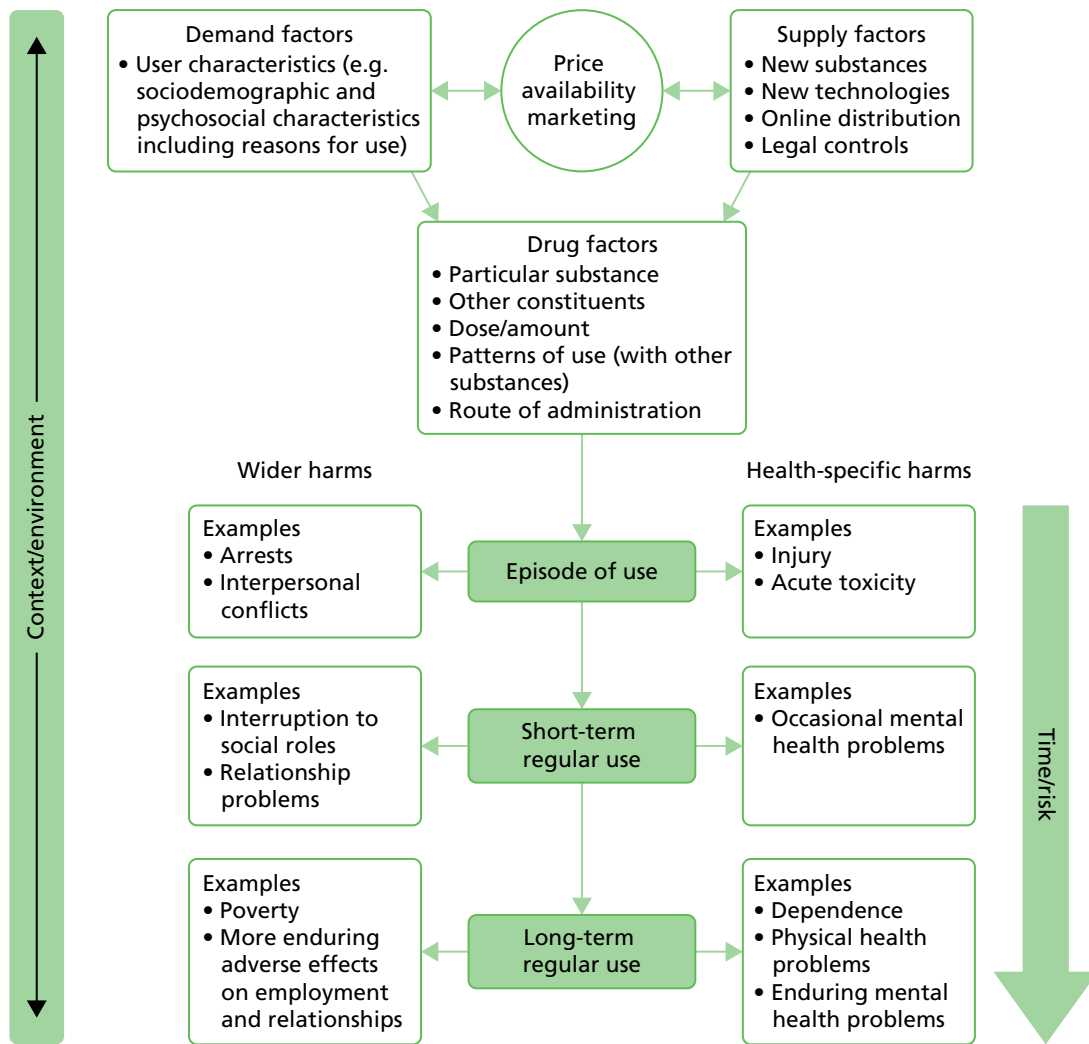


FIGURE 14 A model of risks and harms attributable to NPS use.

risk. Other drug use, both licit and illicit, should be expected to be implicated in the production of harm where other drugs are being used, and it will be rare that none are.

Problems also manifest themselves at levels beyond the individual user, for example involving family members and local communities.^{1053,1054} Harms to society, for example, include the costs of health care, crime and law enforcement.¹⁰⁵⁵ Health impacts incurred by NPS users can be aggregated with measures of physical and/or mental health, quality-adjusted life-years (QALYs) lost, and by applying a monetary value to QALYs lost. Impacts on education among young people can lead to adult employment and economic productivity harms, to which an economic cost can be attributed.

Box 1 provides a thought experiment. There are no obvious problems with NPS use, and one possibility is that there is no role for public health responses and that the Smith family just get on with their lives. Alternatively, we suggest that a prevention orientation, informed by appreciation of risk generation over time, offers the most appropriate long-term public health response. This suggests the need to intervene environmentally, and early, in order to prevent harms, which may develop to become more widespread and more intractable in the absence of prevention.

BOX 1 A portrait of NPS use in the 'Smith family'

The Smiths (father Peter, mother Jane, 18-year-old son Tom, 16-year-old daughter Karen, and 14-year-old son Jack) are an unremarkable family. Both parents work locally and receive family credits to supplement their incomes. The children are doing OK at school, and the school itself is not bad. Tom does not know what he will do after leaving school next summer and Karen is thinking about going to college. Outside school they do the same things as their friends: Tom plays football, Karen plays computer games and spends a lot of time online, and Tom and Jack are into music. They are comfortable in their home, which they part-own, and live in an area that used to have a problem with burglaries.

There are no big health problems in the family. They are not into sports or exercise, apart from Tom. Peter drinks more alcohol than is good for his health, although he definitely would not consider himself an alcoholic or feel comfortable talking to his general practitioner about his drinking. He misses work occasionally on Mondays. Jane has times when she is depressed, for which she takes medication. She drinks occasionally and gave up smoking 5 years ago.

Tom does not smoke. He usually goes to nightclubs at the weekend, where he takes drugs that are sold to him and his friends such as ecstasy and mephedrone. He also usually drinks alcohol in bars before going on to clubs. Karen smokes a few cigarettes each day and has a joint most days. She smokes herbal cannabis and sometimes spice, a synthetic cannabinoid, with her 18-year-old boyfriend and his friends. She tends to smoke spice when they are out of cannabis or when they hear it is particularly good. Her mum worries about her. The group she smokes with have a reputation for getting into trouble. Jack has got really drunk twice, and drinks alcohol only at parties with his friends. Jack has not used any drugs because, he says, he does not like smoking and has heard bad things about pills and powders.

Table 8 offers a presentation of how a systems-based prevention approach may be applied in this situation. This presentation is illustrative, as it is also possible to conceptualise levels differently, for example separating family and peers, in such a system. Note that there is no compelling logic to any NPS-only response, as factors that impact on NPS use do not appear to differ from those that impact on the use of other drugs. Interventions may be designed to target a single level (e.g. family), and may be effective in so doing. Their effectiveness, however, will be limited by the influence of variables in other levels of this system, which is important to assess for intervention decision-making. This presentation calls attention to the adequacy of existing responses and their longer-term consequences, as decisions not to intervene, or to intervene weakly, will also have consequences that should be considered.

TABLE 8 Examples of public health opportunities for responding to risk

Approach	National	Local	Family and peers	Individual
Health	Health services and public health policies; tobacco control policies	Local health service provisions and public health actions	Parental general practice and other NHS contacts; peer network intervention projects; health promotion campaigns	NHS contacts (e.g. general practice, sexual health services, A&E); online and telephone helplines; counselling services
Multisectoral	Housing, employment, education and welfare and economic policies; drug and alcohol policies	Policing, education, community development, licensing and other local authority policies and services	School drug education; youth services provisions; family support services; community groups	School mentoring and counselling; criminal justice system contacts

How well does this approach address health inequalities issues? This is important to consider explicitly, as whole-population approaches have been shown to alter the shape of the distribution of risk within a population as it moves to the left (i.e. less risk for the population as a whole but greater absolute or relative risk in subgroups), as has happened, for example, in relation to tobacco.¹⁰⁵⁶ This happens because those with more psychosocial resources for health gain greater health benefits than those with fewer resources, for whom such inequalities exert pervasive health effects.¹⁰⁵⁶ It is also well established that problematic drug use is more concentrated in deprived communities.^{1057–1059} This consideration suggests the need for an integrated strategy of multilevel whole-population and vulnerable subpopulation interventions that address the environmental causes of the distribution of risk within populations. Capacity to incorporate attention to health inequalities and their associated social determinants at the local level may already exist owing to the devolved nature of the UK public health system.¹⁰⁶⁰

A priori data needs

Having considered hypothetical determinants of NPS use, risk and harm, and the breadth of possible responses, attention to the empirical data needed to inform public health decision-making is warranted. Acute health and wider problems will be experienced following particular episodes of use, most likely in relation to intoxication or direct poisoning (see *Figure 14*).¹⁰²⁴ Presentations to health services and community safety indicators may provide data on trends in the potency and toxicity of NPS, taking account of possible sources of information bias in existing routine monitoring systems. Chronic mental health, physical health and social problems may develop over the longer term as a consequence of regular use, with risk accumulating over time as involvement in drug use continues. Where drug use escalates, and consumption becomes heavier, risks will accumulate faster.¹⁰²² Existing routine data sources are quite likely to be relatively insensitive to changes in patterning of risks, and prevalence and incidence of harms, unless they become severe. Dedicated research studies or highly sophisticated monitoring approaches may be more likely to be needed to provide more detailed investigations of these sorts of issues.

This discussion has largely avoided disaggregating the category of NPS, as the points made may be seen to apply with greater or lesser force to all NPS. Dedicated attention to individual NPS drug types is also needed, as the public health burden associated with each will vary according to the harms that are consequent on their use and to their use prevalence. Capacity to identify new NPS early, particularly those that are more potent or more toxic, and to track their spread, is foundational to appropriately calibrating the required responses. Indeed, distinctions between NPS and existing drugs may be expected to reduce over time, with particular NPS drug types considered alongside more established drugs if and when they become more prevalent.

Gradual deterioration of organ function as a result of toxicity may be a key biological mechanism involved in stable longer-term patterns of use and this will be difficult to detect early in all but the most severe instances. The development of dependence may occur at different rates for different drugs and patterns of use,¹⁰⁶¹ although it is largely driven by the extent of involvement in drug use.¹⁰⁶² Dependence may occur in isolation from other psychosocial difficulties, although this is rare in addiction treatment populations.¹⁰⁶³ Dependence itself is also an important mediator of other harms.¹⁰²⁴ Scrutiny of routine health services data will be useful for the examination of trends in dependence and other presenting problems,¹⁰⁶⁴ and will be quite likely to need to be supplemented by dedicated studies that capture population data on the prevalence of dependence and other problems.

There are two key issues revealed by this preliminary consideration of data needs. First, existing data sources are likely to be profoundly biased towards both severe and episodic problems and less likely to be directly informative about patterns of use, risk and harm in the general population over the longer term. Second, it is assumed that NPS use is identifiable, either as a result of self-presentation or toxicology, the provision for which will vary across settings. There may be many circumstances in which this is problematic, for example when episodic or regular use occurs alongside other drug use and/or when it is not clear what the cause of the problem may be or the contribution of NPS to it. NPS markets may be thought of as more complex drug markets, where products may be branded without any necessary correspondence to

contents, and consumers may be more willing to accept unbranded and unknown content. As part of an effective pharmacovigilance system, simple case finding approaches may need to rely in the first instance on generic screening tools for drug use, which appear to be effective for other forms of drug use, prior to more in-depth drug use assessment.¹⁰⁶⁵ Again, data from health-care services and other sectors will identify NPS use where it is most obvious, and will be vulnerable to missing the contribution that NPS use makes to other presenting problems (e.g. mental health). Communicating the risks associated with particular NPS drug types poses challenges even when such data are in place.

Basic epidemiological data on the prevalence and incidence of NPS use and problems may be difficult to obtain in a timely manner owing to rapidly changing trends, hence the prominence of toxicological surveillance and the development of EWSs in the existing first wave of responses to NPS.^{909,982,1066}

Qualitative and quantitative studies investigating patterns of use in potentially important subpopulations (such as homeless people, those with serious long-term mental health problems and prisoners), or derived from emergency health-care presentations, can be informative on issues such as constituents, doses and other drugs being used simultaneously.^{757,761} The more such studies give rigorous attention to sampling, the more straightforward the consideration of generalisability will be.

Novel psychoactive substance data collection can be added to existing large population cohort studies.¹⁰⁶⁷ 'Prevention systems' approaches,¹⁰⁶⁸ as hypothesised here to be relevant to NPS use, require strong health services research investment on both NPS use and drug use more broadly. Observational studies of the actual operation of prevention systems, with robust designs capable of identifying key characteristics associated with effectiveness are needed, as are evaluation studies of any innovations.¹⁰⁶⁴

A consideration of NPS data needs also calls attention to the scrutiny of the adequacy of the existing drug research infrastructure. The past year prevalence of ecstasy use declined among 16- to 24-year-olds from approximately 6.8% in 2001/2 to average approximately 3.8% over the past 5 years.¹⁰²⁰ It is not known to what extent, if any, this may be due to NPS use and/or whether other factors may be responsible for this fall. There have also been reductions in the prevalence of alcohol consumption among young people across the world,¹⁰⁶⁹ and a similar question could be posed. We suggest that consideration of the need to build the NPS evidence base should examine such inter-relationships and pay attention to the research capacity for drug and alcohol research more generally.

Validity issues

We now offer a brief assessment of the validity of the underlying assumptions and discuss some study implications. We suggest that there are five key logical steps taken in building this framework for which counterfactual reasoning can be applied as follows.

1. NPS are not in fact like other drugs; there is something different about them.
2. The complex systems conceptualisation is not appropriate for NPS.
3. The life-course approach is inapplicable to NPS.
4. The prevention system cannot or will not operate in the way proposed; the multilevel contribution of system elements is unattainable, even if desirable.
5. A high-risk population approach may be preferable only as it is easier to implement.

Steps 1–3 are dealt with together because individually and collectively they are foundational to much thinking in contemporary public health. It is either implausible that they are true, or it is the case that existing public health evidence and ideas are much weaker than they seem. We prefer the former explanation. Although the production, distribution and retail of NPS may have features that distinguish them from other drugs, in other respects the user populations and drivers of demand and supply are similar, and in the future they may be even more so.

There are, of course, likely to be limits to the extent to which approaches to NPS can be informed by comparisons to addressing challenges such as public mental health, climate change or obesity. Perhaps this is less true of drawing on thinking about other forms of drug use, although a key weakness in this area is that arguably too much existing thinking about risk and harm occurs at the individual rather than the population level (reflecting the historical development of addiction sciences for alcohol and drugs in particular). Drawing together population-level data on risk and harm may be a sensible response to this conceptual weakness. Similarly, although the prospect of early (in the life course) interventions for prevention may be alluring, what are the clinical, public health and wider public policy responses to harms that are occurring now, and how extensively do they provide a firm foundation on which to build?

Step 4 is difficult to rebut. Although multisectoral contributions self-evidently have some part to play, it is highly aspirational that they can work in synergy to meaningfully form a system, as is proposed. This will require resources and high-level political commitments that may seem far-fetched in times of austerity in public sector finances. Although a counter argument in terms of the long-term costs and consequences may seem reasonable, this does not diminish the extent to which major efforts to initiate and maintain such systems are probably required. This is a serious objection.

Step 5 is valid in its own terms and is also particularly limited in respect of the neglect of action on upstream determinants. This ignores much that has been learnt in public health about the importance of prevention. High-risk subpopulations may be difficult to reliably identify, particularly where evidence is limited. It should be noted that we do not suggest avoiding the targeting of high-risk subpopulations but rather that this should be undertaken alongside whole-population interventions in line with the strategic approach developed by Rose.¹⁰⁴²

If the counterfactual reasoning to both steps 4 and 5 appears attractive, one might look more bleakly on the prospect of influencing, never mind exercising control over, future trends in drug use. One may also be sceptically inclined towards researchers calling for more research, although we suggest that there is a strong case that existing evidence is not adequate to inform public health strategic responses. This does not necessarily mean that new research is needed in all cases, as existing data collection efforts may be usefully extended, even though the need to build a more secure research platform is an overarching conclusion that we do draw. We may be wrong in our thinking and we invite readers to judge the adequacy of our approach and the conceptual findings themselves. A favourable assessment may lead the reader to be interested in the research recommendations presented in the next chapter. A more critical reader may like to test the assumptions that we have made here (and transparently reported), and/or the evidence gap analysis in the review, to produce a different research agenda.

Implications

Assessing the population impacts of the use of, and possible responses to, NPS thus requires the capture of routine data, the generation of scientific data and the modelling of these data. Modelling may be particularly important early on to help inform coherent policy strategies, for example on potential future impacts on health-care resources, as well as helping to identify epidemiological and other research priorities. The value of such early models is bounded by the assumptions used in the models themselves, which may need to be crude in the absence of high-quality empirical data. The nature of contemporary drug trends poses big challenges to conventional practices in research and in informing policy-making with research summed up as 'how to speed up science, increase knowledge and get responsible regulatory policies enacted.'¹⁰⁷⁰ The regulation of drugs arguably shares this problem with other cultural forces in which the internet is central, from organised crime to consumer protection, offering opportunities for knowledge transfer.¹⁰⁷¹

As the NPS phenomenon is global in character, comparative studies of the diffusion of new drugs in other countries and continents should be valuable. The UK, and Europe as a whole, have so far avoided the epidemics of methamphetamines and prescription opioid use seen elsewhere. It is reasonable to suppose that future generations of NPS will have effects on users that are similar to those of existing drugs, and

that a more extensive and complex range of drugs might be used. In the future, the most optimistic scenario possible is that the most harmful drugs are largely avoided because they are harmful, regardless of their attractiveness. In such a scenario, harmful drugs are still likely to be used by vulnerable or high-risk populations, complicating and making more intractable existing problems and probably deepening health inequalities. Cross-national studies using quasi-experimental designs may have capacity to be informative about the effectiveness of different policy measures and approaches.

There is a dose–response relationship between the prevalence of many forms of drug use and the consequent public health and societal harms and the shape of the risk functions vary for different drugs.^{1022,1024} Public health approaches thus seek to find ways to manage demand and supply. The need to embrace the complexity and daunting scale of the challenge is widely recognised, so it is timely to develop public health approaches to drugs both new and old, and to promote the use of scientific evidence in shaping society's evolving responses.

Conclusions

The set of questions that we identified before we began the development of this conceptual framework (see *Chapter 2, Research questions*) and the review findings indicate that the literature is at an early stage of development in all cases. The substantive content of the conceptual framework presented here is thus largely unchanged by the review.

In the planning of this study we had anticipated a more mature empirical literature that would lead to the refinement of the conceptual material (e.g. drawing attention to the ways in which the NPS phenomenon poses challenges to public health that are at least somewhat distinct from those faced elsewhere). However, we found no reason to change the conceptual content on the basis of what has been published to date on NPS. Therefore, it is important to emphasise that this conceptual work is fundamentally hypothetical in nature, not having been developed with the aid of empirical research on NPS. As the research literature develops, this necessarily preliminary conceptual work will therefore need to be revisited, with a view to elaborating the strengths and limitations of this model. The disjunction between the empirical review and the conceptual framework findings is worthy of careful attention in developing research recommendations and drawing conclusions based on the overall NPS-UK study (see *Chapter 5*).

Chapter 4 Public involvement

Background

Public involvement for this project involved engagement with policy-makers, researchers and NPS users and their carers in the UK as stakeholders in informing the study design and processes, interpreting the findings, and validating the study recommendations. During the preparation of the proposal only, we discussed the project with the Scientific Director of the EMCDDA at the European level, with the Chief Executive of Drugscope and with a member of the ACMD.

Also relevant to PI is the work done with the steering group. The NPS-UK steering group consisted of five researchers who were independent of the research team, namely an expert on addictions treatment and prevention, policy and interventions, one on addictions clinical issues and NPS, another on NPS and EWSs, and two on systematic reviews and complex interventions in public health. All five researchers also act in different capacities to inform policy with evidence and occupy policy roles. Three do so specifically in relation to NPS as well as other drugs, and two are involved in public health. We had also recruited a researcher who is a NPS user to incorporate the user perspective; however, they pulled out and we were unsuccessful in recruiting another NPS user to the steering group. Two steering committee meetings took place in June and October 2016, supplemented by meetings and calls with individual members of the committee. PI relevance of steering committee inputs is judged highest in relation to the stage 1 conceptual framework that we developed. We also involved the different stakeholders in the interpretation of and reflection on our findings and research recommendations, as well as on the research process itself. The methods used and findings from this process are detailed below.

Recruitment and engagement

Policy-makers

Public involvement work on this project involved engagement with purposively selected policy actors with responsibilities directly relevant to NPS, and, in one case, we selected an addictions policy actor without any NPS role. This involved face-to-face meetings, as well as telephone and e-mail discussions.

We first discussed the stage 1 conceptual framework with both the external policy actors and with the steering committee (with whom we also discussed the scoping review findings at that point). In a second round of contacts, the draft final report was discussed either by telephone with individuals or during the steering committee meeting, with additional comments also received by e-mail.

Novel psychoactive substance users and user carers

We recruited NPS users for PI through flyers sent to the following key organisations that work with NPS users or networks: Crew2000 and Newcastle City Council. We also recruited by posting recruitment messages on Bluelight.org, which is an online drug user forum, as well as on The Loop Facebook (Facebook, Inc., Menlo Park, CA, USA) page [We are the loop (Manchester)]. The Loop is involved in conducting forensic testing of drugs at UK festivals and nightclubs and provides associated welfare support. Its Facebook page provides information to drug users including NPS users. We supplemented this recruitment strategy by making one-to-one contact with key individuals within these organisations, as well as other individuals who are connected to other NPS user networks, either via e-mail or telephone. To be able to contribute as a PI member, one had to be a current NPS/legal high user or user carer and be resident in the UK.

Individuals who were interested in participating contacted the researcher (NDM) by e-mail and were then sent an e-mail and an information sheet with a summary of the project and what participation as a PI member would entail. This included being sent two sets of documents to comment on: one containing a summary of the findings from the systematic review and the conceptual framework, and the other containing the research recommendations made in light of the findings. Each set of document would take 30–60 minutes to read and consider. They were also informed that they could choose to decline anything that was not suitable for them and withdraw at any time. Potential PI contributors were also informed that their preferences for how contact was made and maintained would be respected, as well as preserving anonymity and confidentiality as they required. We offered £10 for commenting on each of the document sets as compensation for time.

What we learnt

Feedback from policy-makers and the steering group

Feedback was gathered through face-to-face meetings with three staff from Public Health England (two of whom had specific responsibilities for NPS and one of whom did not) in January 2016, e-mail comments from the Home Office Drugs and Alcohol Research Team and Drug and Alcohol Policy Unit, and a follow-up discussion by telephone with one member of staff from the former in the spring.

The stage 1 conceptual framework document was seen to be highly congruent with both scientific and policy perspectives and to combine both in ways that were useful. The public health orientation was also seen to be complementary to more clinically focused endeavours such as NEPTUNE. There was strong support for not 'reinventing the wheel' for NPS and articulating perspectives on NPS separate from those for other drugs. Indeed, 'NPS' as a category or label was viewed to have limited utility, as this was obviously not a unitary phenomenon, and attention to the specific issues and harms involved in each new drug type was recommended. It was also suggested that there was much to be learnt from earlier epidemics of new drugs in places other than the UK. One example given concerned MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) compounds produced during the manufacture of MPPP (1-methyl-4-phenyl-4-propionoxypiperidine, a synthetic opioid), which led to irreversible Parkinson's disease in six drug users in California.

We also learnt that coverage of existing responses, which tend to be more treatment than prevention orientated, was seen to be limited, and the document was not very practical. It was nonetheless seen to be valuable in offering a broader context for existing responses.

We were also able to be informed about developments including forthcoming Public Health England and Home Office plans, and established connections with the Clinical Network Working Group and other forums via which we distributed calls for information.

Comments on the draft final report conveyed appreciation of the review findings, scale and challenges involved in summarising such a large body of literature in a relatively short space of time. They strongly endorsed the importance of the evidence gap analysis and the broad thrust of the research recommendations made. Comments were received on individual research recommendations and these led to textual refinements in some cases, although not to substantive content changes.

These efforts at policy engagement were quite modest and limited principally by time available. Two particular limitations should be borne in mind. First, we had intended to engage with the Department of Health, and to have done so would have been valuable. Second, the movement of the key contact and resource constraints within the Home Office precluded any contribution in the second round of contacts. This work nonetheless provides a useful basis for dissemination and broader knowledge exchange work that will take place after the completion of the project itself.

Feedback from novel psychoactive substance users and user carers

Four individual NPS users expressed interest in being PI contributors to the project. Of these, three provided correct e-mail addresses and were contacted and recruited in July and August 2016. Their preference was to be contacted by e-mail throughout their involvement, with no telephone or any other means of contact. These three individuals were kept up-to-date about the project through e-mail. They were then sent one set of documents in October 2016, with a 2-week deadline for return of any comments on the findings from the systematic review, conceptual framework and the research recommendations made in light of the findings. Only one NPS user responded with comments via e-mail.

The Newcastle User Carer Forum agreed to host a discussion of the NPS-UK project and its findings and recommendations for 1 hour as part of their regular fortnightly forum meetings. This discussion occurred in October 2016 with two discussion facilitators (a researcher and the Newcastle City Council Service User Involvement Officer), and was attended by five male forum members, all of whom were in drug recovery and volunteering as peer supporters for drug users in treatment or seeking treatment. Their ages ranged from late 20s to mid-50s.

The views on the NPS user and the five Newcastle User Carer Forum members are reported below.

Novel psychoactive substance use and problems

The findings of the scoping review and narrative synthesis concurred with the user carer forum members' observation from the field that NPS/legal highs are mainly used by young people aged 11–18 years. The reasons for use include the fact that they are cheaper and easier to get and that the police do not know how to deal with them. For many of these users, 'legal' translated to 'good stuff' or being safe. However, many users of other drugs who switch to NPS usually switched back to their old drug owing to NPS being much stronger and exhibiting worse side effects. They reported that a number of people in drug treatment who use NPS show signs of dependency on NPS, particularly craving.

However, the NPS user's view was quite different; from his experience on online drug forums, NPS users tended to be mid- to late-20s to mid-40s but not exclusively male. They agreed with the side effects profile of NPS, with the exception of gastrointestinal manifestations, which he viewed as rare. They also agreed that NPS tend to have 'stronger' side effects and that many users tend to switch to other illicit drugs.

Responses

Again, the user carer forum members agreed with the review findings on legislative controls for NPS. They indicated that in Newcastle the UK blanket ban of NPS in 2016 had resulted in the closure of all headshops, a decrease in availability and an increase in price (underground market). They had witnessed a massive decrease in use in Newcastle, even among those seeking treatment for drug use, with a switch to illicit drugs for many NPS users. Hence, they viewed the blanket ban of NPS in the UK as a good strategy.

The NPS user, however, felt that not all banning strategies had been as successful as intended and had resulted in some negative impact as well. The piecemeal approach had led to more dangerous drugs appearing on the market. However, the blanket ban had led to people, particularly those who were already addicted to NPS, feeling 'stranded'. They highlighted that there had been a huge slump in NPS-related post counts on online drug forums since the blanket ban, not only owing to a decrease in supply but also because more people are now not willing to disclose their NPS use. This was viewed as potentially having a negative impact on harm reduction and treatment seeking, and on routinely collected data where NPS use and consequences could be underestimated.

In terms of the views on our proposed conceptual framework in *Chapter 3*, all five user carer forum attendees, as well as the NPS user recruited from the online drug forum, agreed that it was an appropriate framework, as NPS are not different from older or illicit drugs; hence, the responses should be applicable for all drugs and not only for NPS. They, however, highlighted the potential need to distinguish between

individual drug types when considering the health-related consequences, as different drugs will have different toxicity profiles.

Research recommendations

In terms of research recommendations, user carer forum members recommended more investment in interventions, for example examining which treatments are effective and how services can be made more effective. They highlighted the need to explore in greater detail the use of peer counsellors or peer supporters and to invest in educating them so that they also understand the science of drug use and drug treatment for them to be more effective in delivering care. They reiterated the need to consider NPS in the context of drug use in general and to explore interventions that are already known to work for other drugs. They also recommended exploring why people use drugs and engaging more with frontline staff in treatment services and A&E, as well as the police and paramedics to understand some of the problems they face in dealing with users of NPS.

Reflections on the approach used in carrying out the project

The forum members and the NPS user highly commended the approach taken by the NPS-UK project as being rigorous and thorough, particularly in terms of looking at how the approach to other drugs has developed and how it may be applicable to NPS.

Conclusions

Our PI strategy was successful in engaging a small selection of stakeholders, who provided a useful sounding board to test emerging findings and to generate some lines of enquiry that would need to be tested by more qualitative research to provide a definitive assessment of impact on users.

Public involvement activities had demonstrable value in validating our study design, findings and recommendations. The project was successful in engaging with policy-makers and researchers at different stages of the research process. However, we were less successful with NPS user involvement, despite the efforts described above. The feedback that we received from other researchers who have conducted similar work in the area was that there was a need for investment in trust and building mutually beneficial relationships with NPS users over time. This could be done, for example, through advice provision on some of the problems that might be encountered as a result of NPS use to enhance willingness to engage with research projects such as this. However, for short-term projects such as this, implementing this approach is challenging and would need significant early investment. The sustainability of NPS user involvement throughout the project also proved difficult owing to a lack of willingness on the part of NPS users to be contacted in ways other than e-mail. Although there is a clear need to move beyond an expert driven discourse on NPS and drug use by involving NPS users and others affected by NPS, our project experience with NPS user involvement indicates a need to develop methods for PI that take into account the nature of the subject.

Chapter 5 Research recommendations

This chapter provides a brief integrative overview of earlier chapters, by way of introducing the research recommendations. *Chapter 2* found that there were many evidence gaps in relation to the original set of research questions that we identified a priori. We selected a number of areas that were judged to warrant fuller presentation and synthesis of data, without there being a substantial basis for a full systematic review. Following this, we concluded that this literature was at an early stage of development in its capacity to inform strategic public health responses. This conclusion was reached through the contextualisation of review findings within a conceptual framework developed for the purposes of this research. This sought to address what an evidence-informed public health approach to NPS use in the UK might look like. The framework was initially developed prior to the review, and the developmental process is described in detail in *Chapter 3*. We used this framework to interpret the data from the review, and we subsequently revised the conceptual material in minor ways in light of the review data, as there was no rationale for substantive change. Stakeholder contributions are described in *Chapter 4*. Together, the conceptual framework and review indicate a need for a major research effort to be directed at NPS, which should address NPS together with other forms of licit and illicit drug use.

Research recommendations were developed from two distinct data sources. First, research recommendations were made in studies included in the review. This data source offers the perspectives of the authors who have been involved in accumulating the existing research literature and assessing how it needs to be developed further. Second, we use the conceptual framework for NPS developed by the authors of this report to identify what may be missing from this literature.

Research recommendations made by the authors of primary studies in the four bodies of existing literature selected for narrative synthesis (UK prevalence surveys and qualitative studies, policy evaluation studies and systematic reviews) were extracted and coded independently by two reviewers. The resulting codes were similar and were integrated by means of paying attention to detailed content and frequency, as well as by discussion among the reviewers. This led to higher-level coding to produce recommendations in three broad thematic areas, namely research relating to pharmacology, epidemiology and intervention research. Many recommendations previously made were quite generic in nature, and the detailed content of the recommendations proposed adds substance to earlier recommendations based on the review work, thus involving the interpretation of the authors.

Work on the conceptual framework paid particular attention to possible research data needs, as part of the elaboration of a hypothesised evidence-informed public health approach to NPS. This involved the identification of material that is both present in and absent from the other data source. As the conceptual material has quite a different evidential status to previously identified research recommendations, we have sought to use a transparent approach in our handling of it.

The research recommendations are targeted at both researchers and commissioners of research, with a view to inform discussions between both parties about, and to enable decision-making on, future research needs and how they may be met. Research recommendations targeting researchers were primarily based on the synthesis of prior research recommendations. Recommendations for research commissioners were based on the conceptual framework and on conclusions drawn by the researchers across the project as a whole. It was intended that these different approaches would be complementary and that overlaps between material from both sources would be particularly informative. The key recommendations are thus those that are drawn from both data sources. It is noteworthy how far the conceptual framework based on evidence from other parts of the public health literature reflects and builds on the recommendations previously made by authors of the NPS literature.

Study limitations

This chapter has thus far concentrated on the process of generating the research recommendations. Attention should also be given to wider limitations of the NPS-UK study in respect of implications for drawing conclusions and interpreting the resulting research recommendations.

By its nature, a study such as this is not capable of in-depth interrogation of the issues identified as warranting further research. For example, although issues concerning existing evidence on prevalence rates based on self-reported drug use in surveys may be described, consideration of how these issues may be most appropriately addressed is necessarily limited. This example relates to a body of evidence chosen for narrative synthesis, and these cautionary remarks apply with greater force to bodies of evidence not selected. Although a scoping review can map existing research, the breadth of the literature examined necessarily constrains the ability to investigate study limitations or risk of bias in any depth. Therefore, it is appropriate to be careful about how evidence from primary studies is presented and used in this study. With these caveats in mind, we suggest that the findings of the scoping review study should be regarded as providing a reliable broad overview of existing research in this area, permitting identification of the evidence gaps, and thus serving as a platform from which future research needs may be considered.

The disjunction between the scoping review and the conceptual framework findings is worthy of careful attention, and we invite readers to consider two alternative explanations that would challenge our conclusions. It is possible that we have not captured relevant empirical research that should have been included. We suggest that this is highly unlikely to be the case for peer-reviewed literature, particularly studies that are published in scientific journals. We acknowledge the risk that relevant grey literature that is not peer reviewed may not have been fully captured. Our inclusion of a category of 'responses' that permits letters, commentaries and other material that does not constitute research per se is particularly noteworthy. This means that there may be other material espousing views about appropriate responses that may have been missed. We have no specific grounds for concern in this regard.

The other possibility is that our conceptual work based on wider bodies of evidence has not synthesised relevant material in a sufficiently rigorous way. As we did not develop a dedicated methodology for this strand of the work, the limitations of which may be carefully assessed, we do regard this as presenting a risk to our conclusions, and hence state them below in a way that draws attention to this possibility. Our approach throughout has been to be as transparent as possible about both the handling of evidence and the processes of inference generation, so that readers may assess the limitations of our study.

Statement of the Novel Psychoactive Substances in the UK Project research recommendations

The research recommendations have been generated using the methodological approach previously described. Key recommendations are identified as such (in bold below) because they emerged both from the research recommendations identified in the primary studies included in the review and from the conceptual framework developing a hypothesised public health approach to NPS. The nine key recommendations are derived from the full set of 20 research recommendations as follows:

Research recommendations for researchers (with key recommendations in bold)

Pharmacology-related research

1. **Evaluate the effectiveness and sustainability of the existing pharmacovigilance system for NPS and the effects of planned innovations.**
2. **Evaluate the pharmacological, toxicological and related scientific base needed to inform the pharmacovigilance and public health surveillance systems.**

3. Undertake studies of the simultaneous use of multiple substances. Such studies should pay attention to detailed contents, potency, toxicity, doses and other psychopharmacological and other individual factors.

Epidemiology and related research

4. **Evaluate the effectiveness and sustainability of the existing public health surveillance system for monitoring NPS markets and other new online drug trends. This evaluation should cover monitoring actions, both quantitative and qualitative research and associated commissioning arrangements, and be cognisant of opportunities for innovations such as test-purchasing new brands online as they become available.**
5. **Develop the behavioural epidemiology and related science of patterns and correlates of NPS use and problems in the context of involvement in alcohol, tobacco and other drug use.**
6. **Use cohort study designs to better understand the determinants of NPS use and related physical health, mental health and psychosocial problems, and how patterns of involvement and consequences change over time.**
7. Develop the study of NPS use in subpopulations (in addition to, rather than instead of, general population studies). Priority groups could include psychiatric patients with severe mental illness, prisoners, homeless people, existing defined populations of drug users, including MSM and adolescents.
8. Undertake methodological research on NPS behavioural measurement, including the validity of self-report, psychometrics and online survey design.

Interventions

9. **Develop the science of prevention of NPS and other drug use. This should include evaluation of existing interventions and the development and evaluation of novel interventions addressing both proximal and distal determinants of NPS and related drug use, and how risks should be communicated to different groups.**
10. **Evaluate the public health impacts of legislative prohibitions of NPS use or supply, and other major policy initiatives.**
11. Evaluate the effectiveness of existing psychosocial interventions for drug users in relation to NPS outcomes. In addition, develop and evaluate other novel treatment interventions for NPS and other drug use in light of the limitations of the effectiveness of existing interventions.

Recommendations for research commissioners

12. **Consider using the research recommendations presented here as a possible basis for conducting a formal research priority-setting exercise using consensus development methods (such as those developed by the James Lind Alliance).**
13. **Evaluate existing strategic provision for, and develop as necessary, a long-term planning system for research on NPS and other drug use.**
14. Consider designing systems for investigating the drug dependence potential of different types of NPS at optimally early points in epidemics if indicated by the outcomes of research relating to Recommendation 2 above. These data should aim to inform assessments of future prevalence and potential problems and implications for treatment interventions.
15. Evaluate the existing burden of, and responses to, NPS and other drug use in generic and specialist services, and the contributions made therein to prevent and treat problems.
16. Develop the contribution of economics to this subject area. Possible study foci include evaluation of the societal costs of NPS and other drug use, modelling the possible benefits and costs of a range of policy and intervention options, and gaining a better understanding of the influences of price, availability and marketing on demand and supply.

17. Develop research capacity for the design, implementation and rigorous evaluation in comparative studies of any emerging local or regional multilevel strategic responses. Such approaches could include provision for the identification of the national policy influences on observed NPS and other drug outcomes.
18. Strengthen the contribution of social sciences to the study of NPS and other drug use. These approaches should build on methodological advances on similar forms of online-mediated behaviour.
19. Develop empirical research on the public understanding of drug use more broadly, including NPS use, and how this may be enhanced.
20. Move beyond an expert driven discourse on NPS and drug use by developing methods for patient and public involvement. These methods should be capable of dealing with the controversial nature of this subject, engage local, national and international policy actors, and take a long-term view of how societies may adapt to technology-driven problems in the context of globalisation.

Conclusions

The research recommendations presented here cover broadly similar areas to earlier UK expert research recommendations. They are also more detailed in content, partly because they arise from a systematic search and review of the already large and rapidly growing body of research literature, and use a transparent methodology for producing recommendations.

The UK Government Home Office Expert Panel Report 2014⁹²⁸ recommended various kinds of data collection to inform surveillance systems in health and non-health settings, alongside research recommendations on prevention and treatment, as it was not possible at that time to provide recommendations on evidence-based intervention delivery owing to the absence of available evidence. The Home Office Expert Panel Report thus provides some validation support for Recommendations 1, 2, 4, 5, 7, 9 and 11 above (all key recommendations here, with the exception of 7 and 11).

The NPS expert report prepared by Fraser⁹¹⁹ for the Scottish Government, also in 2014, identified evidence gaps in relation to epidemiology, the changing nature of drug markets, including NPS markets, acute and longer-term consequences, policy-level interventions and the applicability of existing interventions, and considered possible new approaches, including psychosocial treatments for NPS users. The Scottish Government document thus provides some validation support for Recommendations 4–6 and 9–11 inclusive and 15 (all key recommendations here, with the exception of 11 and 15).

Other expert reports could also be used for comparison purposes. For example, the 2016 EMCDDA⁹¹² report on health responses to new psychoactive substances was not designed to make research recommendations and notes, for example, the lack of data on use, harms and effectiveness. The report does, however, endorse the targeting of subgroups and the adaptation of existing interventions to incorporate NPS, in line with Recommendations 7 and 11 here.

We conclude with two sets of observations on the research recommendations presented here. First, caution should be exercised in relation to the interpretation of the set of recommendations for research commissioners, hence the articulation of Key Recommendations 12 and 13, which also draw on support from sources other than the conceptual framework. All other recommendations for research commissioners should be regarded as primarily originating in bodies of research evidence other than that existing for NPS, as interpreted by the authors. Further consideration is needed to determine whether the validity of this set of recommendations should be enhanced via further work with research commissioners, policy-makers, researchers and the public. Second, it is noteworthy that all the key recommendations for researchers are supported by earlier UK expert reports and have not yet been acted on. We suggest that the case for decision-making on commissioning new research based on the present recommendations is both strong and urgent.

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Contributions of authors

All authors were involved in the conduct of this research, including data interpretation and drafting the report, and have approved the final version of the report.

Noreen Dadirai Mdege (Research Fellow, Addiction) was responsible for the day-to-day running of the research project. She conducted the scoping review and narrative synthesis, contributed to the conceptual framework development, and led on the drafting of *Chapters 1* (with JM), *2* and *4*.

Nick Meader (Research Fellow, Centre for Reviews and Dissemination) conducted the scoping review and narrative synthesis, contributed to conceptual framework development and made revisions to all chapters.

Charlie Lloyd (Reader, Addiction) contributed to the conceptual framework development.

Steve Parrott (Reader, Health Economics) contributed to the health economics aspects of the conceptual framework development.

Jim McCambridge (Professor, Addictive Behaviours and Public Health) led on the design and conduct of, and had overall responsibility for, all research components. He led on the drafting of *Chapters 1* (with NDM), *3* and *5*.

Data sharing statement

As this is a review study, there are no primary data available for sharing.

References

1. Great Britain. *Psychoactive Substances Act 2016*. London: The Stationery Office; 2016.
2. Home Office. *Drug Misuse: Findings from the 2013/14 Crime Survey for England and Wales*. London: Home Office; 2014.
3. ACMD. *Consideration of the Novel Psychoactive Substances ('Legal Highs')*. London: ACMD; 2011.
4. HM Government. *Drug Strategy 2010 – Annual Review – May 2012*. London: Home Office; 2012.
5. Sumnall HR, Evans-Brown M, McVeigh J. Social, policy, and public health perspectives on new psychoactive substances. *Drug Test Anal* 2011;**3**:515–23. <https://doi.org/10.1002/dta.310>
6. The Gallup Organisation. *Youth Attitudes on Drugs: Analytical Report*. Luxembourg City: The Gallup Organisation; 2011.
7. Wood DM, Greene SL, Dargan PI. Emergency department presentations in determining the effectiveness of drug control in the United Kingdom: mephedrone (4-methylmethcathinone) control appears to be effective using this model. *Emerg Med J* 2013;**30**:70–1. <https://doi.org/10.1136/emered-2011-200747>
8. Winstock AR, Barratt MJ. The 12-month prevalence and nature of adverse experiences resulting in emergency medical presentations associated with the use of synthetic cannabinoid products. *Hum Psychopharmacol* 2013;**28**:390–3. <https://doi.org/10.1002/hup.2292>
9. Plumb J, McDonnell WM, Anderson KT, Crouch BI, Caravati EM. *Adverse Effects from Pediatric Exposures to Spice (Cannabinoid Agonists)*. 2012 Annual Meeting of the North American Congress of Clinical Toxicology (NACCT), Las Vegas, NV, 1–6 October 2012.
10. Murphy CM, Dulaney AR, Beuhler MC, Kacinko S. 'Bath salts' and 'plant food' products: the experience of one regional US poison center. *J Med Toxicol* 2013;**9**:42–8. <https://doi.org/10.1007/s13181-012-0243-1>
11. Wilkins C. A critical first assessment of the new pre-market approval regime for new psychoactive substances (NPS) in New Zealand. *Addiction* 2014;**109**:1580–6. <https://doi.org/10.1111/add.12484>
12. Griffiths P, Evans-Brown M, Sedefov R. Getting up to speed with the public health and regulatory challenges posed by new psychoactive substances in the information age. *Addiction* 2013;**108**:1700–3. <https://doi.org/10.1111/add.12287>
13. Inman I, Carr J, Hupert W, King S, Whitecross R. *2010/11 Scottish Crime and Justice Survey: Drug Use*. Edinburgh: The Scottish Government; 2012.
14. Home Office. *Drug Misuse Declared: Findings from the 2011/12 Crime Survey for England and Wales*. London: Home Office; 2012.
15. Winstock A, Mitcheson L, Ramsey J, Davies S, Puchnarewicz M, Marsden J. Mephedrone: use, subjective effects and health risks. *Addiction* 2011;**106**:1991–6. <https://doi.org/10.1111/j.1360-0443.2011.03502.x>
16. Schifano F, Corkery J, Ghodse AH. Suspected and confirmed fatalities associated with mephedrone (4-methylmethcathinone, 'meow meow') in the United Kingdom. *J Clin Psychopharmacol* 2012;**32**:710–14. <https://doi.org/10.1097/JCP.0b013e318266c70c>
17. EMCDDA. *Action on New Drugs*. Lisbon: EMCDDA; 2014.
18. Hughes B, Griffiths P. Regulatory approaches to new psychoactive substances (NPS) in the European Union. *Addiction* 2014;**109**:1591–3. <https://doi.org/10.1111/add.12610>

19. Novel Psychoactive Treatment UK Network (NEPTUNE). *Guidance on the Clinical Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances*. London: NEPTUNE; 2015.
20. HM Government. *Reducing Demand, Restricting Supply, Building Recovery: Supporting People to Live a Drug Free Life*. London: HM Government; 2010.
21. Fischer B, Keates A, Bühringer G, Reimer J, Rehm J. Non-medical use of prescription opioids and prescription opioid-related harms: why so markedly higher in North America compared to the rest of the world? *Addiction* 2014;**109**:177–81. <https://doi.org/10.1111/add.12224>
22. Mdege N, Meader N, McCambridge J. *A Systematic Review of What is Known about Novel Psychoactive Substance Use, Related Problems and Responses from a Public Health Perspective*. PROSPERO 2016:CRD42016026415 2016. URL: www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016026415 (accessed 29 June 2016).
23. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009;**339**:b2535. <https://doi.org/10.1136/bmj.b2535>
24. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Social Research Methodology* 2005;**8**:1–14. <https://doi.org/10.1080/1364557032000119616>
25. Abagiu AO, Marinescu AG, Niculescu IT, Koulosousas A, Paris E, Mardarescu M. 5 years of legal highs in Romania-consequences and solutions. *Alcohol Alcohol* 2014;**49**:i5. <https://doi.org/10.1093/alcac/agu052.13>
26. Adamowicz P, Lechowicz W. The influence of synthetic cannabinoid UR-144 on human psychomotor performance – a case report demonstrating road traffic risks. *Traffic Inj Prev* 2015;**16**:754–9. <https://doi.org/10.1080/15389588.2015.1018990>
27. Adamowicz P, Tokarczyk B, Stanaszek R, Slopianka M. Fatal mephedrone intoxication – a case report. *J Anal Toxicol* 2013;**37**:37–42. <https://doi.org/10.1093/jat/bks085>
28. Adamowicz P, Zuba D, Byrska B. Fatal intoxication with 3-methyl-N-methylcathinone (3-MMC) and 5-(2-aminopropyl)benzofuran (5-APB). *Forensic Sci Int* 2014;**245**:126–32. <https://doi.org/10.1016/j.forsciint.2014.10.016>
29. Adams RD, Bateman DN. The TOXBASE new product and unusual cases reporting scheme-naphyrone. *Clin Toxicol* 2012;**50**:299.
30. Abbott R, Smith DE. The new designer drug wave: a clinical, toxicological, and legal analysis. *J Psychoactive Drugs* 2015;**47**:368–71. <https://doi.org/10.1080/02791072.2015.1094591>
31. Abouchedid R, Thurtle N, Yamamoto T, Ho J, Bailey G, Hudson S, et al. Analytical confirmation of the synthetic cannabinoid receptor agonists (SCRAs) present in a cohort of presentations with acute recreational drug toxicity to an emergency department (ED) in London, UK. *Clin Toxicol* 2016;**54**:472–3.
32. Adamowicz P. Fatal intoxication with synthetic cannabinoid MDMB-CHMICA. *Forensic Sci Int* 2016;**261**:e5–10. <https://doi.org/10.1016/j.forsciint.2016.02.024>
33. Adamowicz P, Gieroń J. Acute intoxication of four individuals following use of the synthetic cannabinoid MAB-CHMINACA. *Clin Toxicol* 2016;**54**:650–4. <https://doi.org/10.1080/15563650.2016.1190016>
34. Adamowicz P, Gieroń J, Gil D, Lechowicz W, Skulska A, Tokarczyk B. The prevalence of new psychoactive substances in biological material – a three-year review of casework in Poland. *Drug Test Anal* 2016;**8**:63–70. <https://doi.org/10.1002/dta.1924>

35. Addy PH, Garcia-Romeu A, Metzger M, Wade J. The subjective experience of acute, experimentally-induced *Salvia divinorum* inebriation. *J Psychopharmacol* 2015;**29**:426–35. <https://doi.org/10.1177/0269881115570081>
36. Adebamiro A, Perazella MA. Recurrent acute kidney injury following bath salts intoxication. *Am J Kidney Dis* 2012;**59**:273–5. <https://doi.org/10.1053/j.ajkd.2011.10.012>
37. Ahern NR, Greenberg CS. Psychoactive herb use and youth: a closer look at *salvia divinorum*. *J Psychosoc Nurs Ment Health Serv* 2011;**49**:16–19. <https://doi.org/10.3928/02793695-20110705-05>
38. Airuehia E, Walker LY, Nittler J. A review of ‘bath salts’: evolving designer drugs of abuse. *J Child Adolesc Subst Abuse* 2015;**24**:186–90. <https://doi.org/10.1080/1067828X.2013.803942>
39. Alansari M, Hamilton D. Nephrotoxicity of BZP-based herbal party pills: a New Zealand case report. *N Z Med J* 2006;**119**:U1959.
40. Albadareen R, Lowry J, Thornton S, Heshmati A. An unusual prolonged presentation of synthetic cathinone encephalopathy responsive to steroids: a case report. *Neurology* 2014;**82**(Suppl. P3.334).
41. Albertson DN, Grubbs LE. Subjective effects of *Salvia divinorum*: LSD- or marijuana-like? *J Psychoactive Drugs* 2009;**41**:213–7. <https://doi.org/10.1080/02791072.2009.10400531>
42. Alhadi S, Tiwari A, Vohra R, Gerona R, Acharya J, Bilello K. High times, low sats: diffuse pulmonary infiltrates associated with chronic synthetic cannabinoid use. *J Med Toxicol* 2013;**9**:199–206. <https://doi.org/10.1007/s13181-013-0288-9>
43. Alison D, Dargan PI, Heyerdahl F, Hvoda KE, Yates C, Giraudon I, et al. Four months surveillance of recreational drug use in Europe: first report from the European Drug Emergencies Network (Euro-DEN) project. *Clin Toxicol* 2014;**52**:703.
44. Alverio C, Reddy A, Hernandez E, Renner JA. Synthetic cannabis ‘spice,’ more potent than natural cannabis and may have increased risk for psychosis? *Am J Addict* 2012;**21**:381–2.
45. Anderson C, Morrell C, Marchevsky D. A novel psychoactive substance poses a new challenge in the management of paranoid schizophrenia. *BMJ Case Rep* 2015;**2015**:bcr2015209573. <https://doi.org/10.1136/bcr-2015-209573>
46. Andrabi S, Greene S, Moukaddam N, Moukkadam N, Li B. New drugs of abuse and withdrawal syndromes. *Emerg Med Clin North Am* 2015;**33**:779–95. <https://doi.org/10.1016/j.emc.2015.07.006>
47. Aksel G, Bozan O, Kayaci M, Guneyssel O, Sezgin SB. Rising threat; bonsai. *Turk J Emerg Med* 2015;**15**:75–8. <https://doi.org/10.5505/1304.7361.2015.80388>
48. Albertson TE, Chenoweth JA, Colby DK, Sutter ME. The changing drug culture: emerging drugs of abuse and legal highs. *FP Essent* 2016;**441**:18–24.
49. Almarza E, Martinez MA, Quintela O, Ballesteros S. Bath salts (synthetic cathinones): two cases with forensic implications. *Clin Toxicol* 2016;**54**:496–7.
50. Angelats M, Galindo L, Grifell M, Palma A, Martinez L, Pujol L, et al. PCP analogues in samples of Barcelona from 2009 to 2015. *Eur Psychiatry* 2016;**33**(Suppl.):117. <https://doi.org/10.1016/j.eurpsy.2016.01.128>
51. Antill T, Jakkoju A, Dieguez J, Laskhmiprasad L. Lactic acidosis: a rare manifestation of synthetic marijuana intoxication. *J La State Med Soc* 2015;**167**:155.

52. Araújo AM, Carvalho F, Bastos Mde L, Guedes de Pinho P, Carvalho M. The hallucinogenic world of tryptamines: an updated review. *Arch Toxicol* 2015;**89**:1151–73. <https://doi.org/10.1007/s00204-015-1513-x>
53. Archer JR, Hudson S, Jackson O, Yamamoto T, Lovett C, Lee HM, *et al*. Analysis of anonymized pooled urine in nine UK cities: variation in classical recreational drug, novel psychoactive substance and anabolic steroid use. *QJM* 2015;**108**:929–33. <https://doi.org/10.1093/qjmed/hcv058>
54. Archer JRH, Hudson S, Yamamoto T, Hudson S, Wood DM. Trend analysis of novel psychoactive substances (NPS) detected in pooled urine samples from street urinals in London, UK over 18 months. *Clin Toxicol (Phila)* 2016;**54**:409.
55. Argamany JR, Reveles KR, Duhon B. Synthetic cannabinoid hyperemesis resulting in rhabdomyolysis and acute renal failure. *Am J Emerg Med* 2016;**34**:765.e1–2. <https://doi.org/10.1016/j.ajem.2015.08.051>
56. Anne S, Tse R, Cala AD. A fatal case of isolated methiopropamine (1-(thiophen-2-yl)-2-methylaminopropane) toxicity: a case report. *Am J Forensic Med Pathol* 2015;**36**:205–6. <https://doi.org/10.1097/PAF.0000000000000170>
57. Antoniou T, Juurlink DN. Synthetic cannabinoids. *CMAJ* 2014;**186**:210. <https://doi.org/10.1503/cmaj.130510>
58. Appel J, Kim-Appel D. The rise of a new psychoactive agent: *Salvia divinorum*. *Int J Ment Health Addiction* 2007;**5**:248–53. <https://doi.org/10.1007/s11469-007-9086-4>
59. Archer JR, Dargan PI, Lee HM, Hudson S, Wood DM. Trend analysis of anonymised pooled urine from portable street urinals in central London identifies variation in the use of novel psychoactive substances. *Clin Toxicol (Phila)* 2014;**52**:160–5. <https://doi.org/10.3109/15563650.2014.885982>
60. Armenian P, Gerona RR. The electric Kool-Aid NBOMe test: LC-TOF/MS confirmed 2C-C-NBOMe (25C) intoxication at Burning Man. *Am J Emerg Med* 2014;**32**:1444.e3–5. <https://doi.org/10.1016/j.ajem.2014.04.047>
61. Arndt T, Claussen U, Güssregen B, Schröfel S, Stürzer B, Werle A, Wolf G. Kratom alkaloids and O-desmethyltramadol in urine of a 'Krypton' herbal mixture consumer. *Forensic Sci Int* 2011;**208**:47–52. <https://doi.org/10.1016/j.forsciint.2010.10.025>
62. Aromatario M, Bottoni E, Santoni M, Ciallella C. New 'lethal highs': a case of a deadly cocktail of GHB and Mephedrone. *Forensic Sci Int* 2012;**223**:e38–41. <https://doi.org/10.1016/j.forsciint.2012.09.014>
63. Arora A, Kumar A, Raza MN. 'Legal high' associated Wallenberg syndrome. *BMJ Case Rep* 2013;**2013**:bcr2013009693. <https://doi.org/10.1136/bcr-2013-009693>
64. Ascioglu F. New psycho-active substances: the legal procedure used in European Union countries and Turkey. *Klinik Psikofarmakoloji Bulteni* 2010;**20**:334–9.
65. Atik SU, Dedeoğlu R, Varol F, Çam H, Eroğlu AG, Saltık L. Cardiovascular side effects related with use of synthetic cannabinoids 'bonzai': two case reports. *Turk Pediatri Ars* 2015;**50**:61–4. <https://doi.org/10.5152/tpa.2015.2609>
66. Backberg M, Westerbergh J, Yasir AS, Lindeman E, Helander A. Trends in intoxications of novel psychoactive substances in Sweden during 2012. *Clin Toxicol* 2013;**51**:256–7.
67. Baggott MJ, Erowid E, Erowid F, Galloway GP, Mendelson J. Use patterns and self-reported effects of *Salvia divinorum*: an internet-based survey. *Drug Alcohol Depend* 2010;**111**:250–6. <https://doi.org/10.1016/j.drugalcdep.2010.05.003>
68. Bajaj N, Mullen D, Wylie S. Dependence and psychosis with 4-methylmethcathinone (mephedrone) use. *BMJ Case Rep* 2010;**2010**:bcr0220102780. <https://doi.org/10.1136/bcr.02.2010.2780>

69. Banerji S, Deutsch CM, Bronstein AC. Spice ain't so nice. *Clin Toxicol* 2010;**48**:632.
70. Banks ML, Worst TJ, Rusyniak DE, Sprague JE. Synthetic cathinones ('bath salts'). *J Emerg Med* 2014;**46**:632–42. <https://doi.org/10.1016/j.jemermed.2013.11.104>
71. Aydin Sunbul E, Sunbul M, Terzi A, Calli S, Koca E, Bilici R, Citak S. The effect of synthetic cannabinoids on p-wave dispersion: an observational study. *Med Princ Pract* 2016;**25**:483–7. <https://doi.org/10.1159/000447516>
72. Azam MA. Sociodemographic variables and concurrent substance use are not predictors of synthetic cannabis use. *Biol Psychiatry* 2016;**1**:915.
73. Barnett RY, Baker DD, Kelly NE, McGuire CE, Fassette TC, Gorniak JM. A fatal intoxication of 2,5-dimethoxy-4-chloroamphetamine: a case report. *J Anal Toxicol* 2014;**38**:589–91. <https://doi.org/10.1093/jat/bku087>
74. Barratt MJ, Cakic V, Lenton S. Patterns of synthetic cannabinoid use in Australia. *Drug Alcohol Rev* 2013;**32**:141–6. <https://doi.org/10.1111/j.1465-3362.2012.00519.x>
75. Bauer A, Schopfer J, Schwerer M, Sachs H, Zinka B, Graw M, *et al.* Fatality after intake of para-methoxyamphetamine (PMA) and amphetamine: a case report. *Rechtsmedizin* 2013;**23**:347.
76. Batisse A, Fortias M, Bourgogne E, Djeddar S. A French case series of 21 synthetic cathinones abuse. *Fundam Clin Pharmacol* 2013;**27**:102.
77. Baumann MH. Awash in a sea of 'bath salts': implications for biomedical research and public health. *Addiction* 2014;**109**:1577–9. <https://doi.org/10.1111/add.12601>
78. Baumeister D, Tojo LM, Tracy DK. Legal highs: staying on top of the flood of novel psychoactive substances. *Ther Adv Psychopharmacol* 2015;**5**:97–132. <https://doi.org/10.1177/2045125314559539>
79. Bebartha VS, Ramirez S, Varney SM. Spice: a new 'legal' herbal mixture abused by young active duty military personnel. *Subst Abus* 2012;**33**:191–4. <https://doi.org/10.1080/08897077.2011.637610>
80. Bebartha VS, Ramirez S, Varney SM. Complication of spice use in a deployed combat setting-seizure while on duty. *Am J Addict* 2012;**21**:496–7. <https://doi.org/10.1111/j.1521-0391.2012.00264.x>
81. Behonick G, Shanks KG, Firchau DJ, Mathur G, Lynch CF, Nashelsky M, *et al.* Four postmortem case reports with quantitative detection of the synthetic cannabinoid, 5F-PB-22. *J Anal Toxicol* 2014;**38**:559–62. <https://doi.org/10.1093/jat/bku048>
82. Bell J, Collins R. Gamma-butyrolactone (GBL) dependence and withdrawal. *Addiction* 2011;**106**:442–7. <https://doi.org/10.1111/j.1360-0443.2010.03145.x>
83. Belton P, Sharngoe T, Maguire FM, Polhemus M. Cardiac infection and sepsis in 3 intravenous bath salts drug users. *Clin Infect Dis* 2013;**56**:e102–4. <https://doi.org/10.1093/cid/cit095>
84. Benford DM, Caplan JP. Psychiatric sequelae of Spice, K2, and synthetic cannabinoid receptor agonists. *Psychosomatics* 2011;**52**:295. <https://doi.org/10.1016/j.psym.2011.01.004>
85. Baumann MH, Volkow ND. Abuse of new psychoactive substances: threats and solutions. *Neuropsychopharmacology* 2016;**41**:663–5. <https://doi.org/10.1038/npp.2015.260>
86. Benzer TI, Nejad SH, Flood JG. Case records of the Massachusetts General Hospital. Case 40-2013. A 36-year-old man with agitation and paranoia. *N Engl J Med* 2013;**369**:2536–45. <https://doi.org/10.1056/NEJMcp1304051>
87. Berkowitz EA, Henry TS, Veeraraghavan S, Staton GW, Gal AA. Pulmonary effects of synthetic marijuana: chest radiography and CT findings. *AJR Am J Roentgenol* 2015;**204**:750–7. <https://doi.org/10.2214/AJR.14.13138>

88. Bernson-Leung ME, Leung LY, Kumar S. Synthetic cannabis and acute ischemic stroke. *J Stroke Cerebrovasc Dis* 2014;**23**:1239–41. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.07.030>
89. Berry JD, Srisung W, Prabhakar S. Synthetic cannabinoids and acute kidney injury. *J Investig Med* 2014;**62**:502–3.
90. Berry-Cabán CS, Ee J, Ingram V, Berry CE, Kim EH. Synthetic cannabinoid overdose in a 20-year-old male US soldier. *Subst Abus* 2013;**34**:70–2. <https://doi.org/10.1080/08897077.2012.677754>
91. Berry-Cabán CS, Kleinschmidt PE, Rao DS, Jenkins J. Synthetic cannabinoid and cathinone use among US soldiers. *US Army Med Dep J* 2012;Oct-Dec:19–24.
92. Bersani FS, Corazza O, Albano G, Valeriani G, Santacroce R, Bolzan Mariotti Posocco F, et al. 25C-NBOMe: preliminary data on pharmacology, psychoactive effects, and toxicity of a new potent and dangerous hallucinogenic drug. *Biomed Res Int* 2014;**2014**:734749. <https://doi.org/10.1155/2014/734749>
93. Besli GE, Ikiz MA, Yildirim S, Saltik S. Synthetic cannabinoid abuse in adolescents: a case series. *J Emerg Med* 2015;**49**:644–50. <https://doi.org/10.1016/j.jemermed.2015.06.053>
94. Bhanushali GK, Jain G, Fatima H, Leisch LJ, Thornley-Brown D. AKI associated with synthetic cannabinoids: a case series. *Clin J Am Soc Nephrol* 2013;**8**:523–6. <https://doi.org/10.2215/CJN.05690612>
95. Bhatti S, Wu W. Organic and synthetic cannabinoid use in adolescents. *Pediatr Ann* 2013;**42**:31–5. <https://doi.org/10.3928/00904481-20121221-16>
96. Bick BL, Szostek JH, Mangan TF. Synthetic cannabinoid leading to cannabinoid hyperemesis syndrome. *Mayo Clin Proc* 2014;**89**:1168–9. <https://doi.org/10.1016/j.mayocp.2014.06.013>
97. Bigdeli I, Corazza O, Aslanpour Z, Schifano F. Novel psychoactive substances (NPS): a study on Persian language websites. *Iran J Public Health* 2013;**42**:511–15.
98. Bilinski P, Holownia P, Kapka-Skrzypczak L, Wojtyla A. Designer drug (DD) abuse in Poland; a review of the psychoactive and toxic properties of substances found from seizures of illegal drug products and the legal consequences thereof. Part I – cannabinoids and cathinones. *Ann Agric Environ Med* 2012;**19**:857–70.
99. Bilinski P, Holownia P, Kapka-Skrzypczak L, Wojtyla A. Designer drug (DD) abuse in Poland; a review of the psychoactive and toxic properties of substances found from seizures of illegal drug products and the legal consequences thereof. Part II – piperazines/piperidines, phenylethylamines, tryptamines and miscellaneous ‘others’. *Ann Agric Environ Med* 2012;**19**:871–82.
100. Biliński P, Kapka-Skrzypczak L, Jabłoński P. Determining the scale of designer drugs (DD) abuse and risk to public health in Poland through an epidemiological study in adolescents. *Ann Agric Environ Med* 2012;**19**:357–64.
101. Bonar EE, Ashrafioun L, Ilgen MA. Synthetic cannabinoid use among patients in residential substance use disorder treatment: prevalence, motives, and correlates. *Drug Alcohol Depend* 2014;**143**:268–71. <https://doi.org/10.1016/j.drugalcdep.2014.07.009>
102. Bonnici KS, Dargan PI, Wood DM. Novel psychoactive substances or ‘legal highs’. *Br J Hosp Med* 2015;**76**:C130–4. <https://doi.org/10.12968/hmed.2015.76.9.C130>
103. Bilgrei OR. From ‘herbal highs’ to the ‘heroin of cannabis’: exploring the evolving discourse on synthetic cannabinoid use in a Norwegian Internet drug forum. *Int J Drug Policy* 2016;**29**:1–8. <https://doi.org/10.1016/j.drugpo.2016.01.011>
104. Booth RE. ‘Krokodil’ and other home-produced drugs for injection: a perspective from Ukraine. *Int J Drug Policy* 2013;**24**:277–8. <https://doi.org/10.1016/j.drugpo.2013.05.009>

105. Borek HA, Holstege CP. Hyperthermia and multiorgan failure after abuse of 'bath salts' containing 3,4-methylenedioxypropylone. *Ann Emerg Med* 2012;**60**:103–5. <https://doi.org/10.1016/j.annemergmed.2012.01.005>
106. Bosak A, LoVecchio F, Levine M. Recurrent seizures and serotonin syndrome following '2C-I' ingestion. *J Med Toxicol* 2013;**9**:196–8. <https://doi.org/10.1007/s13181-013-0287-x>
107. Boshuisen K, Arends JE, Rutgers DR, Frijns CJ. A young man with hemiplegia after inhaling the bath salt 'Ivory Wave'. *Neurology* 2012;**78**:1533–4. <https://doi.org/10.1212/WNL.0b013e3182553c70>
108. Bossong MG, Brunt TM, Van Dijk JP, Rigter SM, Hoek J, Goldschmidt HM, Niesink RJ. mCPP: an undesired addition to the ecstasy market. *J Psychopharmacol* 2010;**24**:1395–401. <https://doi.org/10.1177/0269881109102541>
109. Bottei E. First report of drug concentrations of the synthetic cannabinoid 5F-PB-22 found on post-mortem testing. *Clin Toxicol* 2014;**52**:750.
110. Bowden-Jones O. Club drugs and Europe: from epidemiology to treatment. *Sucht* 2012;**58**:92.
111. Bowden-Jones O. 'Legal highs' and other 'club drugs': why the song and dance? *Psychiatrist* 2013;**37**:185–7. <https://doi.org/10.1192/pb.bp.113.042713>
112. Bozkurt M, Umut G, Evren C, Karabulut V. Clinical characteristics and laboratory test results of patients admitted to outpatient clinic for synthetic cannabinoid usage. *Dusunen Adam* 2014;**27**:328–34. <https://doi.org/10.5350/DAJPN2014270407>
113. Brandt SD, King LA, Evans-Brown M. The new drug phenomenon. *Drug Test Anal* 2014;**6**:587–97. <https://doi.org/10.1002/dta.1686>
114. Brents LK, Prather PL. The K2/Spice phenomenon: emergence, identification, legislation and metabolic characterization of synthetic cannabinoids in herbal incense products. *Drug Metab Rev* 2014;**46**:72–85. <https://doi.org/10.3109/03602532.2013.839700>
115. Bertol E, Mari F, Boscolo Berto R, Mannaioni G, Vaiano F, Favretto D. A mixed MDPV and benzodiazepine intoxication in a chronic drug abuser: determination of MDPV metabolites by LC-HRMS and discussion of the case. *Forensic Sci Int* 2014;**243**:149–55. <https://doi.org/10.1016/j.forsciint.2014.08.002>
116. Bhattacharya IS, Watson F, Bruce M. A case of γ -butyrolactone associated with severe withdrawal delirium and acute renal failure. *Eur Addict Res* 2011;**17**:169–71. <https://doi.org/10.1159/000324343>
117. Bretteville-Jensen AL, Tuv SS, Bilgri OR, Fjeld B, Bachs L. Synthetic cannabinoids and cathinones: prevalence and markets. *Forensic Sci Rev* 2013;**25**:7–26.
118. Brewer TL, Collins M. A review of clinical manifestations in adolescent and young adults after use of synthetic cannabinoids. *J Spec Pediatr Nurs* 2014;**19**:119–26. <https://doi.org/10.1111/jspn.12057>
119. Brown JA, Gunja N, Buckley NA. Synthetic cannabinoids: impact of Australian legislation; is the problem chronic or chronic? *Clin Toxicol* 2014;**52**:364–5.
120. Bruneel CA, Lakhdar CB, Vaillant NG. Are 'Legal Highs' users satisfied? Evidence from online customer comments. *Subst Use Misuse* 2014;**49**:364–73. <https://doi.org/10.3109/10826084.2013.841243>
121. Bruno R, Matthews AJ, Dunn M, Alati R, McIlwraith F, Hickey S, et al. Emerging psychoactive substance use among regular ecstasy users in Australia. *Drug Alcohol Depend* 2012;**124**:19–25. <https://doi.org/10.1016/j.drugalcdep.2011.11.020>

122. Bulbena-Cabre A, Dunn NR, Swift RG. Synthetic cannabis 'K2' intoxication and psychiatric manifestations. *CNS Spectrums* 2013;**18**:344–5.
123. Burch HJ, Clarke EJ, Hubbard AM, Scott-Ham M. Concentrations of drugs determined in blood samples collected from suspected drugged drivers in England and Wales. *J Forensic Leg Med* 2013;**20**:278–89. <https://doi.org/10.1016/j.jflm.2012.10.005>
124. Burda AM, Strugala MJ, Wahl MS, Dimaano JQ, DesLauriers CA. DOM – an old street drug making a resurgence. *Clin Toxicol* 2009;**47**:755.
125. Burish MJ, Thoren KL, Madou M, Toossi S, Shah M. Hallucinogens causing seizures? A case report of the synthetic amphetamine 2,5-dimethoxy-4-chloroamphetamine. *Neurohospitalist* 2015;**5**:32–4. <https://doi.org/10.1177/1941874414528939>
126. Burns L, Roxburgh A, Matthews A, Bruno R, Lenton S, Van Buskirk J. The rise of new psychoactive substance use in Australia. *Drug Test Anal* 2014;**6**:846–9. <https://doi.org/10.1002/dta.1626>
127. Busardò FP, Kyriakou C, Napoletano S, Marinelli E, Zaami S. Mephedrone related fatalities: a review. *Eur Rev Med Pharmacol Sci* 2015;**19**:3777–90.
128. Brunt TM, Nagy C, Bucheli A, Martins D, Ugarte M, Beduwe C, et al. Drug testing in Europe: monitoring results of the Trans European Drug Information (TEDI) project. *Drug Test Anal* 2016;**17**:17.
129. Buser GL, Gerona RR, Horowitz BZ, Vian KP, Troxell ML, Hendrickson RG, et al. Acute kidney injury associated with smoking synthetic cannabinoid. *Clin Toxicol* 2014;**52**:664–73. <https://doi.org/10.3109/15563650.2014.932365>
130. Butler K, Hayes BD, Howell F. Status epilepticus following use of synthetic marijuana. *Clin Toxicol* 2012;**50**:708.
131. Butler RA, Sheridan JL. Highs and lows: patterns of use, positive and negative effects of benzylopipezazine-containing party pills (BZP-party pills) amongst young people in New Zealand. *Harm Reduct J* 2007;**4**:18. <https://doi.org/10.1186/1477-7517-4-18>
132. Capriola M. Synthetic cathinone abuse. *Clin Pharmacol* 2013;**5**:109–15. <https://doi.org/10.2147/CPAA.S42832>
133. Carbone P, Carbone DL, Carstairs S, Luzi SA. Sudden cardiac death associated with methylone use. *Am J Clin Pathol* 2012;**138**:A323. <https://doi.org/10.1093/ajcp/138.suppl2.50>
134. Carhart-Harris RL, King LA, Nutt DJ. A web-based survey on mephedrone. *Drug Alcohol Depend* 2011;**118**:19–22. <https://doi.org/10.1016/j.drugalcdep.2011.02.011>
135. Carroll KS, Alston W, Marsal ES, Harris A. Substance abuse treatment: spice and bath salt addiction – so what's next? *J Hum Behav Soc Environ* 2014;**24**:573–81. <https://doi.org/10.1080/10911359.2014.914821>
136. Casselman I, Heinrich M. Novel use patterns of *Salvia divinorum*: unobtrusive observation using YouTube™. *J Ethnopharmacol* 2011;**138**:662–7. <https://doi.org/10.1016/j.jep.2011.07.065>
137. Castaneto MS, Gorelick DA, Desrosiers NA, Hartman RL, Pirard S, Huestis MA. Synthetic cannabinoids: epidemiology, pharmacodynamics, and clinical implications. *Drug Alcohol Depend* 2014;**144**:12–41. <https://doi.org/10.1016/j.drugalcdep.2014.08.005>
138. Castellanos D, Singh S, Thornton G, Avila M, Moreno A. Synthetic cannabinoid use: a case series of adolescents. *J Adolesc Health* 2011;**49**:347–9. <https://doi.org/10.1016/j.jadohealth.2011.08.002>
139. Castellanos D, Thornton G. Synthetic cannabinoid use: recognition and management. *J Psychiatr Pract* 2012;**18**:86–93. <https://doi.org/10.1097/01.pra.0000413274.09305.9c>
140. Calles JL, Jr. *Novel Drugs of Abuse*. Hauppauge, NY: Nova Science Publishers; 2015.

141. Caroway M, Scott J, Thakar CV. Mechanisms of rhabdomyolysis induced AKI in the intensive care unit: a case series. *Am J Kidney Dis* 2016;**67**:A31. <https://doi.org/10.1053/j.ajkd.2016.03.059>
142. Castellanos D, Gralnik LM. Synthetic cannabinoids 2015: an update for pediatricians in clinical practice. *World J Clin Pediatr* 2016;**5**:16–24. <https://doi.org/10.5409/wjcp.v5.i1.16>
143. Catlyn K, Moguillansky N, Mehta H, Jantz M, Patel V. Synthetic cannabinoids as a cause for black carbonaceous bronchoalveolar lavage. *Chest* 2013;**144**:23A. <https://doi.org/10.1378/chest.1703301>
144. Caviness CM, Tzilos G, Anderson BJ, Stein MD. Synthetic Cannabinoids: use and Predictors in a Community Sample of Young Adults. *Subst Abus* 2015;**36**:368–73. <https://doi.org/10.1080/08897077.2014.959151>
145. Celofiga A, Koprivsek J, Klavz J. Use of synthetic cannabinoids in patients with psychotic disorders: case series. *J Dual Diagn* 2014;**10**:168–73. <https://doi.org/10.1080/15504263.2014.929364>
146. Centers for Disease Control and Prevention. Emergency department visits after use of a drug sold as 'bath salts' – Michigan, November 13, 2010–March 31, 2011. *MMWR Morb Mortal Wkly Rep* 2011;**60**:624–7.
147. Centers for Disease Control and Prevention. Notes from the field: severe illness associated with reported use of synthetic marijuana – Colorado, August–September 2013. *MMWR Morb Mortal Wkly Rep* 2013;**62**:1016–17.
148. Centers for Disease Control and Prevention. Notes from the field: severe illness associated with synthetic cannabinoid use – Brunswick, Georgia, 2013. *MMWR Morb Mortal Wkly Rep* 2013;**62**:939.
149. Centers for Disease Control and Prevention. Acute kidney injury associated with synthetic cannabinoid use – multiple states, 2012. *MMWR Morb Mortal Wkly Rep* 2013;**62**:93–8.
150. Chan WL, Wood DM, Hudson S, Dargan PI. Acute psychosis associated with recreational use of benzofuran 6-(2-aminopropyl)benzofuran (6-APB) and cannabis. *J Med Toxicol* 2013;**9**:278–81. <https://doi.org/10.1007/s13181-013-0306-y>
151. Champion KE, Newton NC, Stapinski LA, Teesson M. Effectiveness of a universal Internet-based prevention program for ecstasy and new psychoactive substances: a cluster randomised controlled trial. *Addiction* 2016;**16**:16. <https://doi.org/10.1111/add.13345>
152. Chase PB. Signs of synthetic cannabinoid vs. marijuana intoxication as determined by police drug recognition experts. *Clin Toxicol* 2013;**51**:667.
153. Chavant F, Boucher A, Le Boisselier R, Deheul S, Debruyne D. New synthetic drugs in addictovigilance. *Therapie* 2015;**70**:167–89. <https://doi.org/10.2515/therapie/2015001>
154. Chavarin A, Nogue S, Castaneda-Pomeda M, Gil V. The dangers of buying 'research chemicals' online, bromo-dragonfly mislabelled as 2C-B Fly: a confirmed case report, and its follow up in 'research chemical' specific social media. *Clin Toxicol* 2013;**51**:347.
155. Chen C, Kostakis C, Irvine RJ, White JM. Increases in use of novel synthetic stimulant are not directly linked to decreased use of 3,4-methylenedioxy-N-methylamphetamine (MDMA). *Forensic Sci Int* 2013;**231**:278–83. <https://doi.org/10.1016/j.forsciint.2013.06.007>
156. Cheng FK, Robinson T, Domingo C, Ally M, Kim CH, Itzkowitz S. Spicing up the differential for cyclic vomiting: a case of synthetic-cannabinoid induced hyperemesis syndrome. *Am J Gastroenterol* 2012;**107**:S268–9.
157. Chillemi E, Martinotti G, Bonifaci L, Santacroce, R, Cinosi E, Lupi M, et al. Epidemiology of novel psychoactive substances in an Italian sample. *Eur Neuropsychopharmacol* 2014;**24**:S683. [https://doi.org/10.1016/S0924-977X\(14\)71101-0](https://doi.org/10.1016/S0924-977X(14)71101-0)

158. Choi H, Neto MR. 'Bath salts': bad new kids on the block. *Chest* 2012;**142**:984A–984B. <http://dx.doi.org/10.1378/chest.1390017>
159. Chung E, Waters L, Mercey D, Edwards S. High rates of recreational drug use (RDU) in HIV+ men who have sex with men (MSM) with sexually transmitted infections (STI). *HIV Med* 2014;**15**:50.
160. Chase PB, Hawkins J, Mosier J, Jimenez E, Boesen K, Logan BK, *et al.* Differential physiological and behavioral cues observed in individuals smoking botanical marijuana versus synthetic cannabinoid drugs. *Clin Toxicol (Phila)* 2016;**54**:14–9. <https://doi.org/10.3109/15563650.2015.1101769>
161. Chinnadurai T, Shrestha S, Ayinla R. A curious case of inhalation fever caused by synthetic cannabinoid. *Am J Case Rep* 2016;**17**:379–83. <https://doi.org/10.12659/AJCR.898500>
162. Christie G, MacFarlane V. Synthetic cannabinoid presentations decline following ban. *Drug Alcohol Rev* 2016;**35**:E3–4. <https://doi.org/10.1111/dar.12352>
163. Cinosi E, Corazza O, Santacroce R, Lupi M, Acciavatti T, Martinotti G, di Giannantonio M. New drugs on the Internet: the case of Camfetamine. *Biomed Res Int* 2014;**2014**:419026. <https://doi.org/10.1155/2014/419026>
164. Clark BC, Georgekutty J, Berul CI. Myocardial ischemia secondary to synthetic cannabinoid (K2) use in pediatric patients. *J Pediatr* 2015;**167**:757–61.e1. <https://doi.org/10.1016/j.jpeds.2015.06.001>
165. Cohen BM, Butler R. BZP-party pills: a review of research on benzylpiperazine as a recreational drug. *Int J Drug Policy* 2011;**22**:95–101. <https://doi.org/10.1016/j.drugpo.2010.12.002>
166. Cohen J, Morrison S, Greenberg J, Saidinejad M. Clinical presentation of intoxication due to synthetic cannabinoids. *Pediatrics* 2012;**129**:e1064–7. <https://doi.org/10.1542/peds.2011-1797>
167. Corazza O, Assi S, Simonato P, Corkery J, Bersani FS, Demetrovics Z, *et al.* Promoting innovation and excellence to face the rapid diffusion of novel psychoactive substances in the EU: the outcomes of the ReDNet project. *Hum Psychopharmacol* 2013;**28**:317–23. <https://doi.org/10.1002/hup.2299>
168. Corazza O, Schifano F, Farre M, Deluca P, Davey Z, Torrens M, *et al.* Designer drugs on the internet: a phenomenon out-of-control? The emergence of hallucinogenic drug Bromo-Dragonfly. *Curr Clin Pharmacol* 2011;**6**:125–9. <https://doi.org/10.2174/157488411796151129>
169. Corazza O, Schifano F, Simonato P, Fergus S, Assi S, Stair J, *et al.* Phenomenon of new drugs on the Internet: the case of ketamine derivative methoxetamine. *Hum Psychopharmacol* 2012;**27**:145–9. <https://doi.org/10.1002/hup.1242>
170. Corazza O, Simonato P, Corkery J, Trincas G, Schifano F. 'Legal highs': safe and legal 'heavens'? A study on the diffusion, knowledge and risk awareness of novel psychoactive drugs among students in the UK. *Riv Psichiatr* 2014;**49**:89–94. <https://doi.org/10.1708/1461.16147>
171. Corazza O, Valeriani G, Bersani FS, Corkery J, Martinotti G, Bersani G, *et al.* 'Spice,' 'kryptonite,' 'black mamba': an overview of brand names and marketing strategies of novel psychoactive substances on the web. *J Psychoactive Drugs* 2014;**46**:287–94. <https://doi.org/10.1080/02791072.2014.944291>
172. Corkery JM, Durkin E, Elliott S, Schifano F, Ghodse AH. The recreational tryptamine 5-MeO-DALT (N,N-diallyl-5-methoxytryptamine): a brief review. *Prog Neuropsychopharmacol Biol Psychiatry* 2012;**39**:259–62. <https://doi.org/10.1016/j.pnpbp.2012.05.022>

173. Corkery JM, Elliott S, Schifano F, Corazza O, Ghodse AH. 2-DPMP (desoxypropipradrol, 2-benzhydrylpiperidine, 2-phenylmethylpiperidine) and D2PM (diphenyl-2-pyrrolidin-2-yl-methanol, diphenylprolinol): a preliminary review. *Prog Neuropsychopharmacol Biol Psychiatry* 2012;**39**:253–8. <https://doi.org/10.1016/j.pnpbp.2012.05.021>
174. Corkery JM, Elliott S, Schifano F, Corazza O, Ghodse AH. MDAI (5,6-methylenedioxy-2-aminoindane; 6,7-dihydro-5H-cyclopenta[f][1,3]benzodioxol-6-amine; 'sparkle'; 'mindy') toxicity: a brief overview and update. *Hum Psychopharmacol* 2013;**28**:345–55. <https://doi.org/10.1002/hup.2298>
175. Corkery JM, Schifano F, Ghodse AH. Phenazepam abuse in the UK: an emerging problem causing serious adverse health problems, including death. *Hum Psychopharmacol* 2012;**27**:254–61. <https://doi.org/10.1002/hup.2222>
176. Cinosi E, Martinotti G, Simonato P, Singh D, Demetrovics Z, Roman-Urrestarazu A, *et al.* Following 'the Roots' of Kratom (*Mitragyna speciosa*): the evolution of an enhancer from a traditional use to increase work and productivity in Southeast Asia to a recreational psychoactive drug in Western Countries. *Biomed Res Int* 2015;**2015**:968786. <http://dx.doi.org/10.1155/2015/968786> (accessed 29 June 2016).
177. Clements-Nolle K, Lensch T, Larson S, Yang W. Prevalence and correlates of any and frequent synthetic cannabinoid use in a representative sample of high school students. *Subst Use Misuse* 2016;**51**:1139–46. <https://doi.org/10.3109/10826084.2016.1160121>
178. Cooper ZD. Adverse effects of synthetic cannabinoids: management of acute toxicity and withdrawal. *Curr Psychiatry Rep* 2016;**18**:52. <https://doi.org/10.1007/s11920-016-0694-1>
179. Cosby SH, Peters KL, Quinn A, Bentley A. Mephedrone (methylenedioxymethamphetamine) in toxicology casework: a Northern Ireland perspective. *J Anal Toxicol* 2013;**37**:74–82. <https://doi.org/10.1093/jat/bks094>
180. Cottencin O, Rolland B, Karila L. New designer drugs (synthetic cannabinoids and synthetic cathinones): review of literature. *Curr Pharm Des* 2014;**20**:4106–11. <https://doi.org/10.2174/13816128113199990622>
181. Csák R, Demetrovics Z, Rácz J. Transition to injecting 3,4-methylene-dioxy-pyrovalerone (MDPV) among needle exchange program participants in Hungary. *J Psychopharmacol* 2013;**27**:559–63. <https://doi.org/10.1177/0269881113480987>
182. Currie CL. Epidemiology of adolescent *Salvia divinorum* use in Canada. *Drug Alcohol Depend* 2013;**128**:166–70. <https://doi.org/10.1016/j.drugalcdep.2012.08.008>
183. Dalgarno P. Subjective effects of *Salvia divinorum*. *J Psychoactive Drugs* 2007;**39**:143–9. <https://doi.org/10.1080/02791072.2007.10399872>
184. Dargan PI, Albert S, Wood DM. Mephedrone use and associated adverse effects in school and college/university students before the UK legislation change. *QJM* 2010;**103**:875–9. <https://doi.org/10.1093/qjmed/hcq134>
185. Dargan PI, Button J, Davies S, Ramsey J, George S, Holt DW, Wood DM. The first reported UK fatality related to gamma-butyrolactone (GBL) ingestion. *J R Soc Med* 2009;**102**:546–7. <https://doi.org/10.1258/jrsm.2009.090283>
186. Dargan PI, Hudson S, Ramsey J, Wood DM. The impact of changes in UK classification of the synthetic cannabinoid receptor agonists in 'Spice'. *Int J Drug Policy* 2011;**22**:274–7. <https://doi.org/10.1016/j.drugpo.2011.02.006>
187. Dargan PI, Sedefov R, Gallegos A, Wood DM. The pharmacology and toxicology of the synthetic cathinone mephedrone (4-methylmethcathinone). *Drug Test Anal* 2011;**3**:454–63. <https://doi.org/10.1002/dta.312>

188. Coulon P, Gorji A. Tightrope or slackline? The neuroscience of psychoactive substances. *Trends Pharmacol Sci* 2016;**37**:511–21. <https://doi.org/10.1016/j.tips.2016.04.004>
189. Crevani M, Chiara F, Papa P, Roda E, Lonati D, Giampreti A, *et al.* Novel psychoactive substance (NPS) consumption in binge drinkers: a new and potentially dangerous health risk. *Clin Toxicol* 2016;**54**:385.
190. Cunningham SM, Haikal NA, Kraner JC. Fatal intoxication with acetyl fentanyl. *J Forensic Sci* 2015;**21**:21.
191. Dart RC, Bronstein AC, Spyker DA, Cantilena LR, Seifert SA, Heard SE, Krenzelok EP. Poisoning in the United States: 2012 emergency medicine report of the National Poison Data System. *Ann Emerg Med* 2015;**65**:416–22. <https://doi.org/10.1016/j.annemergmed.2014.11.001>
192. Daskalopoulou M, Rodger A, Phillips AN, Sherr L, Speakman A, Collins S, *et al.* Recreational drug use, polydrug use, and sexual behaviour in HIV-diagnosed men who have sex with men in the UK: results from the cross-sectional ASTRA study. *Lancet HIV* 2014;**1**:e22–31. [https://doi.org/10.1016/S2352-3018\(14\)70001-3](https://doi.org/10.1016/S2352-3018(14)70001-3)
193. Davis C, Boddington D. Teenage cardiac arrest following abuse of synthetic cannabis. *Heart Lung Circ* 2015;**24**:e162–3. <https://doi.org/10.1016/j.hlc.2015.04.176>
194. de Havenon A, Chin B, Thomas KC, Afra P. The secret 'spice': an undetectable toxic cause of seizure. *Neurohospitalist* 2011;**1**:182–6. <https://doi.org/10.1177/1941874411417977>
195. Dean BV, Stellpflug SJ, Burnett AM, Engebretsen KM. 2C or not 2C: phenethylamine designer drug review. *J Med Toxicol* 2013;**9**:172–8. <https://doi.org/10.1007/s13181-013-0295-x>
196. Debruyne D, Le Boisselier R. Emerging drugs of abuse: current perspectives on synthetic cannabinoids. *Subst Abuse Rehabil* 2015;**6**:113–29. <https://doi.org/10.2147/SAR.S73586>
197. Deluca P, Davey Z, Corazza O, Di Furia L, Farre M, Flesland LH, *et al.* Identifying emerging trends in recreational drug use; outcomes from the Psychonaut Web Mapping Project. *Prog Neuropsychopharmacol Biol Psychiatry* 2012;**39**:221–6. <https://doi.org/10.1016/j.pnpbp.2012.07.011>
198. Davies BB, Bayard C, Larson SJ, Zarwell LW, Mitchell RA. Retrospective analysis of synthetic cannabinoid metabolites in urine of individuals suspected of driving impaired. *J Anal Toxicol* 2016;**40**:89–96. <https://doi.org/10.1093/jat/bkv136>
199. Demirci H, Coşar R, Çiftçi Ö, Sarı IK. Atypical diabetic ketoacidosis: case report. *Balkan Med J* 2015;**32**:124–6. <https://doi.org/10.5152/balkanmedj.2015.15123>
200. Derungs A, Schietzel S, Meyer MR, Maurer HH, Krähenbühl S, Liechti ME. Sympathomimetic toxicity in a case of analytically confirmed recreational use of naphyrone (naphthylpyrovalerone). *Clin Toxicol* 2011;**49**:691–3. <https://doi.org/10.3109/15563650.2011.592838>
201. Derungs A, Schwaninger AE, Mansella G, Bingisser R, Kraemer T, Liechti ME. Symptoms, toxicities, and analytical results for a patient after smoking herbs containing the novel synthetic cannabinoid MAM-2201. *Forensic Toxicol* 2013;**31**:164–71. <https://doi.org/10.1007/s11419-012-0166-1>
202. Dickson AJ, Vorce SP, Levine B, Past MR. Multiple-drug toxicity caused by the coadministration of 4-methylmethcathinone (mephedrone) and heroin. *J Anal Toxicol* 2010;**34**:162–8. <https://doi.org/10.1093/jat/34.3.162>
203. Dines AM, Wood DM, Yates C, Heyerdahl F, Hovda KE, Giraudon I, *et al.* The European Drug Emergencies Network (Euro-DEN) project a model for multi-centre data collection on acute recreational drug toxicity. *Clin Toxicol* 2015;**53**:647–8. <https://doi.org/10.3109/15563650.2015.1088157>

204. Drees JC, Stone JA, Wu AH. Morbidity involving the hallucinogenic designer amines MDA and 2C-I. *J Forensic Sci* 2009;**54**:1485–7. <https://doi.org/10.1111/j.1556-4029.2009.01199.x>
205. Doğan S, Akman C, Yılmaz A, Kalafat UM, Ocağ T. A hypothermic case with giant Osborn waves and atrial fibrillation after using synthetic cannabinoid. *Anatol J Cardiol* 2016;**16**:E1. <https://doi.org/10.14744/AnatolJCardiol.2015.6856>
206. Dolengevich-Segal H, Rodríguez-Salgado B, Gómez-Arnau J, Sánchez-Mateos D. Severe psychosis, drug dependence, and Hepatitis C related to slamming mephedrone. *Case Rep Psychiatry* 2016;**2016**:8379562. <https://doi.org/10.1155/2016/8379562>
207. US Department of Justice, Drug Enforcement Administration. Schedules of controlled substances: temporary placement of butyryl fentanyl and beta-hydroxythiofentanyl into Schedule I. Final order. *Fed Regist* 2016;**81**:29492–6.
208. US Department of Justice, Drug Enforcement Administration. Schedules of controlled substances: temporary placement of the synthetic cannabinoid MAB-CHMINACA into Schedule I. Final order. *Fed Regist* 2016;**81**:6171–5.
209. Duffert A. Current challenges and problems in the field of new psychoactive substances in Germany from a law enforcement perspective. *Drug Test Anal* 2014;**6**:876–8. <https://doi.org/10.1002/dta.1604>
210. Dugan S, Roesler J, Westbrook A, Bilden E, Anderson D, Van Deelen N, *et al.* The high cost of bath salts: a study of the health care burden of illicit synthetic drug use in Duluth, Minnesota. *Minn Med* 2014;**97**:34–7.
211. Dunne FJ, Jaffar K, Hashmi S. Legal highs – not so new and still growing in popularity. *BJMP* 2015;**8**:25–33.
212. Durand D, Delgado LL, de la Parra-Pellot DM, Nichols-Vinueza D. Psychosis and severe rhabdomyolysis associated with synthetic cannabinoid use: a case report. *Clin Schizophr Relat Psychoses* 2015;**8**:205–8. <https://doi.org/10.3371/CSRP.DUDE.031513>
213. Durham M. Ivory wave: the next mephedrone? *Emerg Med J* 2011;**28**:1059–60. <https://doi.org/10.1136/emj.2011.112920>
214. Dybdal-Hargreaves NF, Holder ND, Ottoson PE, Sweeney MD, Williams T. Mephedrone: public health risk, mechanisms of action, and behavioral effects. *Eur J Pharmacol* 2013;**714**:32–40. <https://doi.org/10.1016/j.ejphar.2013.05.024>
215. Egan KL, Suerken CK, Reboussin BA, Spangler J, Wagoner KG, Sutfin EL, *et al.* K2 and Spice use among a cohort of college students in southeast region of the USA. *Am J Drug Alcohol Abuse* 2015;**41**:317–22. <https://doi.org/10.3109/00952990.2015.1043438>
216. Eiden C, Mathieu O, Cathala P, Debruyne D, Baccino E, Petit P, Peyriere H. Toxicity and death following recreational use of 2-pyrrolidino valerophenone. *Clin Toxicol* 2013;**51**:899–903. <https://doi.org/10.3109/15563650.2013.847187>
217. El-Higaya E, Ahmed M, Hallahan B. Whack induced psychosis: a case series. *Ir J Psychol Med* 2011;**28**:S11–S13. <https://doi.org/10.1017/S0790966700011915>
218. El-Khoury J, Sahakian N. The association of Salvia divinorum and psychotic disorders: a review of the literature and case series. *J Psychoactive Drugs* 2015;**47**:286–92. <https://doi.org/10.1080/02791072.2015.1073815>
219. Elliott S, Smith C. Investigation of the first deaths in the United Kingdom involving the detection and quantitation of the piperazines BZP and 3-TFMP. *J Anal Toxicol* 2008;**32**:172–7. <https://doi.org/10.1093/jat/32.2.172>

220. Egan KL, Erasquin JT, Milroy JJ, Wyrick DL. Synthetic cannabinoid use and descriptive norms among collegiate student-athletes. *J Psychoactive Drugs* 2016;**48**:166–72. <https://doi.org/10.1080/02791072.2016.1186305>
221. Elliott S, Evans J. A 3-year review of new psychoactive substances in casework. *Forensic Sci Int* 2014;**243**:55–60. <https://doi.org/10.1016/j.forsciint.2014.04.017>
222. Elliott SP, Brandt SD, Wallach J, Morris H, Kavanagh PV. First reported fatalities associated with the 'research chemical' 2-methoxydiphenidine. *J Anal Toxicol* 2015;**39**:287–93. <https://doi.org/10.1093/jat/bkv006>
223. Every-Palmer S. Warning: legal synthetic cannabinoid-receptor agonists such as JWH-018 may precipitate psychosis in vulnerable individuals. *Addiction* 2010;**105**:1859–60. <https://doi.org/10.1111/j.1360-0443.2010.03119.x>
224. Every-Palmer S. Synthetic cannabinoid JWH-018 and psychosis: an explorative study. *Drug Alcohol Depend* 2011;**117**:152–7. <https://doi.org/10.1016/j.drugalcdep.2011.01.012>
225. Evren C, Bozkurt M. Synthetic cannabinoids: crisis of the decade. *Dusunen Adam* 2013;**26**:1–11.
226. Elliott SP, Brandt SD, Smith C. The first reported fatality associated with the synthetic opioid 3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide (U-47700) and implications for forensic analysis. *Drug Test Anal* 2016;**27**:27. <https://doi.org/10.1002/dta.1984>
227. Elsheshtawy M, Sriganesh P, Virparia V, Patel F, Khanna A. Synthetic marijuana induced acute nonischemic left ventricular dysfunction. *Case Rep Cardiol* 2016;**2016**:9625758. <https://doi.org/10.1155/2016/9625758>
228. Evans-Brown M. Toxicovigilance of new psychoactive substances – perspectives from the EU Early Warning System. *Toxicol Lett* 2015;**1**:S5. <https://doi.org/10.1016/j.toxlet.2015.08.031>
229. Ezaki J, Ro A, Hasegawa M, Kibayashi K. Fatal overdose from synthetic cannabinoids and cathinones in Japan: demographics and autopsy findings. *Am J Drug Alcohol Abuse* 2016;**42**:520–9. <https://doi.org/10.3109/00952990.2016.1172594>
230. Ezquiaga I, Grifell M, Galindo L, Martínez L, Palma A, Quintana P, et al. 25I-NBOMe: the legal LSD. *Eur Psychiatry* 2016;**33**:S72–3. <https://doi.org/10.1016/j.eurpsy.2016.01.006>
231. Farre M, Perez-Mana C, De Souza E, Mateus J, Theunisen E, Kuypers K, et al. Interactions between mephedrone and alcohol in humans: cardiovascular and subjective effects. *Eur Psychiatry* 2016;**33**:S115. <https://doi.org/10.1016/j.eurpsy.2016.01.122>
232. Fassette T, Martinez A. An impaired driver found to be under the influence of methoxetamine. *J Anal Toxicol* 2016;**40**:700–2. <https://doi.org/10.1093/jat/bkw054>
233. Fattore L. Synthetic cannabinoids – further evidence supporting the relationship between cannabinoids and psychosis. *Biol Psychiatry* 2016;**79**:539–48. <https://doi.org/10.1016/j.biopsych.2016.02.001>
234. Fernandez D, Hammer J, De Olano J, Nelson LS, Hoffman RS, Su MK. A synthetic cannabinoid receptor agonist (AB-FUBINACA)-associated fatality. *Clin Toxicol* 2016;**54**:408.
235. Finkelstein Y, Goel G, Hutson JR, Armstrong J, Baum CR, Wax P, et al. Drug misuse in adolescents presenting to the emergency department [published online ahead of print October 13 2015]. *Pediatr Emerg Care* 2015. <https://doi.org/10.1097/PEC.0000000000000571>
236. Faircloth J, Khandheria B, Shum S. Case report: adverse reaction to synthetic marijuana. *Am J Addict* 2012;**21**:289–90. <https://doi.org/10.1111/j.1521-0391.2012.00220.x>
237. Farre M, Gonzalez D, Marsa F, Caudevila F, Ventura M, Pérez-Mañá C, et al. New psychoactive drugs in Spain: results of two surveys. *Basic Clin Pharmacol Toxicol* 2012;**111**:39.

238. Fass JA, Fass AD, Garcia AS. Synthetic cathinones (bath salts): legal status and patterns of abuse. *Ann Pharmacother* 2012;**46**:436–41. <https://doi.org/10.1345/aph.1Q628>
239. Fattore L, Fratta W. Beyond THC: the new generation of cannabinoid designer drugs. *Front Behav Neurosci* 2011;**5**:60. <https://doi.org/10.3389/fnbeh.2011.00060>
240. Ford JA, Watkins WC, Blumenstein L. Correlates of Salvia divinorum use in a national sample: findings from the 2009 National Survey on Drug Use and Health. *Addict Behav* 2011;**36**:1032–7. <https://doi.org/10.1016/j.addbeh.2011.06.004>
241. Forrester MB. Adolescent synthetic cannabinoid exposures reported to Texas poison centers. *Pediatr Emerg Care* 2012;**28**:985–9. <https://doi.org/10.1097/PEC.0b013e31826c9a97>
242. Forrester MB. Synthetic cathinone exposures reported to Texas poison centers. *Am J Drug Alcohol Abuse* 2012;**38**:609–15. <https://doi.org/10.3109/00952990.2012.677890>
243. Forrester MB. NBOMe designer drug exposures reported to Texas poison centers. *J Addict Dis* 2014;**33**:196–201. <https://doi.org/10.1080/10550887.2014.950027>
244. Forrester MB, Baker SD, Roth B. Adolescent 2C series phenethylamine derivative exposures reported to poison centers. *Clin Toxicol* 2013;**51**:669–70.
245. Forrester MB, Haywood T. Geographic distribution of synthetic cannabinoid exposures reported to Texas poison centers. *Am J Drug Alcohol Abuse* 2012;**38**:603–8. <https://doi.org/10.3109/00952990.2012.670339>
246. Forrester MB, Kleinschmidt K. Combined synthetic cannabinoid-synthetic cathinone exposures reported to poison centers. *Clin Toxicol* 2012;**50**:610.
247. Forrester MB, Kleinschmidt K, Gardner M. A comparison of synthetic cannabinoid exposures near the Mexican border vs. those distant from the border. *Clin Toxicol* 2012;**50**:613.
248. Forrester MB, Kleinschmidt K, Schwarz E, Young A. Synthetic cannabinoid and marijuana exposures reported to poison centers. *Hum Exp Toxicol* 2012;**31**:1006–11. <https://doi.org/10.1177/0960327111421945>
249. Forrester MB, Leung L, Kleinschmidt K. Comparison of ingested versus inhaled synthetic cathinone exposures. *Clin Toxicol* 2012;**50**:705–6.
250. Forrester MB, Leung L, Kleinschmidt K. Comparison of synthetic cannabinoid and methylenedioxymethamphetamine (MDMA) exposures. *Clin Toxicol* 2012;**50**:706–7.
251. Forrester MB, Kleinschmidt K, Schwarz E, Young A. Synthetic cannabinoid exposures reported to Texas poison centers. *J Addict Dis* 2011;**30**:351–8. <https://doi.org/10.1080/10550887.2011.609807>
252. Ford LT, Berg JD. ANNALS EXPRESS: analysis of legal high materials by UPLC-MS/TOF as part of a toxicology vigilance system. What are the most popular novel psychoactive substances in the UK? *Ann Clin Biochem* 2016;**10**:10.
253. Freeman TP, Curran HV. Supply always comes on the heels of demand: what effects do control strategies have on drug users themselves? *Addiction* 2012;**107**:1903–5. <https://doi.org/10.1111/j.1360-0443.2012.04032.x>
254. Freeman TP, Morgan CJ, Vaughn-Jones J, Hussain N, Karimi K, Curran HV. Cognitive and subjective effects of mephedrone and factors influencing use of a 'new legal high'. *Addiction* 2012;**107**:792–800. <https://doi.org/10.1111/j.1360-0443.2011.03719.x>
255. Froberg BA, Bauer BD. Pneumothorax, pneumomediastinum, and subcutaneous emphysema after synthetic cannabinoid use. *Clin Toxicol* 2012;**50**:705.

256. Froberg BA, Levine M, Engebretsen KM, McKeown NJ, Kostic M, Rosenbaum CD, *et al.* Clinical presentations and medical complications after exposure to substances labeled as 'bath salts': a ToxIC preliminary report. *Clin Toxicol* 2012;**50**:704–5.
257. Fröhlich S, Lambe E, O'Dea J. Acute liver failure following recreational use of psychotropic 'head shop' compounds. *Ir J Med Sci* 2011;**180**:263–4. <https://doi.org/10.1007/s11845-010-0636-6>
258. Gahr M, Freudenmann RW, Hiemke C, Gunst IM, Connemann BJ, Schönfeldt-Lecuona C. Desomorphine goes 'crocodile'. *J Addict Dis* 2012;**31**:407–12. <https://doi.org/10.1080/10550887.2012.735570>
259. Gaillard YP, Cuquel AC, Boucher A, Romeuf L, Bevalot F, Prevosto JM, Menard JM. A fatality following ingestion of the designer drug meta-chlorophenylpiperazine (mCPP) in an asthmatic – HPLC-MS/MS detection in biofluids and hair. *J Forensic Sci* 2013;**58**:263–9. <https://doi.org/10.1111/j.1556-4029.2012.02254.x>
260. Gallagher CT, Assi S, Stair JL, Fergus S, Corazza O, Corkery JM, Schifano F. 5,6-Methylenedioxy-2-aminoindane: from laboratory curiosity to 'legal high'. *Hum Psychopharmacol* 2012;**27**:106–12. <https://doi.org/10.1002/hup.1255>
261. Garrett G, Sweeney M. The serotonin syndrome as a result of mephedrone toxicity. *BMJ Case Rep* 2010;**2010**:bcr0420102925. <https://doi.org/10.1136/bcr.04.2010.2925>
262. Frinculescu A, Lyall CL, Ramsey J, Miserez B. Variation in commercial smoking mixtures containing third-generation synthetic cannabinoids. *Drug Test Anal* 2016;**9**:327–33. <https://doi.org/10.1002/dta.1975>
263. Galbis-Reig D. A case report of kratom addiction and withdrawal. *WMJ* 2016;**115**:49–52.
264. Galindo L, Grifell M, Quintana P, Palma A, Tirado J, Ventura M, *et al.* The synthetic cannabinoids: JWH, four years of analysis. *Eur Psychiatry* 2016;**33**:S115–S116. <https://doi.org/10.1016/j.eurpsy.2016.01.123>
265. Gee P, Jackson S, Easton J. Another bitter pill: a case of toxicity from DMAA party pills. *N Z Med J* 2010;**123**:124–7.
266. German CL, Fleckenstein AE, Hanson GR. Bath salts and synthetic cathinones: an emerging designer drug phenomenon. *Life Sci* 2014;**97**:2–8. <https://doi.org/10.1016/j.lfs.2013.07.023>
267. Gerona RRL, Birsdall E, Wu AH. Non-targeted analysis of synthetic cannabinoids in two intoxication cases involving herbal incense products. *Am J Clin Pathol* 2011;**136**:474–5.
268. Gerostamoulos D, Drummer OH, Woodford NW. Deaths linked to synthetic cannabinoids. *Forensic Sci Med Pathol* 2015;**11**:478. <https://doi.org/10.1007/s12024-015-9669-5>
269. Giese C, Igoe D, Gibbons Z, Hurley C, Stokes S, McNamara S, *et al.* Injection of new psychoactive substance snow blow associated with recently acquired HIV infections among homeless people who inject drugs in Dublin, Ireland, 2015. *Euro Surveill* 2015;**20**:pii=30036. <https://doi.org/10.2807/1560-7917.ES.2015.20.40.30036>
270. Gil D, Adamowicz P, Skulska A, Tokarczyk B, Stanaszek R. Analysis of 4-MEC in biological and non-biological material – three case reports. *Forensic Sci Int* 2013;**228**:e11–15. <https://doi.org/10.1016/j.forsciint.2013.03.011>
271. Glennon RA. Bath salts, mephedrone, and methylenedioxypropylvalerone as emerging illicit drugs that will need targeted therapeutic intervention. *Adv Pharmacol* 2014;**69**:581–620. <https://doi.org/10.1016/B978-0-12-420118-7.00015-9>
272. Gilani F. Novel psychoactive substances: the rising wave of 'legal highs'. *Br J Gen Pract* 2016;**66**:8–9. <https://doi.org/10.3399/bjgp16X683053>

273. Gjerde H, Nordfjærn T, Bretteville-Jensen AL, Edland-Gryt M, Furuhaugen H, Karinen R, Øiestad EL. Comparison of drugs used by nightclub patrons and criminal offenders in Oslo, Norway. *Forensic Sci Int* 2016;**265**:1–5. <https://doi.org/10.1016/j.forsciint.2015.12.029>
274. Glass G, Park S, Fisse D, Cazanave S, Katz H. Case study for neurorehabilitation of hypoxic encephalopathy secondary to synthetic marijuana use. *J Head Trauma Rehabil* 2015;**30**:E70.
275. Glue P, Al-Shaqsi S, Hancock D, Gale C, Strong B, Schep L. Hospitalisation associated with use of the synthetic cannabinoid K2. *N Z Med J* 2013;**126**:18–23.
276. Glue P, Courts J, MacDonald M, Gale C, Mason E. Implementation of the 2013 Psychoactive Substances Act and mental health harms from synthetic cannabinoids. *N Z Med J* 2015;**128**:15–18.
277. Goggin LS, Gately N, Bridle RI. Novel psychoactive substance and other drug use by young adults in Western Australia. *J Psychoactive Drugs* 2015;**47**:140–8. <https://doi.org/10.1080/02791072.2015.1031413>
278. González D, Riba J, Bouso JC, Gómez-Jarabo G, Barbanoj MJ. Pattern of use and subjective effects of *Salvia divinorum* among recreational users. *Drug Alcohol Depend* 2006;**85**:157–62. <https://doi.org/10.1016/j.drugalcdep.2006.04.001>
279. González D, Ventura M, Caudevilla F, Torrens M, Farre M. Consumption of new psychoactive substances in a Spanish sample of research chemical users. *Hum Psychopharmacol* 2013;**28**:332–40. <https://doi.org/10.1002/hup.2323>
280. Gonzalez ML, Royce ME. Tonic-clonic seizures associated with K2 use: a case report. *J Pharm Pract* 2012;**25**:300–1.
281. Goss CH. Legal Highs. Learn how to identify and treat patients under the influence of so-called legal substances of abuse. *JEMS* 2015;**40**:62–7.
282. Gray BA, Holland C. Implications of psychoactive ‘bath salts’ use during pregnancy. *Nurs Womens Health* 2014;**18**:220–30. <https://doi.org/10.1111/1751-486X.12123>
283. Green D, Barry P, Green HD. Central cyanosis on a psychiatric unit treated at the Salford Royal Hospital. *Thorax* 2014;**69**:1157–8. <https://doi.org/10.1136/thoraxjnl-2014-205769>
284. Green JA. Partying on? Life after BZP-based party pills. *N Z Med J* 2008;**121**:35–42.
285. Grapp M, Sauer C, Vidal C, Müller D. GC-MS analysis of the designer drug α -pyrrolidinovalerophenone and its metabolites in urine and blood in an acute poisoning case. *Forensic Sci Int* 2016;**259**:e14–19. <https://doi.org/10.1016/j.forsciint.2015.12.020>
286. Gray R, Bressington D, Hughes E, Ivanecka A. A systematic review of the effects of novel psychoactive substances ‘legal highs’ on people with severe mental illness. *J Psychiatr Ment Health Nurs* 2016;**23**:267–81. <https://doi.org/10.1111/jpm.12297>
287. Griffith DJ, Mackintosh CL, Inverarity D. *Staphylococcus aureus* bacteraemia associated with injected new psychoactive substances. *Epidemiol Infect* 2016;**144**:1257–66. <https://doi.org/10.1017/S095026881500271X>
288. Gudsoorkar VS, Perez JA, Jr. A new differential diagnosis: synthetic cannabinoids-associated acute renal failure. *Methodist Debaquey Cardiovasc J* 2015;**11**:189–91. <https://doi.org/10.14797/mdcj-11-3-189>
289. Gugelmann H, Gerona R, Leibovich SA, Anderson I, Kim S, Durrani T. Seizures and rhabdomyolysis with a novel phenethylamine: 2,5-dimethoxy-4-chloroamphetamine (DOC). *Clin Toxicol* 2014;**52**:709.

290. Gugelmann H, Gerona R, Li C, Tsutaoka B, Olson KR, Lung D. 'Crazy Monkey' poisons man and dog: human and canine seizures due to PB-22, a novel synthetic cannabinoid. *Clin Toxicol* 2014;**52**:635–8. <https://doi.org/10.3109/15563650.2014.925562>
291. Gugelmann H, Kim S, Bigelow J, Friesen M, Olson KR, Gerona R. Cardiogenic shock from a novel phenethylamine: 3,4-methylenedioxybutanphenamine (MDB, aka BDB) intoxication. *Clin Toxicol* 2014;**52**:708–9.
292. Gunderson EW. Synthetic cannabinoids: a new frontier of designer drugs. *Ann Intern Med* 2013;**159**:563–4. <https://doi.org/10.7326/0003-4819-159-8-201310150-00707>
293. Gunderson EW, Haughey HM, Ait-Daoud N, Joshi AS, Hart CL. 'Spice' and 'K2' herbal highs: a case series and systematic review of the clinical effects and biopsychosocial implications of synthetic cannabinoid use in humans. *Am J Addict* 2012;**21**:320–6. <https://doi.org/10.1111/j.1521-0391.2012.00240.x>
294. Gunderson EW, Haughey HM, Ait-Daoud N, Joshi AS, Hart CL. A survey of synthetic cannabinoid consumption by current cannabis users. *Subst Abus* 2014;**35**:184–9. <https://doi.org/10.1080/08897077.2013.846288>
295. Gunderson EW, Kirkpatrick MG, Willing LM, Holstege CP. Intranasal substituted cathinone 'bath salts' psychosis potentially exacerbated by diphenhydramine. *J Addict Med* 2013;**7**:163–8. <https://doi.org/10.1097/ADM.0b013e31829084d5>
296. Gunderson EW, Kirkpatrick MG, Willing LM, Holstege CP. Substituted cathinone products: a new trend in 'bath salts' and other designer stimulant drug use. *J Addict Med* 2013;**7**:153–62. <https://doi.org/10.1097/ADM.0b013e31829084b7>
297. Gunja N, Kuligowski K, Paul PG, Collins M, Anderson R, Kwan J. Acute agitation and chest pain from 5-fluoro-AKB48: a novel synthetic cannabinoid. *Clin Toxicol* 2014;**52**:364.
298. Gurney SM, Scott KS, Kacinko SL, Presley BC, Logan BK. Pharmacology, toxicology, and adverse effects of synthetic cannabinoid drugs. *Forensic Sci Rev* 2014;**26**:53–78.
299. Gutierrez KM, Cooper TV. Investigating correlates of synthetic marijuana and Salvia use in light and intermittent smokers and college students in a predominantly Hispanic sample. *Exp Clin Psychopharmacol* 2014;**22**:524–9. <https://doi.org/10.1037/a0038014>
300. Hagerkvist R, Hulten P, Personne M. Increasing abuse of new cathinone derivatives in Sweden – a poisons centre study for the years 2008–2009. *Clin Toxicol* 2010;**48**:291–2.
301. Hammersley R. Dangers of banning spice and the synthetic cannabinoid agonists. *Addiction* 2010;**105**:373. <https://doi.org/10.1111/j.1360-0443.2009.02845.x>
302. Hammond WA. 'Bath salts': a new high, not found in the hygiene AISLE. *J Gen Intern Med* 2012;**27**:S508–9.
303. Harris CR, Brown A. Synthetic cannabinoid intoxication: a case series and review. *J Emerg Med* 2013;**44**:360–6. <https://doi.org/10.1016/j.jemermed.2012.07.061>
304. Heath TS, Burroughs Z, Thompson AJ, Tecklenburg FW. Acute intoxication caused by a synthetic cannabinoid in two adolescents. *J Pediatr Pharmacol Ther* 2012;**17**:177–81. <https://doi.org/10.5863/1551-6776-17.2.177>
305. Gutierrez KM, Cooper TV. The use of social networking sites: a risk factor for using alcohol, marijuana, and synthetic cannabinoids? *Drug Alcohol Depend* 2016;**163**:247–50. <https://doi.org/10.1016/j.drugalcdep.2016.03.021>
306. Hagan KS, Reidy L. Detection of synthetic cathinones in victims of sexual assault. *Forensic Sci Int* 2015;**257**:71–5. <https://doi.org/10.1016/j.forsciint.2015.07.040>

307. Heikman P, Sundstrom M, Pelander A, Ojanpera I. New psychoactive substances as part of polydrug abuse within opioid maintenance treatment revealed by comprehensive high-resolution mass spectrometric urine drug screening. *Hum Psychopharmacol Clin Exp* 2016;**31**:44–52. <https://doi.org/10.1002/hup.2512>
308. Helander A, Bäckberg M, Beck O. Intoxications involving the fentanyl analogs acetylfentanyl, 4-methoxybutyrfentanyl and furanylfentanyl: results from the Swedish STRIDA project. *Clin Toxicol* 2016;**54**:324–32. <https://doi.org/10.3109/15563650.2016.1139715>
309. Hermanns-Clausen M, Kithinji J, Spehl M, Angerer V, Franz F, Eyer F, Auwärter V. Adverse effects after the use of JWH-210 – a case series from the EU Spice II plus project. *Drug Test Anal* 2016;**8**:1030–8. <https://doi.org/10.1002/dta.1936>
310. Hermanns-Clausen M, Muller D, Kithinji J, Angerer V, Franz F, Eyer F, et al. Acute side effects after consumption of the novel synthetic cannabinoids AB-CHMINACA and MDMB-CHMICA. *Clin Toxicol* 2016;**54**:378.
311. Hess C, Stockhausen S, Kernbach-Wighton G, Madea B. Death due to diabetic ketoacidosis: induction by the consumption of synthetic cannabinoids? *Forensic Sci Int* 2015;**257**:e6–11. <https://doi.org/10.1016/j.forsciint.2015.08.012>
312. Hieger MA, Rose SR, Cumpston KL, Stromberg PE, Miller S, Wills BK. Severe poisoning after self-reported use of 2-(4-iodo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine, a novel substituted amphetamine: a case series. *Am J Emerg Med* 2015;**33**:1843.e1–3.
313. Heltsley R, Shelby MK, Crouch DJ, Black DL, Robert TA, Marshall L, et al. Prevalence of synthetic cannabinoids in U.S. athletes: initial findings. *J Anal Toxicol* 2012;**36**:588–93. <https://doi.org/10.1093/jat/bks066>
314. Hermanns-Clausen M, Kneisel S, Auwarter V. Acute intoxications by herbal blends containing synthetic cannabinoids. *Clin Toxicol* 2012;**50**:340.
315. Hermanns-Clausen M, Sauer O, Gerber G, Faerber E, Koch IE, Hentschel H, et al. New ‘Herbal drugs’ of abuse: spice and smoke. *Clin Toxicol* 2009;**47**:452.
316. Hill M, Warrick B, Nedzlek C, Lehr B, Mowry J, Smolinske S, et al. Multi-state toxicosurveillance of ‘bath salts’ presenting to the emergency department. *Ann Emerg Med* 2011;**58**:S325. <https://doi.org/10.1016/j.annemergmed.2011.06.469>
317. Hill SL, Cooper GA, Jackson G, Lupton DJ, Bradberry S, Thomas SHL. What’s on the ‘Spice’ rack? Synthetic cannabinoid receptor agonist toxicity reported to the UK National Poisons Information Service. *Clin Toxicol* 2013;**51**:345.
318. Hill SL, Doris T, Gurung S, Katebe S, Lomas A, Dunn M, et al. Severe clinical toxicity associated with analytically confirmed recreational use of 25I-NBOMe: case series. *Clin Toxicol* 2013;**51**:487–92. <https://doi.org/10.3109/15563650.2013.802795>
319. Hill SL, Harbon SC, Coulson J, Cooper GA, Jackson G, Lupton DJ, et al. Methoxetamine toxicity reported to the National Poisons Information Service: clinical characteristics and patterns of enquiries (including the period of the introduction of the UK’s first Temporary Class Drug Order). *Emerg Med J* 2014;**31**:45–7. <https://doi.org/10.1136/emered-2012-202251>
320. Hill SL, Dunn M, Najafi J, Abouchedid R, Dargan PI, Wood DM, et al. Identification of novel psychoactive substances in biological samples from patients with severe clinical toxicity in the UK: preliminary results from the Identification Of Novel psychoActive substances (IONA) study. *Clin Toxicol* 2016;**54**:380.

321. Hill SL, Najafi J, Dunn M, Acheampong P, Kamour A, Grundlingh J, *et al.* Clinical toxicity following analytically confirmed use of the synthetic cannabinoid receptor agonist MDMB-CHMICA. A report from the Identification Of Novel psychoActive substances (IONA) study. *Clin Toxicol (Phila)* 2016;**54**:638–43. <https://doi.org/10.1080/15563650.2016.1190980>
322. Hinds CJ. Have you heard of the 'party drug' GBL (gamma butyrolactone)? A survey of health workers' knowledge of this potentially fatal drug. *Aust N Z J Psychiatry* 2015;**49**:1069. <https://doi.org/10.1177/0004867415605620>
323. Hirapara K, Aggarwal R. Synthetic cannabis and myocardial infarction: a complication less known! *Psychosomatics* 2015;**56**:712–13. <https://doi.org/10.1016/j.psych.2015.07.009>
324. Hockenhuil J, Murphy KG, Paterson S. Mephedrone use is increasing in London. *Lancet* 2016;**387**:1719–20. [https://doi.org/10.1016/S0140-6736\(16\)30258-6](https://doi.org/10.1016/S0140-6736(16)30258-6)
325. Hohmann N, Mikus G, Czock D. Effects and risks associated with novel psychoactive substances: mislabeling and sale as bath salts, spice, and research chemicals. *Dtsch Arztebl Int* 2014;**111**:139–47. <https://doi.org/10.3238/arztebl.2014.0139>
326. Hopkins CY, Gilchrist BL. A case of cannabinoid hyperemesis syndrome caused by synthetic cannabinoids. *J Emerg Med* 2013;**45**:544–6. <https://doi.org/10.1016/j.jemermed.2012.11.034>
327. Hoyte CO, Jacob J, Monte AA, Al-Jumaan M, Bronstein AC, Heard KJ. A characterization of synthetic cannabinoid exposures reported to the National Poison Data System in 2010. *Ann Emerg Med* 2012;**60**:435–8. <https://doi.org/10.1016/j.annemergmed.2012.03.007>
328. Hu X, Primack BA, Barnett TE, Cook RL. College students and use of K2: an emerging drug of abuse in young persons. *Subst Abuse Treat Prev Policy* 2011;**6**:16. <https://doi.org/10.1186/1747-597X-6-16>
329. Huang HH, Bai YM. Persistent psychosis after ingestion of a single tablet of '2C-B'. *Prog Neuropsychopharmacol Biol Psychiatry* 2011;**35**:293–4. <https://doi.org/10.1016/j.pnpbp.2010.10.018>
330. Ibrahim S, Al-Saffar F, Wannenburg T. A unique case of cardiac arrest following K2 abuse. *Case Rep Cardiol* 2014;**2014**:120607. <https://doi.org/10.1155/2014/120607>
331. Ide A, Ide T, Kamijo Y, Nishikawa T, Yoshimura K, Mekari M, *et al.* A case series of acute intoxication with new psychoactive drugs in Japan: a vicious spiral of 'Law' and 'Market'. *Clin Toxicol* 2013;**51**:345.
332. Imam SF, Patel H, Mahmoud M, Prakash NA, King MS, Fremont RD. Bath salts intoxication: a case series. *J Emerg Med* 2013;**45**:361–5. <https://doi.org/10.1016/j.jemermed.2013.04.017>
333. Institóris L, Árok Z, Seprenyi K, Varga T, Sára-Klausz G, Keller É, *et al.* Frequency and structure of stimulant designer drug consumption among suspected drug users in Budapest and South-East Hungary in 2012–2013. *Forensic Sci Int* 2015;**248**:181–6. <https://doi.org/10.1016/j.forsciint.2015.01.002>
334. Institóris L, Arok Z, Zacher G, Reka Toth A, Kereszty E, Varga T. Serum, urine and oral fluid concentration of stimulant-type designer drugs in intoxicated drug users. *Rechtsmedizin* 2012;**22**:287.
335. Iwanicki JL, Cao DJ, Hoppe J, Hoyte CO, Bronstein AC, Lavonas EJ, *et al.* Novel synthetic cannabinoid outbreak causing severe illness. *Clin Toxicol* 2014;**52**:402.
336. Jaenicke NJ, Pogoda W, Paulke A, Wunder C, Toennes SW. Retrospective analysis of synthetic cannabinoids in serum samples – epidemiology and consumption patterns. *Forensic Sci Int* 2014;**242**:81–7. <https://doi.org/10.1016/j.forsciint.2014.06.010>

337. Inci R, Kelekci KH, Oguz N, Karaca S, Karadas B, Bayrakci A. Dermatological aspects of synthetic cannabinoid addiction. *Cutan Ocul Toxicol* 2017;**36**. <https://doi.org/10.3109/15569527.2016.1169541>
338. James D, Adams RD, Spears R, Cooper G, Lupton DJ, Thompson JP, *et al*. Clinical characteristics of mephedrone toxicity reported to the UK National Poisons Information Service. *Emerg Med J* 2011;**28**:686–9. <https://doi.org/10.1136/emj.2010.096636>
339. Jan RK, Lin JC, Lee H, Sheridan JL, Kydd RR, Kirk IJ, Russell BR. Determining the subjective effects of TFMPP in human males. *Psychopharmacology* 2010;**211**:347–53. <https://doi.org/10.1007/s00213-010-1911-y>
340. Johnson LA, Johnson RL, Alfonzo C. Spice: a legal marijuana equivalent. *Mil Med* 2011;**176**:718–20. <https://doi.org/10.7205/MILMED-D-10-00356>
341. Johnson LA, Johnson RL, Portier RB. Current 'legal highs'. *J Emerg Med* 2013;**44**:1108–15. <https://doi.org/10.1016/j.jemermed.2012.09.147>
342. Johnson PS, Johnson MW. Investigation of 'bath salts' use patterns within an online sample of users in the United States. *J Psychoactive Drugs* 2014;**46**:369–78. <https://doi.org/10.1080/02791072.2014.962717>
343. Jolliff HA, Holmes CT, Holmes KA, Clifton DC, Jenkins JJ. 'Bath Salts' abuse: a poison center study of the clinical effects and outcomes. *Clin Toxicol* 2013;**51**:678–9.
344. Joshi S, Singh G. A case study on the temporal correlation of acute psychosis with the use of a new recreational drug named NRG3. *Eur Psychiatry* 2012;**27**:1. [https://doi.org/10.1016/s0924-9338\(12\)75032-0](https://doi.org/10.1016/s0924-9338(12)75032-0)
345. John ME, Thomas-Rozza C, Hahn D. Bath salts abuse leading to new onset psychosis and potential for violence [published online ahead of print June 20 2014]. *Clin Schizophr Relat Psychoses* 2014. <https://doi.org/10.3371/CSRP.JORO.061314>
346. Jones P, Rai BP, Doig S, Ahammed N. Priapism associated with novel psychoactive substance abuse. *Cent European J Urol* 2015;**68**:447–9. <https://doi.org/10.5173/cej.2015.676>
347. Jovel A, Felthous A, Bhattacharyya A. Delirium due to intoxication from the novel synthetic tryptamine 5-MeO-DALT. *J Forensic Sci* 2014;**59**:844–6. <https://doi.org/10.1111/1556-4029.12367>
348. Kadaria D, Sinclair SE. A case of acute agitation with a negative urine drug screen: a new wave of 'legal' drugs of abuse. *Tenn Med* 2012;**105**:31–2.
349. Kamat AS, Aliashkevich AF, Denton JR, Fitzjohn TP. Headache after substance abuse: a diagnostic dilemma. *J Clin Neurosci* 2012;**19**:464–6. <https://doi.org/10.1016/j.jocn.2011.07.028>
350. Kamel M, Thajudeen B. A case of acute kidney injury and calcium oxalate deposition associated with synthetic cannabinoids. *Saudi J Kidney Dis Transpl* 2015;**26**:802–3. <https://doi.org/10.4103/1319-2442.160222>
351. Kamijo Y, Takai M, Fujita Y, Hirose Y, Iwasaki Y, Ishihara S, *et al*. A multicenter retrospective survey of poisoning after consumption of products containing synthetic chemicals in Japan. *Intern Med* 2014;**53**:2439–45. <https://doi.org/10.2169/internalmedicine.53.2344>
352. Kamour A, James D, Lupton DJ, Cooper G, Eddleston M, Vale A, *et al*. Patterns of presentation and clinical features of toxicity after reported use of ([2-aminopropyl]-2,3-dihydrobenzofurans), the 'benzofuran' compounds. A report from the United Kingdom National Poisons Information Service. *Clin Toxicol (Phila)* 2014;**52**:1025–31. <https://doi.org/10.3109/15563650.2014.973115>
353. Kamour A, James D, Lupton DJ, Eddleston M, Thompson JP, Vale JA, *et al*. Patterns of presentation and clinical toxicity after reported intravenous use of mephedrone in the United Kingdom. A report from the UK National Poisons Information Service. *Clin Toxicol* 2014;**52**:367–8.

354. Kamour A, James D, Spears R, Cooper G, Lupton DJ, Eddleston M, *et al.* Patterns of presentation and clinical toxicity after reported use of alpha methyltryptamine in the United Kingdom. A report from the UK National Poisons Information Service. *Clin Toxicol* 2014;**52**:192–7. <https://doi.org/10.3109/15563650.2014.885983>
355. Kankaanpää A, Ariniemi K, Heinonen M, Kuoppasalmi K, Gunnar T. Use of illicit stimulant drugs in Finland: a wastewater study in ten major cities. *Sci Total Environ* 2014;**487**:696–702. <https://doi.org/10.1016/j.scitotenv.2013.11.095>
356. Kamijo Y, Takai M, Fujita Y, Sakamoto T. A multicenter retrospective survey of poisoning after consumption of products containing novel psychoactive substances from 2013 to 2014 in Japan. *Am J Drug Alcohol Abuse* 2016;**42**:513–9. <https://doi.org/10.1080/00952990.2016.1176177>
357. Kane EM, Hinson JS, Jordan CD, Paziana K, Sauber NJ, Rothman RE, Stolbach AI. Bradycardia and hypotension after synthetic cannabinoid use: a case series. *Am J Emerg Med* 2016;**34**:2055.e1–2055.e2. <https://doi.org/10.1016/j.ajem.2016.03.007>
358. Kapitány-Fövény M, Kertész M, Winstock A, Deluca P, Corazza O, Farkas J, *et al.* Substitutional potential of mephedrone: an analysis of the subjective effects. *Hum Psychopharmacol* 2013;**28**:308–16. <https://doi.org/10.1002/hup.2297>
359. Kapka-Skrzypczak L, Kulpa P, Sawicki K, Cyranka M, Wojtyła A, Kruszewski M. Legal highs – legal aspects and legislative solutions. *Ann Agric Environ Med* 2011;**18**:304–9.
360. Karch SB. Cathinone neurotoxicity ('The '3Ms'). *Curr Neuropharmacol* 2015;**13**:21–5. <https://doi.org/10.2174/1570159X13666141210225009>
361. Karila L, Megarbane B, Cottencin O, Lejoyeux M. Synthetic cathinones: a new public health problem. *Curr Neuropharmacol* 2015;**13**:12–20. <https://doi.org/10.2174/1570159X13666141210224137>
362. Kasick DP, McKnight CA, Klisovic E. 'Bath salt' ingestion leading to severe intoxication delirium: two cases and a brief review of the emergence of mephedrone use. *Am J Drug Alcohol Abuse* 2012;**38**:176–80. <https://doi.org/10.3109/00952990.2011.643999>
363. Kasper AM, Ridpath AD, Arnold JK, Chatham-Stephens K, Morrison M, Olayinka O, *et al.* Severe illness associated with reported use of synthetic cannabinoids – Mississippi, April 2015. *MMWR Morb Mortal Wkly Rep* 2015;**64**:1121–2. <https://doi.org/10.15585/mmwr.mm6439a7>
364. Katselou M, Papoutsis I, Nikolaou P, Spiliopoulou C, Athanaselis S. A 'krokodil' emerges from the murky waters of addiction. Abuse trends of an old drug. *Life Sci* 2014;**102**:81–7. <https://doi.org/10.1016/j.lfs.2014.03.008>
365. Katselou M, Papoutsis I, Nikolaou P, Spiliopoulou C, Athanaselis S. 5-(2-aminopropyl)indole: a new player in the drama of 'legal highs' alerts the community. *Drug Alcohol Rev* 2015;**34**:51–7. <https://doi.org/10.1111/dar.12136>
366. Karila L, Billieux J, Benyamina A, Lancon C, Cottencin O. The effects and risks associated to mephedrone and methylone in humans: a review of the preliminary evidences. *Brain Res Bull* 2016;**126**:61–7. <https://doi.org/10.1016/j.brainresbull.2016.03.005>
367. Karinen R, Tuv SS, Rogde S, Peres MD, Johansen U, Frost J, *et al.* Lethal poisonings with AH-7921 in combination with other substances. *Forensic Sci Int* 2014;**244**:e21–4. <https://doi.org/10.1016/j.forsciint.2014.08.013>
368. Katz DP, Bhattacharya D, Bhattacharya S, Deruiter J, Clark CR, Suppiramaniam V, Dhanasekaran M. Synthetic cathinones: 'a khat and mouse game'. *Toxicol Lett* 2014;**229**:349–56. <https://doi.org/10.1016/j.toxlet.2014.06.020>

369. Kavanagh PV, Power JD. New psychoactive substances legislation in Ireland – perspectives from academia. *Drug Test Anal* 2014;**6**:884–91. <https://doi.org/10.1002/dta.1598>
370. Kazory A, Aiyer R. Synthetic marijuana and acute kidney injury: an unforeseen association. *Clin Kidney J* 2013;**6**:330–3. <https://doi.org/10.1093/ckj/sft047>
371. Kegler R, Buttner A, Nowotnik J, Rucker G, Rentsch D. Trends in drug consumption at a music festival over five years. *Rechtsmedizin* 2014;**24**:366–7.
372. Kelly BC. Legally tripping: a qualitative profile of *Salvia divinorum* use among young adults. *J Psychoactive Drugs* 2011;**43**:46–54. <https://doi.org/10.1080/02791072.2011.566500>
373. Kelly BC, Wells BE, Pawson M, Leclair A, Parsons JT, Golub SA. Novel psychoactive drug use among younger adults involved in US nightlife scenes. *Drug Alcohol Rev* 2013;**32**:588–93. <https://doi.org/10.1111/dar.12058>
374. Kersten BP, McLaughlin ME. Toxicology and management of novel psychoactive drugs. *J Pharm Pract* 2015;**28**:50–65. <https://doi.org/10.1177/0897190014544814>
375. Katselou M, Papoutsis I, Nikolaou P, Spiliopoulou C, Athanaselis S. AH-7921: the list of new psychoactive opioids is expanded. *Forensic Toxicol* 2015;**33**:195–201. <https://doi.org/10.1007/s11419-015-0271-z>
376. Katselou M, Papoutsis I, Nikolaou P, Spiliopoulou C, Athanaselis S. Alpha-PVP ('flakka'): a new synthetic cathinone invades the drug arena. *Forensic Toxicol* 2016;**34**:41–50. <https://doi.org/10.1007/s11419-015-0298-1>
377. Katz DP, Deruiter J, Bhattacharya D, Ahuja M, Bhattacharya S, Clark CR, et al. Benzylpiperazine: 'a messy drug'. *Drug Alcohol Depend* 2016;**164**:1–7. <https://doi.org/10.1016/j.drugalcdep.2016.04.010>
378. Katz KD, Leonetti AL, Bailey BC, Surmaitis RM, Eustice ER, Kacinko S, Wheatley SM. Case series of synthetic cannabinoid intoxication from one toxicology center. *West J Emerg Med* 2016;**17**:290–4. <https://doi.org/10.5811/westjem.2016.2.29519>
379. Kemp AM, Clark MS, Dobbs T, Galli R, Sherman J, Cox R. Top 10 facts you need to know about synthetic cannabinoids: not so nice spice. *Am J Med* 2016;**129**:240–4.e1. <https://doi.org/10.1016/j.amjmed.2015.10.008>
380. Khan M, Pace L, Truong A, Gordon M, Moukaddam N. Catatonia secondary to synthetic cannabinoid use in two patients with no previous psychosis. *Am J Addict* 2016;**25**:25–7. <https://doi.org/10.1111/ajad.12318>
381. Kilian A, Huppke B, Groeneveld A, Schaper A. Phenethylamines – they have known, but have they loved? Mass intoxication with 2C-E in northern Germany. *Clin Toxicol* 2016;**54**:381.
382. Klavž J, Gorenjak M, Marinšek M. Suicide attempt with a mix of synthetic cannabinoids and synthetic cathinones: case report of non-fatal intoxication with AB-CHMINACA, AB-FUBINACA, alpha-PHP, alpha-PVP and 4-CMC. *Forensic Sci Int* 2016;**265**:121–4. <https://doi.org/10.1016/j.forsciint.2016.01.018>
383. Keshava K, Boggs CL, Ripple MG, Allan CH, Levine B, Jufer-Phipps R, et al. Methylenedioxypropylvalerone ('bath salts'), related death: case report and review of the literature. *J Forensic Sci* 2013;**58**:1654–9. <https://doi.org/10.1111/1556-4029.12202>
384. Khan S, Shaheen F, Sarwar H, Molina J, Mushtaq S. 'Bath salts'-induced psychosis in a young woman. *Prim Care Companion CNS Disord* 2013;**15**:PCC.12101417. <https://doi.org/10.4088/PCC.12101417>

385. Khan U, van Nuijs AL, Li J, Maho W, Du P, Li K, *et al.* Application of a sewage-based approach to assess the use of ten illicit drugs in four Chinese megacities. *Sci Total Environ* 2014;**487**:710–21. <https://doi.org/10.1016/j.scitotenv.2014.01.043>
386. Khanagavi J, Phatak P, Kolte D, Aronow WS, Lanier G. Synthetic cannabinoids-induced thrombotic microangiopathy leading to acute heart failure. *Circulation* 2013;**128**:A18135.
387. Khullar V, Jain A, Sattari M. Emergence of a new class of recreational drugs – a case for caution. *J Gen Intern Med* 2013;**28**:S321.
388. Kikura-Hanajiri R, Kawamura NU, Goda Y. Changes in the prevalence of new psychoactive substances before and after the introduction of the generic scheduling of synthetic cannabinoids in Japan. *Drug Test Anal* 2014;**6**:832–9. <https://doi.org/10.1002/dta.1584>
389. Kirschner RI, Nipper HC, Studts PK, Jacobitz KL. Fatalities following parenteral injection of MDPV sold as 'hookah cleaner'. *Clin Toxicol* 2012;**50**:702–3.
390. Kleinschmidt K, Forrester MB. Bath salts & synthetic cannabinoids-initial experience & comparisons. *Clin Toxicol* 2011;**49**:528.
391. Kleinschmidt K, Forrester MB. A comparison of ingested versus inhaled synthetic cannabinoids. *Clin Toxicol* 2011;**49**:530–1.
392. Kolli V, Sharma A, Amani M, Bestha D, Chaturvedi R. 'Meow meow' (mephedrone) and catatonia. *Innov Clin Neurosci* 2013;**10**:11–12.
393. Korya D, Kapoor A, Labiner D. Ischemic stroke in a 28-year-old woman after smoking synthetic THC. *Neurology* 2013;**80**:P06.250.
394. Kovacs K, Zacher G, Reka Toth A, Harmath A, Kereszty E, Varga T. Designer drug related intoxications in Hungary – clinical experiences. *Rechtsmedizin* 2012;**22**:341–2.
395. Kraemer T. From room odorizers, bath salts and plant food-new psychoactive substances on the rise. *Toxicol Lett* 2013;**221**:S2. <https://doi.org/10.1016/j.toxlet.2013.06.002>
396. Kriikku P, Wilhelm L, Schwarz O, Rintatalo J. New designer drug of abuse: 3,4-Methylenedioxypropylvalerone (MDPV). Findings from apprehended drivers in Finland. *Forensic Sci Int* 2011;**210**:195–200. <https://doi.org/10.1016/j.forsciint.2011.03.015>
397. Krabseth HM, Tuv SS, Strand MC, Karinen R, Wiik E, Vevelstad M, *et al.* Novel psychoactive substances. *Tidsskr Nor Laegeforen* 2016;**136**:714–17. <https://doi.org/10.4045/tidsskr.15.1278>
398. Kramer CL, Wetzel DR, Wijdicks EF. Devastating delayed leukoencephalopathy associated with bath salt inhalation. *Neurocrit Care* 2016;**24**:454–8. <https://doi.org/10.1007/s12028-015-0226-6>
399. Kristofic JJ, Chmiel JD, Jackson GF, Vorce SP, Holler JM, Robinson SL, Bosy TZ. Detection of 25C-NBOMe in three related cases. *J Anal Toxicol* 2016;**40**:466–72. <https://doi.org/10.1093/jat/bkw035>
400. Labay LM, Caruso JL, Gilson TP, Phipps RJ, Knight LD, Lemos NP, *et al.* Synthetic cannabinoid drug use as a cause or contributory cause of death. *Forensic Sci Int* 2016;**260**:31–9. <https://doi.org/10.1016/j.forsciint.2015.12.046>
401. Lafferty C, Smith L, Coull A, Shanley J. The experience of an increase in the injection of ethylphenidate in Lothian April 2014–March 2015. *Scott Med J* 2016;**61**:74–83. <https://doi.org/10.1177/0036933016649871>
402. Kronstrand R, Roman M, Andersson M, Eklund A. Toxicological findings of synthetic cannabinoids in recreational users. *J Anal Toxicol* 2013;**37**:534–41. <https://doi.org/10.1093/jat/bkt068>

403. Kronstrand R, Roman M, Dahlgren M, Thelander G, Wikström M, Druid H. A cluster of deaths involving 5-(2-aminopropyl)indole (5-IT). *J Anal Toxicol* 2013;**37**:542–6. <https://doi.org/10.1093/jat/bkt058>
404. Kronstrand R, Thelander G, Lindstedt D, Roman M, Kugelberg FC. Fatal intoxications associated with the designer opioid AH-7921. *J Anal Toxicol* 2014;**38**:599–604. <https://doi.org/10.1093/jat/bku057>
405. Kudo K, Usumoto Y, Kikura-Hanajiri R, Sameshima N, Tsuji A, Ikeda N. A fatal case of poisoning related to new cathinone designer drugs, 4-methoxy PV8, PV9, and 4-methoxy PV9, and a dissociative agent, diphenidine. *Leg Med* 2015;**17**:421–6. <https://doi.org/10.1016/j.legalmed.2015.06.005>
406. Kueppers VB, Cooke CT. 25I-NBOMe related death in Australia: a case report. *Forensic Sci Int* 2015;**249**:e15–18. <https://doi.org/10.1016/j.forsciint.2015.02.010>
407. Kulhawik D, Walecki J. Toxic lung injury in a patient addicted to 'legal highs' – case study. *Pol J Radiol* 2015;**80**:62–6. <https://doi.org/10.12659/PJR.892334>
408. Kyle PB, Iverson RB, Gajagowni RG, Spencer L. Illicit bath salts: not for bathing. *J Miss State Med Assoc* 2011;**52**:375–7.
409. Kyriakou C, Marinelli E, Frati P, Santurro A, Afxentiou M, Zaami S, et al. NBOMe: new potent hallucinogens – pharmacology, analytical methods, toxicities, fatalities: a review. *Eur Rev Med Pharmacol Sci* 2015;**19**:3270–81.
410. Laizure SC. Addiction to the synthetic cannabinoid analog AM-2201. *Pharmacotherapy* 2013;**33**:e236.
411. Lajoie TM, Rich A. 'Bath salts': a new drug epidemic—a case report. *Am J Addict* 2012;**21**:572–3. <https://doi.org/10.1111/j.1521-0391.2012.00286.x>
412. Lajtai A, Lakatos A, Erzsebet G, Zrinyi Z, Mayer M, Porpaczy Z, et al. Several designer drugs in the specimen of a chronic drug user. *Clin Chem Lab Med* 2012;**50**:eA42.
413. Lange JE, Daniel J, Homer K, Reed MB, Clapp JD. Salvia divinorum: effects and use among YouTube users. *Drug Alcohol Depend* 2010;**108**:138–40. <https://doi.org/10.1016/j.drugalcdep.2009.11.010>
414. Lange JE, Reed MB, Croff JM, Clapp JD. College student use of Salvia divinorum. *Drug Alcohol Depend* 2008;**94**:263–6. <https://doi.org/10.1016/j.drugalcdep.2007.10.018>
415. Lank PM, Pines E, Mycyk M. Are emergency physicians prepared to manage synthetic cannabinoid intoxication? *Clin Toxicol* 2011;**49**:607–8.
416. Lapoint J, James LP, Moran CL, Nelson LS, Hoffman RS, Moran JH. Severe toxicity following synthetic cannabinoid ingestion. *Clin Toxicol* 2011;**49**:760–4. <https://doi.org/10.3109/15563650.2011.609822>
417. Lawrence A. A bad trip: lawmakers try to stay one step ahead of the chemists manufacturing dangerous synthetic drugs. *State Legis* 2011;**37**:28–9.
418. Lea T, Reynolds R, De Wit J. Mephedrone use among same-sex attracted young people in Sydney, Australia. *Drug Alcohol Rev* 2011;**30**:438–40. <https://doi.org/10.1111/j.1465-3362.2011.00288.x>
419. Lee H, Kydd RR, Lim VK, Kirk IJ, Russell BR. Effects of trifluoromethylphenylpiperazine (TFMPP) on interhemispheric communication. *Psychopharmacology* 2011;**213**:707–14. <https://doi.org/10.1007/s00213-010-2025-2>

420. Laskowski LK, Elbakoush F, Calvo J, Exantus-Bernard G, Fong J, Poklis JL, *et al.* Evolution of the NBOMes: 25C- and 25B- Sold as 25I-NBOMe. *J Med Toxicol* 2015;**11**:237–41. <https://doi.org/10.1007/s13181-014-0445-9>
421. Lauritsen KJ, Rosenberg H. Comparison of outcome expectancies for synthetic cannabinoids and botanical marijuana. *Am J Drug Alcohol Abuse* 2016;**42**:377–84. <https://doi.org/10.3109/00952990.2015.1135158>
422. Lawn W, Borschmann R, Cottrell A, Winstock A. Methoxetamine: prevalence of use in the USA and UK and associated urinary problems. *J Subst Use* 2016;**21**:115–20.
423. Le Roux G, Ferec S, Lelievre B, Bretaudeau-Deguigne M, Abbara C, Turcant A, *et al.* All that glitters is not LSD! *Clin Toxicol* 2016;**54**:404–5.
424. Lee H, Wang GY, Curley LE, Kydd RR, Kirk IJ, Russell BR. Investigation of the effects of 'piperazine-containing party pills' and dexamphetamine on interhemispheric communication using electroencephalography. *Psychopharmacology (Berl)* 2016;**233**:2869–77. <https://doi.org/10.1007/s00213-016-4335-5>
425. Lee H, Wang GY, Curley LE, Sollers JJ, Kydd RR, Kirk IJ, Russell BR. Acute effects of BZP, TFMPP and the combination of BZP and TFMPP in comparison to dexamphetamine on an auditory oddball task using electroencephalography: a single-dose study. *Psychopharmacology* 2016;**233**:863–71. <https://doi.org/10.1007/s00213-015-4165-x>
426. Liakoni E, Dolder PC, Rentsch KM, Liechti ME. Presentations due to acute toxicity of psychoactive substances in an urban emergency department in Switzerland: a case series. *BMC Pharmacol Toxicol* 2016;**17**:25. <https://doi.org/10.1186/s40360-016-0068-7>
427. Lehner KR, Baumann MH. Psychoactive 'bath salts': compounds, mechanisms, and toxicities. *Neuropsychopharmacology* 2013;**38**:243–4. <https://doi.org/10.1038/npp.2012.162>
428. Lekham R, Pedroza M, Bradauskaite G, Raja R. A curious case of acute allograft dysfunction after cannabinoids use. *Am J Kidney Dis* 2014;**63**:A73. <https://doi.org/10.1053/j.ajkd.2014.01.234>
429. Lemos NP. Driving under the influence of synthetic cannabinoid receptor agonist XLR-11. *J Forensic Sci* 2014;**59**:1679–83. <https://doi.org/10.1111/1556-4029.12550>
430. Lenz D, Rothschild MA, Kröner L. Intoxications due to ingestion of gamma-butyrolactone: organ distribution of gamma-hydroxybutyric acid and gamma-butyrolactone. *Ther Drug Monit* 2008;**30**:755–61. <https://doi.org/10.1097/FTD.0b013e3181898c2e>
431. Lenz J, Brown J, Flagg S, Oh R, Batts K, Ditzler T, Johnson J. Cristalius: a case in designer drugs. *Mil Med* 2013;**178**:e893–5. <https://doi.org/10.7205/MILMED-D-12-00393>
432. Levine M, Levitan R, Skolnik A. Compartment syndrome after 'bath salts' use: a case series. *Ann Emerg Med* 2013;**61**:480–3. <https://doi.org/10.1016/j.annemergmed.2012.11.021>
433. Lev-Ran S. A case of treating cathinone dependence and comorbid depression using bupropion. *J Psychoactive Drugs* 2012;**44**:434–6. <https://doi.org/10.1080/02791072.2012.736851>
434. Liechti M. Novel psychoactive substances (designer drugs): overview and pharmacology of modulators of monoamine signaling. *Swiss Med Wkly* 2015;**145**:w14043. <https://doi.org/10.4414/smw.2015.14043>
435. Lin JC, Jan RK, Kydd RR, Russell BR. Subjective effects in humans following administration of party pill drugs BZP and TFMPP alone and in combination. *Drug Test Anal* 2011;**3**:582–5. <https://doi.org/10.1002/dta.285>

436. Lin JC, Jan RK, Lee H, Jensen MA, Kydd RR, Russell BR. Determining the subjective and physiological effects of BZP combined with TFMPP in human males. *Psychopharmacology* 2011;**214**:761–8. <https://doi.org/10.1007/s00213-010-2081-7>
437. Lindsay L, White ML. Herbal marijuana alternatives and bath salts-‘barely legal’ toxic highs. *Clin Pediatr Emerg Med* 2012;**13**:283–91. <https://doi.org/10.1016/j.cpem.2012.09.001>
438. Linsen F, Koning RP, van Laar M, Niesink RJ, Koeter MW, Brunt TM. 4-Fluoroamphetamine in the Netherlands: more than a one-night stand. *Addiction* 2015;**110**:1138–43. <https://doi.org/10.1111/add.12932>
439. Lisi DM. Designer drugs. Patients may be using synthetic cannabinoids more than you think. *JEMS* 2014;**39**:56–9.
440. Locatelli CA, Lonati D, Buscaglia E, Vecchio S, Giampreti A, Petrolini V, *et al.* ‘Synthetic cocaine’ as legal cocaine hides synthetic cannabinoids. *Toxicol Lett* 2013;**221**:S74. <https://doi.org/10.1016/j.toxlet.2013.05.062>
441. Locatelli CA, Lonati D, Giampreti A, Petrolini V, Vecchio S, Rognoni C, *et al.* New synthetic cannabinoids intoxications in Italy: clinical identification and analytical confirmation of cases. *Eur J Emerg Med* 2011;**21**:220. <https://doi.org/10.1016/j.jemermed.2011.06.114>
442. Loeffler G, Hurst D, Penn A, Yung K. Spice, bath salts, and the U.S. military: the emergence of synthetic cannabinoid receptor agonists and cathinones in the U.S. Armed Forces. *Mil Med* 2012;**177**:1041–8. <https://doi.org/10.7205/MILMED-D-12-00180>
443. Loeffler G, Penn A, Ledden B. ‘Bath salt’-induced agitated paranoia: a case series. *J Stud Alcohol Drugs* 2012;**73**:706. <https://doi.org/10.15288/jsad.2012.73.706>
444. Loewinger GC, Oleson EB, Cheer JF. Using dopamine research to generate rational cannabinoid drug policy. *Drug Test Anal* 2013;**5**:22–6. <https://doi.org/10.1002/dta.1410>
445. Loi B, Corkery JM, Claridge H, Goodair C, Chiappini S, Gimeno Clemente C, Schifano F. Deaths of individuals aged 16-24 years in the UK after using mephedrone. *Hum Psychopharmacol* 2015;**30**:225–32. <https://doi.org/10.1002/hup.2423>
446. Liveri K, Constantinou MA, Afxentiou M, Kanari P. A fatal intoxication related to MDPV and pentedrone combined with antipsychotic and antidepressant substances in Cyprus. *Forensic Sci Int* 2016;**265**:160–5. <https://doi.org/10.1016/j.forsciint.2016.02.017>
447. Loeffler G, Delaney E, Hann M. International trends in spice use: prevalence, motivation for use, relationship to other substances, and perception of use and safety for synthetic cannabinoids. *Brain Res Bull* 2016;**126**:8–28. <https://doi.org/10.1016/j.brainresbull.2016.04.013>
448. Lowe DJ, Torrance HJ, Ireland AJ, Bloeck F, Stevenson R. SODAS: surveillance of drugs of abuse study. *Eur J Emerg Med* 2015;**26**:26.
449. Łukasik-Głębocka M, Sommerfeld K, Teżyk A, Zielińska-Psuja B, Panieński P, Żaba C. Flubromazolam – a new life-threatening designer benzodiazepine. *Clin Toxicol* 2016;**54**:66–8. <https://doi.org/10.3109/15563650.2015.1112907>
450. Lung D, Wilson N, Chatenet FT, Lacroix C, Gerona R. Non-targeted screening for novel psychoactive substances among agitated emergency department patients. *Clin Toxicol* 2016;**54**:319–23. <https://doi.org/10.3109/15563650.2016.1139714>
451. Lonati D, Buscaglia E, Papa P, Petrolini VM, Vecchio S, Giampreti A, *et al.* Prevalence of intoxication by new recreational drugs: preliminary data by the Italian network of emergency departments involved in the national early identification system. *Clin Toxicol* 2012;**50**:344.

452. Lonati D, Buscaglia E, Papa P, Valli A, Coccini T, Giampreti A, *et al.* MAM-2201 (analytically confirmed) intoxication after 'Synthacaine' consumption. *Ann Emerg Med* 2014;**64**:629–32. <https://doi.org/10.1016/j.annemergmed.2014.01.007>
453. Louh IK, Freeman WD. A 'spicy' encephalopathy: synthetic cannabinoids as cause of encephalopathy and seizure. *Crit Care* 2014;**18**:553. <https://doi.org/10.1186/s13054-014-0553-6>
454. Louis A, Peterson BL, Couper FJ. XLR-11 and UR-144 in Washington state and state of Alaska driving cases. *J Anal Toxicol* 2014;**38**:563–8. <https://doi.org/10.1093/jat/bku067>
455. Lovett CJ, Measham F, Dargan PI, Wood DM. Limited awareness and use of the novel psychoactive substance methiopropamine in men who have sex with men in South London nightclubs. *Clin Toxicol* 2014;**52**:362.
456. Lowry J, Thornton SL, Albadareen R, Gerona RR. Hot Molly! Methylenedioxybenzylpiperazine use associated with prolonged encephalopathy. *Clin Toxicol* 2014;**52**:706–7.
457. Lubarsky K, Odom A, Bernstein S, Kotbi N. Understanding the dangers of synthetic cannabinoids. *J Addict Med* 2014;**8**:288–9. <https://doi.org/10.1097/ADM.0000000000000040>
458. Luciano RL, Perazella MA. Nephrotoxic effects of designer drugs: synthetic is not better! *Nat Rev Nephrol* 2014;**10**:314–24. <https://doi.org/10.1038/nrneph.2014.44>
459. Lusthof KJ, Oosting R, Maes A, Verschraagen M, Dijkhuizen A, Sprong AG. A case of extreme agitation and death after the use of mephedrone in the Netherlands. *Forensic Sci Int* 2011;**206**:e93–5. <https://doi.org/10.1016/j.forsciint.2010.12.014>
460. Maas A, Wippich C, Madea B, Hess C. Driving under the influence of synthetic phenethylamines: a case series. *Int J Legal Med* 2015;**129**:997–1003. <https://doi.org/10.1007/s00414-015-1150-1>
461. Macfarlane V, Christie G. Synthetic cannabinoid withdrawal: a new demand on detoxification services. *Drug Alcohol Rev* 2015;**34**:147–53. <https://doi.org/10.1111/dar.12225>
462. Mackay K, Taylor M, Bajaj N. The adverse consequences of mephedrone use: a case series. *Psychiatrist* 2011;**35**:203–5. <https://doi.org/10.1192/pb.bp.110.032433>
463. Malaiyandi D, Pandya D, Abraham M, Taqi M, Helms A, Lynch J. Disruption of the blood brain barrier and relative hypertension as the primary disorder in near fatal posterior reversible encephalopathy syndrome. *Neurocritical Care* 2011;**15**:1. <http://dx.doi.org/10.1007/s12028-011-9625-5> (accessed 29 June 2016).
464. Malakooti M, Friedman M, Smith C. Multi-organ failure associated with ingestion of synthetic street drug '25I' (25I-NBOMe). *Crit Care Med* 2013;**41**:A285. <http://dx.doi.org/10.1097/01.ccm.0000440361.58922.cf> (accessed 29 June 2016).
465. Mangewala V, Sarwar SR, Shah K, Singh T. Bath salts-induced psychosis: a case report. *Innov Clin Neurosci* 2013;**10**:10–11.
466. Mangold AR, Bravo TP, Traub SJ, Maher SA, Lipinski CA. Flashback phenomenon and residual neurological deficits after the use of 'bath salt' 3, 4- methylenedioxypropylvalerone. *World J Emerg Med* 2014;**5**:63–6. <https://doi.org/10.5847/wjem.j.1920-8642.2014.01.011>
467. Lurie Y, Neuman G, Lev Dov-Avital I, Kurnik D, Bentur Y. Abuse of synthetic cannabinoids in Israel: reports to the national poison information center 2010–14. *Clin Toxicol* 2016;**54**:403.
468. Mackey HE, Hawksley O. Dystonia not dystopia: effects of the legal high, 'Clockwork Orange'. *BMJ Case Rep* 2015;**2015**:bcr2015212934. <https://doi.org/10.1136/bcr-2015-212934>
469. Mahendran R, Lim HA, Tan JY, Chua SM, Winslow M. Salvia divinorum: an overview of the usage, misuse, and addiction processes. *Asia Pac Psychiatry* 2016;**8**:23–31. <https://doi.org/10.1111/appy.12225>

470. Manseau MW. *Synthetic Cannabinoids: Emergence, Epidemiology, Clinical Effects, and Management*. Arlington, VA: American Psychiatric Publishing, Inc.; 2016.
471. Marillier M, Batisse A, Chevallier C, Djezzar S. Behavioral disorders and new psychoactive substances abuse, a French case series. *Eur Psychiatry* 2016;**33**:S307. <https://doi.org/10.1016/j.eurpsy.2016.01.1050>
472. Martinez Sadurni L, Grifell M, Galindo L, Ezquiaga I, Quintana P, Ventura M, et al. Methylone consumption characterized through samples handled by users. *Eur Psychiatry* 2016;**33**:S117. <https://doi.org/10.1016/j.eurpsy.2016.01.129>
473. Maskell PD, Smith PR, Cole R, Hikin L, Morley SR. Seven fatalities associated with ethylphenidate. *Forensic Sci Int* 2016;**265**:70–4. <https://doi.org/10.1016/j.forsciint.2015.12.045>
474. Marinetti LJ, Antonides HM. Analysis of synthetic cathinones commonly found in bath salts in human performance and postmortem toxicology: method development, drug distribution and interpretation of results. *J Anal Toxicol* 2013;**37**:135–46. <https://doi.org/10.1093/jat/bks136>
475. Martinotti G, Chillemi E, Sarchione F, Lupi M, Fiori F, Di Giannantonio M. Designer drugs: psychoactive effects and diffusion in an Italian university population. *Eur Psychiatry* 2013;**28**. [https://doi.org/10.1016/s0924-9338\(13\)76547-7](https://doi.org/10.1016/s0924-9338(13)76547-7)
476. Martinotti G, Lupi M, Acciavatti T, Cinosi E, Santacroce R, Signorelli MS, et al. Novel psychoactive substances in young adults with and without psychiatric comorbidities. *Biomed Res Int* 2014;**2014**:815424. <http://dx.doi.org/10.1155/2014/815424>
477. Martinotti G, Lupi M, Carlucci L, Cinosi E, Santacroce R, Acciavatti T, et al. Novel psychoactive substances: use and knowledge among adolescents and young adults in urban and rural areas. *Hum Psychopharmacol* 2015;**30**:295–301. <https://doi.org/10.1002/hup.2486>
478. Matsumoto T, Tachimori H, Tanibuchi Y, Takano A, Wada K. Clinical features of patients with designer-drug-related disorder in Japan: a comparison with patients with methamphetamine- and hypnotic/anxiolytic-related disorders. *Psychiatry Clin Neurosci* 2014;**68**:374–82. <https://doi.org/10.1111/pcn.12140>
479. Maxwell P, Jenkins N. Synthetic cannabinomimetics and 'legal highs'. *Australas J Pharm* 2015;**96**:76–8.
480. Mbeah-Bankas H, Marlowe K. Stimulant drug use for referrals to an early detection service: THEDS learning from mephedrone. *Early Interv Psychiatry* 2010;**4**:122.
481. McAuley A, Hecht G, Barnsdale L, Thomson CS, Graham L, Priyadarshi S, Robertson JR. Mortality related to novel psychoactive substances in Scotland, 2012: an exploratory study. *Int J Drug Policy* 2015;**26**:461–7. <https://doi.org/10.1016/j.drugpo.2014.10.010>
482. McClean JM, Anspikian A, Tsuang JW. Bath salt use: a case report and review of the literature. *J Dual Diagn* 2012;**8**:250–6. <https://doi.org/10.1080/15504263.2012.697447>
483. McElrath K, O'Neill C. Experiences with mephedrone pre- and post-legislative controls: perceptions of safety and sources of supply. *Int J Drug Policy* 2011;**22**:120–7. <https://doi.org/10.1016/j.drugpo.2010.11.001>
484. McGraw M, McGraw L. Bath salts: not as harmless as they sound. *J Emerg Nurs* 2012;**38**:582–8. <https://doi.org/10.1016/j.jen.2012.07.025>
485. McGraw MM. Is your patient high on 'bath salts'? these designer drugs sound harmless, but cause dangerous behavior. *Nursing Critical Care* 2012;**7**:31–6. <https://doi.org/10.1097/01.CCN.0000421968.44288.3f>

486. McGuinness TM, Newell D. Risky recreation: synthetic cannabinoids have dangerous effects. *J Psychosoc Nurs Ment Health Serv* 2012;**50**:16–18. <https://doi.org/10.3928/02793695-20120703-04>
487. McKeever RG, Vearrier D, Jacobs D, LaSala G, Okaneku J, Greenberg MI. K2 – not the spice of life; synthetic cannabinoids and ST elevation myocardial infarction: a case report. *J Med Toxicol* 2015;**11**:129–31. <https://doi.org/10.1007/s13181-014-0424-1>
488. McNamara S, Stokes S, Coleman N. Head shop compound abuse amongst attendees of the Drug Treatment Centre Board. *Ir Med J* 2010;**103**:134, 136–7.
489. McQuade D, Hudson S, Dargan PI, Wood DM. First European case of convulsions related to analytically confirmed use of the synthetic cannabinoid receptor agonist AM-2201. *Eur J Clin Pharmacol* 2013;**69**:373–6. <https://doi.org/10.1007/s00228-012-1379-2>
490. Meacher BMC. Drug policy reform – the opportunity presented by ‘legal highs’. *Psychiatrist* 2013;**37**:249–52. <https://doi.org/10.1192/pb.bp.113.043711>
491. Measham F, Wood DM, Dargan PI, Moore K. The rise in legal highs: prevalence and patterns in the use of illegal drugs and first- and second-generation ‘legal highs’ in South London gay dance clubs. *J Subst Use* 2011;**16**:263–72. <https://doi.org/10.3109/14659891.2011.594704>
492. Mehta V. Bath salts’ abuse. *Curr Psychiatr* 2013. URL: www.mdedge.com/currentpsychiatry/article/76916/schizophrenia-other-psychotic-disorders/bath-salts-abuse (accessed 29 June 2016).
493. McCloskey K, Vearrier D, McKeever RG, Greenberg M. E-cigarettes and synthetic cannabinoids: a new trend. *Clin Toxicol* 2016;**54**:390.
494. McIlroy G, Ford L, Khan JM. Acute myocardial infarction, associated with the use of a synthetic adamantyl-cannabinoid: a case report. *BMC Pharmacol Toxicol* 2016;**17**:2. <https://doi.org/10.1186/s40360-016-0045-1>
495. Mieczkowski BP, Chacey M, Schaffernocker T. *Intoxication of Bath Salts Leading to Rhabdomyolysis and Renal Failure: A Case Report*. American Journal of Respiratory and Critical Care Medicine Conference: American Thoracic Society International Conference, ATS 2012;**185**. http://dx.doi.org/10.1164/ajrccm-conference.2012.185.1_MeetingAbstracts.A4621.
496. Miliano C, Serpelloni G, Rimondo C, Mereu M, Marti M, De Luca MA. Neuropharmacology of new psychoactive substances (NPS): focus on the rewarding and reinforcing properties of cannabimimetics and amphetamine-like stimulants. *Front Neurosci* 2016;**10**:153. <https://doi.org/10.3389/fnins.2016.00153>
497. Mistral W. *New Drugs, Old Responses?* New York, NY: Routledge/Taylor & Francis Group; 2016.
498. Meijer KA, Russo RR, Adhvaryu DV. Smoking synthetic marijuana leads to self-mutilation requiring bilateral amputations. *Orthopedics* 2014;**37**:e391–4. <https://doi.org/10.3928/01477447-20140401-62>
499. Baumann MH, Solis E, Watterson LR, Marusich JA, Fantegrossi WE, Wiley JL. Baths salts, spice, and related designer drugs: the science behind the headlines. *J Neurosci* 2014;**34**:15150–8. <https://doi.org/10.1523/JNEUROSCI.3223-14.2014>
500. Miller BL, Stogner JM. Not-so-clean fun: a profile of bath salt users among a college sample in the United States. *J Psychoactive Drugs* 2014;**46**:147–53. <https://doi.org/10.1080/02791072.2013.876520>
501. Mills B, Yepes A, Nugent K. Synthetic cannabinoids. *Am J Med Sci* 2015;**350**:59–62. <https://doi.org/10.1097/MAJ.0000000000000466>

502. Miotto K, Striebel J, Cho AK, Wang C. Clinical and pharmacological aspects of bath salt use: a review of the literature and case reports. *Drug Alcohol Depend* 2013;**132**:1–12. <https://doi.org/10.1016/j.drugalcdep.2013.06.016>
503. Mir A, Obafemi A, Young A, Kane C. Myocardial infarction associated with use of the synthetic cannabinoid K2. *Pediatrics* 2011;**128**:e1622–7. <https://doi.org/10.1542/peds.2010-3823>
504. Misselbrook GP, Hamilton EJ. Out with the old, in with the new? Case reports of the clinical features and acute management of two novel designer drugs. *Acute Med* 2012;**11**:157–60.
505. Miyajima M, Matsumoto T, Ito S. 2C-T-4 intoxication: acute psychosis caused by a designer drug. *Psychiatry Clin Neurosci* 2008;**62**:243. <https://doi.org/10.1111/j.1440-1819.2008.01764.x>
506. Moad J, Kinasewitz G. Don't throw the baby out with the bath....salts. *Chest* 2011;**140**:187A. <https://doi.org/10.1378/chest.1120069>
507. Monte AA, Bronstein AC, Cao DJ, Heard KJ, Hoppe JA, Hoyte CO, et al. An outbreak of exposure to a novel synthetic cannabinoid. *N Engl J Med* 2014;**370**:389–90. <https://doi.org/10.1056/NEJMc1313655>
508. Monteiro P. Smart shops: new intervention guidelines. *Atencion Primaria* 2013;**45**:33.
509. Moore K, Dargan PI, Wood DM, Measham F. Do novel psychoactive substances displace established club drugs, supplement them or act as drugs of initiation? The relationship between mephedrone, ecstasy and cocaine. *Eur Addict Res* 2013;**19**:276–82. <https://doi.org/10.1159/000346678>
510. Haig SD, Kelly C, Morden C. A report of an outbreak of toxicity from a novel drug of abuse: ERIC-3. *Emerg Med J* 2013;**30**:543–5. <https://doi.org/10.1136/emmermed-2012-201631>
511. Moti D, Ahmed M. First use of K2, first seizure. *J Invest Med* 2014;**62**:538.
512. Muller D, Neurath H, Just S, Liebetrau G, Desel H. Novel psychoactive substances: findings in a regional toxicology center in 2014. *Clin Toxicol* 2015;**53**:363.
513. Müller H, Huttner HB, Köhrmann M, Wielopolski JE, Kornhuber J, Sperling W. Panic attack after spice abuse in a patient with ADHD. *Pharmacopsychiatry* 2010;**43**:152–3. <https://doi.org/10.1055/s-0029-1243252>
514. Muller H, Sperling W, Kohrmann M, Huttner HB, Kornhuber J, Maler JM. The synthetic cannabinoid Spice as a trigger for an acute exacerbation of cannabis induced recurrent psychotic episodes. *Schizophr Res* 2010;**118**:309–10. <https://doi.org/10.1016/j.schres.2009.12.001>
515. Murray BL, Murphy CM, Beuhler MC. Death following recreational use of designer drug 'bath salts' containing 3,4-Methylenedioxypyrovalerone (MDPV). *J Med Toxicol* 2012;**8**:69–75. <https://doi.org/10.1007/s13181-011-0196-9>
516. Moore AP, Lesser E. Legal highs, NPS, head shop drugs? Whatever you call them, we need to know more about prevalence. *BJPsych Bull* 2015;**39**:316. <https://doi.org/10.1192/pb.39.6.316a>
517. Mounsey SJ, Dargan PI, Stewart M, Brown A, Newton N, Wood DM. Perceived risk of using novel psychoactive substances in school students: lower in users compared to non-users. *J Subst Use* 2016;**21**:323–6. <https://doi.org/10.3109/14659891.2015.1021870>
518. Muller HH, Kornhuber J, Sperling W. The behavioral profile of spice and synthetic cannabinoids in humans. *Brain Res Bull* 2015;**6**:6.
519. Najafi J, Dunn M, Hill SL, Thomas SHL. Severe clinical toxicity following analytically confirmed use of the synthetic cannabinoid receptor agonist MDMB-CHMICA: a report from the Identification Of Novel psychoActive substance study (IONA). *Clin Toxicol* 2016;**54**:405.

520. Newman M, Denton G, Walker T, Grewal J. The experience of using synthetic cannabinoids: a qualitative analysis of online user self-reports. *Eur Psychiatry* 2016;**33**:S309–10. <https://doi.org/10.1016/j.eurpsy.2016.01.1059>
521. Murray DB, Potts S, Haxton C, Jackson G, Sandilands EA, Ramsey J, et al. 'Ivory wave' toxicity in recreational drug users; integration of clinical and poisons information services to manage legal high poisoning. *Clin Toxicol* 2012;**50**:108–13. <https://doi.org/10.3109/15563650.2011.647992>
522. Musselman ME, Hampton JP. 'Not for human consumption': a review of emerging designer drugs. *Pharmacotherapy* 2014;**34**:745–57. <https://doi.org/10.1002/phar.1424>
523. Musshoff F, Madea B, Kernbach-Wighton G, Bicker W, Kneisel S, Hutter M, Auwärter V. Driving under the influence of synthetic cannabinoids ('Spice'): a case series. *Int J Legal Med* 2014;**128**:59–64. <https://doi.org/10.1007/s00414-013-0864-1>
524. Nacca N, Vatti D, Sullivan R, Sud P, Su M, Marraffa J. The synthetic cannabinoid withdrawal syndrome. *J Addict Med* 2013;**7**:296–8. <https://doi.org/10.1097/ADM.0b013e31828e1881>
525. Namera A, Urabe S, Saito T, Torikoshi-Hatano A, Shiraishi H, Arima Y, et al. A fatal case of 3,4-methylenedioxypyrovalerone poisoning: coexistence of alpha-pyrrolidinobutiophenone and alpha-pyrrolidinovalerophenone in blood and/or hair. *Forensic Toxicol* 2013;**31**:338–43. <https://doi.org/10.1007/s11419-013-0192-7>
526. Nelson ME, Bryant SM, Aks SE. Emerging drugs of abuse. *Emerg Med Clin North Am* 2014;**32**:1–28. <https://doi.org/10.1016/j.emc.2013.09.001>
527. Newberry J, Wodak A, Sellman D, Robinson G. New Zealand's regulation of new psychoactive substances. *BMJ* 2014;**348**:g1534. <https://doi.org/10.1136/bmj.g1534>
528. Nicholson TC. Prevalence of use, epidemiology and toxicity of 'herbal party pills' among those presenting to the emergency department. *Emerg Med Australas* 2006;**18**:180–4. <https://doi.org/10.1111/j.1742-6723.2006.00826.x>
529. Nicol J, Yarema M, Purssell R, Martz, Q, Purssell RA, MacDonald JC, et al. Paramethoxymethamphetamine (PMMA) fatalities in Alberta and British Columbia, Canada. *Clin Toxicol* 2013;**51**:662–3.
530. Ninnemann A, MacPherson L. Query and test for synthetic cannabinoids in drug treatment and research. *Int J Drug Policy* 2015;**26**:531–2. <https://doi.org/10.1016/j.drugpo.2014.11.013>
531. Ninnemann A, Stuart GL. The NBOMe series: a novel, dangerous group of hallucinogenic drugs. *J Stud Alcohol Drugs* 2013;**74**:977–8. <https://doi.org/10.15288/jsad.2013.74.977>
532. Norman J, Grace S, Lloyd C. Legal high groups on the Internet – the creation of new organized deviant groups? *Drugs (Abingdon Engl)* 2014;**21**:14–23. <https://doi.org/10.3109/09687637.2013.769500>
533. Nocerino A, Ilyas N. Unusual toxicities of synthetic marijuana. *J Gen Intern Med* 2016;**1**:S775–S776.
534. Nugteren-van Lonkhuyzen JJ, van Riel AJ, Brunt TM, Hondebrink L. Pharmacokinetics, pharmacodynamics and toxicology of new psychoactive substances (NPS): 2C-B, 4-fluoroamphetamine and benzofurans. *Drug Alcohol Depend* 2015;**157**:18–27. <https://doi.org/10.1016/j.drugalcdep.2015.10.011>
535. Nurmedov S, Yilmaz O, Darcin AE, Noyan OC, Dilbaz N. Frequency of synthetic cannabinoid use and its relationship with socio-demographic characteristics and treatment outcomes in alcohol- and substance-dependent inpatients: a retrospective study. *Klinik Psikofarmakol Bülteni* 2015;**25**:348–54. <https://doi.org/10.5455/bcp.20150207072424>

536. Nyi PP, Lai EP, Lee DY, Biglete SA, Torrecer GI, Anderson IB. Influence of age on *Salvia divinorum* use: results of an Internet survey. *J Psychoactive Drugs* 2010;**42**:385–92. <https://doi.org/10.1080/02791072.2010.10400701>
537. Obafemi AI, Goto C, Drew F, Kleinschmidt K. Synthetic cannabinoid laced brownies. *Clin Toxicol* 2012;**50**:638.
538. O'Brien K, Chatwin C, Jenkins C, Measham F. New psychoactive substances and British drug policy: a view from the cyber-psychonauts. *Drugs (Abingdon Engl)* 2015;**22**:217–23. <https://doi.org/10.3109/09687637.2014.989959>
539. Oğuz S, Kurt F, Tekin D, Suskan E. New challenges of the pediatric emergency department: synthetic cannabinoids. *Turk Pediatri Ars* 2014;**49**:356–7. <https://doi.org/10.5152/tpa.2014.2276>
540. Oliver T, Gheevarghese SJ, Gandhi U, Bhat ZY, Pillai U. 'Krokodil' – a menace slowly spreading across the Atlantic. *Am J Ther* 2015;**22**:231–3. <https://doi.org/10.1097/MJT.000000000000085>
541. Oluwabusi OO, Lobach L, Akhtar U, Youngman B, Ambrosini PJ. Synthetic cannabinoid-induced psychosis: two adolescent cases. *J Child Adolesc Psychopharmacol* 2012;**22**:393–5. <https://doi.org/10.1089/cap.2012.0004>
542. Omer TA, Doherty C. Posterior reversible encephalopathy syndrome (PRES) complicating the 'legal high' mephedrone. *BMJ Case Rep* 2011;**2011**:bcr0220113904. <https://doi.org/10.1136/bcr.02.2011.3904>
543. O'Neill C. Novel psychoactive substances: risks and harms. *Community Pract* 2014;**87**:45–7.
544. O'Neill N. Mephedrone and multiplicity: user accounts of effects and harms. *Contemp Drug Probl* 2014;**41**:417–43. <https://doi.org/10.1177/009145091404100307>
545. Obafemi AI, Kleinschmidt K, Goto C, Fout D. Cluster of acute toxicity from ingestion of synthetic cannabinoid-laced brownies. *J Med Toxicol* 2015;**11**:426–9. <https://doi.org/10.1007/s13181-015-0482-z>
546. Odoardi S, Romolo FS, Strano-Rossi S. A snapshot on NPS in Italy: distribution of drugs in seized materials analysed in an Italian forensic laboratory in the period 2013–2015. *Forensic Sci Int* 2016;**265**:116–20. <https://doi.org/10.1016/j.forsciint.2016.01.037>
547. Orsini J, Blaak C, Tam E, Rajayer S, Morante J, Yeh A, Butala A. The wide and unpredictable scope of synthetic cannabinoids toxicity. *Case Rep Crit Care* 2015;**2015**:542490. <https://doi.org/10.1155/2015/542490>
548. Palamar JJ. 'Bath salt' use among a nationally representative sample of high school seniors in the United States. *Am J Addict* 2015;**24**:488–91. <https://doi.org/10.1111/ajad.12254>
549. Palamar JJ, Acosta P, Sherman S, Ompad DC, Cleland CM. Self-reported use of novel psychoactive substances among attendees of electronic dance music venues. *Am J Drug Alcohol Abuse* 2016;**42**:624–32. <https://doi.org/10.1080/00952990.2016.1181179>
550. Palamar JJ, Salomone A, Vincenti M, Cleland CM. Detection of 'bath salts' and other novel psychoactive substances in hair samples of ecstasy/MDMA/'Molly' users. *Drug Alcohol Depend* 2016;**161**:200–5. <https://doi.org/10.1016/j.drugalcdep.2016.02.001>
551. Onikoyi-Deckon A, Smyth B. Use of new psychoactive substances among teenagers attending a specialized adolescent addiction service in Dublin, before and after a legislative ban on their sale. *Eur Child Adolesc Psychiatry* 2013;**22**:S213.
552. Oprea S, Visan MG, Iliescu R, Florescu S, Nitescu GV. New psychoactive substances and illicit drugs used among 16-year-old high school students in Romania. *Clin Toxicol* 2014;**52**:360.

553. Osterhoudt KC, Cook MD. Clean but not sober: a 16-year-old with restlessness. *Pediatr Emerg Care* 2011;**27**:892–4. <https://doi.org/10.1097/PEC.0b013e318233ed26>
554. Pagano JJ, Penders TM, Lang MC, Professor A, Gooding ZS. The use of ECT in treatment-resistant psychosis secondary to bath salt use. *J ECT* 2013;**29**:152.
555. Paillet-Loilier M, Cesbron A, Le Boisselier R, Bourguine J, Debruyne D. Emerging drugs of abuse: current perspectives on substituted cathinones. *Subst Abuse Rehabil* 2014;**5**:37–52. <https://doi.org/10.2147/SAR.S37257>
556. Palamar JJ, Acosta P. Synthetic cannabinoid use in a nationally representative sample of US high school seniors. *Drug Alcohol Depend* 2015;**149**:194–202. <https://doi.org/10.1016/j.drugalcdep.2015.01.044>
557. Palamar JJ, Martins SS, Su MK, Ompad DC. Self-reported use of novel psychoactive substances in a US nationally representative survey: prevalence, correlates, and a call for new survey methods to prevent underreporting. *Drug Alcohol Depend* 2015;**156**:112–19. <https://doi.org/10.1016/j.drugalcdep.2015.08.028>
558. Pallasch EM, Wahl M, Burda A, Kubic A. Who uses bath salts? Urban vs. rural distribution of PCC cases. *Clin Toxicol* 2013;**51**:680–1.
559. Pandya D, Malaiyandi D, Asi K, Helms A, Lynch J. Methadone and ‘bath salt’ use causing near-fatal posterior reversible encephalopathy syndrome. *Neurology* 2012;**78**:P06.259.
560. Pant S, Deshmukh A, Dholaria B, Kaur V, Ramavaram S, Ukur M, Teran GA. Spicy seizure. *Am J Med Sci* 2012;**344**:67–8. <https://doi.org/10.1097/MAJ.0b013e31824cf5c2>
561. Papanti D, Schifano F, Botteon G, Bertossi F, Mannix J, Vidoni D, et al. ‘Spicephrenia’: a systematic overview of ‘spice’-related psychopathological issues and a case report. *Hum Psychopharmacol* 2013;**28**:379–89. <https://doi.org/10.1002/hup.2312>
562. Papaseit E, Farré M, Schifano F, Torrens M. Emerging drugs in Europe. *Curr Opin Psychiatry* 2014;**27**:243–50. <https://doi.org/10.1097/YCO.0000000000000071>
563. Patel J, Feeney C, Scott J, Yang S, Wu A. The toxic effects of synthetic cannabinoids. *Crit Care Med* 2014;**42**:A1628. <https://doi.org/10.1097/01.ccm.0000458612.93094.0a>
564. Patton AL, Chimalakonda KC, Moran CL, McCain KR, Radominska-Pandya A, James LP, et al. K2 toxicity: fatal case of psychiatric complications following AM2201 exposure. *J Forensic Sci* 2013;**58**:1676–80. <https://doi.org/10.1111/1556-4029.12216>
565. Palamar JJ, Su MK, Hoffman RS. Characteristics of novel psychoactive substance exposures reported to New York City Poison Center, 2011–2014. *Am J Drug Alcohol Abuse* 2016;**42**:39–47. <https://doi.org/10.3109/00952990.2015.1106551>
566. Pap C. Futile fight – trends in poisoning with drugs of abuse in Hungary. *Clin Toxicol* 2016;**54**:408.
567. Papaseit E, Pérez-Mañá C, Mateus JA, Pujadas M, Fonseca F, Torrens M, et al. Human Pharmacology of Mephedrone in Comparison with MDMA. *Neuropsychopharmacology* 2016;**41**:2704–13. <https://doi.org/10.1038/npp.2016.75>
568. Parks C, McKeown D, Torrance HJ. A review of ethylphenidate in deaths in east and west Scotland. *Forensic Sci Int* 2015;**257**:203–8. <https://doi.org/10.1016/j.forsciint.2015.08.008>
569. Patrick ME, O’Malley PM, Kloska DD, Schulenberg JE, Johnston LD, Miech RA, et al. Novel psychoactive substance use by US adolescents: characteristics associated with use of synthetic cannabinoids and synthetic cathinones. *Drug Alcohol Rev* 2016;**35**:586–90. <https://doi.org/10.1111/dar.12372>

570. Penney J, Dargan PI, Padmore J, Wood DM, Norman IJ. Epidemiology of adolescent substance use in London schools. *QJM* 2016;**109**:405–9. <https://doi.org/10.1093/qjmed/hcv171>
571. Pavarin RM. Substance use and related problems: a study on the abuse of recreational and not recreational drugs in Northern Italy. *Ann Ist Super Sanita* 2006;**42**:477–84.
572. Pawlowicz U, Wasilewska A, Olanski W, Stefanowicz M. Epidemiological study of acute poisoning in children: a 5-year retrospective study in the Paediatric University Hospital in Bialystok, Poland. *Emerg Med J* 2013;**30**:712–16. <https://doi.org/10.1136/emered-2012-201376>
573. Peglow S, Buchner J, Briscoe G. Synthetic cannabinoid induced psychosis in a previously nonpsychotic patient. *Am J Addict* 2012;**21**:287–8. <https://doi.org/10.1111/j.1521-0391.2012.00222.x>
574. Pendergraft WF, Herlitz LC, Thornley-Brown D, Rosner M, Niles JL. Nephrotoxic effects of common and emerging drugs of abuse. *Clin J Am Soc Nephrol* 2014;**9**:1996–2005. <https://doi.org/10.2215/CJN.00360114>
575. Penders TM. How to recognize a patient who's high on 'bath salts'. *J Fam Pract* 2012;**61**:210–12.
576. Penders TM, Gestring R. Hallucinatory delirium following use of MDPV: 'Bath Salts'. *Gen Hosp Psychiatry* 2011;**33**:525–6. <https://doi.org/10.1016/j.genhosppsych.2011.05.014>
577. Penders TM, Gestring R. Psychiatric morbidity following use of synthetic cathinones, 'bath salts'. *Am J Addict* 2013;**22**:315.
578. Penders TM, Gestring RE, Vilensky DA. Intoxication delirium following use of synthetic cathinone derivatives. *Am J Drug Alcohol Abuse* 2012;**38**:616–17. <https://doi.org/10.3109/00952990.2012.694535>
579. Penders TM, Gestring RE, Vilensky DA. Excited delirium following use of synthetic cathinones (bath salts). *Gen Hosp Psychiatry* 2012;**34**:647–50. <https://doi.org/10.1016/j.genhosppsych.2012.06.005>
580. Penders TM, Lang MC, Pagano JJ, Gooding ZS. Electroconvulsive therapy improves persistent psychosis after repeated use of methylenedioxypropylvalerone ('bath salts'). *J ECT* 2013;**29**:e59–60. <https://doi.org/10.1097/YCT.0b013e3182887bc2>
581. Perron BE, Ahmedani BK, Vaughn MG, Glass JE, Abdon A, Wu LT. Use of *Salvia divinorum* in a nationally representative sample. *Am J Drug Alcohol Abuse* 2012;**38**:108–13. <https://doi.org/10.3109/00952990.2011.600397>
582. Perrone D, Helgesen RD, Fischer RG. United States drug prohibition and legal highs: how drug testing may lead cannabis users to spice. *Drugs (Abingdon Engl)* 2013;**20**:216–24. <https://doi.org/10.3109/09687637.2012.749392>
583. Petrescu-Ghenea C, Dobrescu I, Anghel GC, Nitescu VG, Boghitoiu DA. Adolescents presenting with designer drug intoxication in a pediatric toxicology department in Bucharest. *Eur Neuropsychopharmacol* 2013;**23**:S616–S617. [https://doi.org/10.1016/S0924-977X\(13\)70979-9](https://doi.org/10.1016/S0924-977X(13)70979-9)
584. Petti T. Marijuana and synthetic marijuana: clinical and public health perspectives. *Eur Child Adolesc Psychiatry* 2013;**22**:S139.
585. Peyrière H, Jacquet JM, Eiden C, Tuillon E, Psomas C, Reynes J. Viral and bacterial risks associated with mephedrone abuse in HIV-infected men who have sex with men. *AIDS* 2013;**27**:2971–2. <https://doi.org/10.1097/QAD.000000000000029>
586. Pichini S, Marchei E, Rotolo MC, Pellegrini M, Pacifici R. Emerging trends in drug use among young people. *Biochimica Clinica* 2013;**37**:S14.

587. Pichini S, Rotolo MC, Garcia J, Girona N, Leal L, García-Algar O, *et al.* Neonatal withdrawal syndrome after chronic maternal consumption of 4-methylethcathinone. *Forensic Sci Int* 2014;**245**:e33–5. <https://doi.org/10.1016/j.forsciint.2014.10.027>
588. Pierre JM. Cannabis, synthetic cannabinoids, and psychosis risk: what the evidence says. *Current Psychiatry* 2011;**10**:49–58.
589. Plumb J, Caravati EM, Anderson KT, McDonnell WM. Spicing things up: pediatric exposures to synthetic cannabinoids. *Acad Emerg Med* 2011;**18**:S74.
590. Plumb J, McDonnell WM, Anderson KT, Crouch BI, Caravati EM. Adverse effects from pediatric exposures to spice (cannabinoid agonists). *Clin Toxicol* 2012;**50**:708.
591. Pohjalainen T, Hoppu K. MDPV exposures reported to the Finnish poison information centre. *Clin Toxicol* 2010;**48**:305.
592. Pettie JM, Dow MA, Greig R, Eddleston M, Dear JW. The impact of legislative control of methylphenidate-based novel psychoactive substances on recreational drug-related admissions to the Royal Infirmary of Edinburgh. *Clin Toxicol* 2016;**54**:399–400.
593. Poklis J, Poklis A, Wolf C, Hathaway C, Arbefeville E, Chrostowski L, *et al.* Two fatal intoxications involving butyryl fentanyl. *J Anal Toxicol* 2016;**40**:703–8. <https://doi.org/10.1093/jat/bkw048>
594. Poklis J, Poklis A, Wolf C, Mainland M, Hair L, Devers K, *et al.* Postmortem tissue distribution of acetyl fentanyl, fentanyl and their respective nor-metabolites analyzed by ultrahigh performance liquid chromatography with tandem mass spectrometry. *Forensic Sci Int* 2015;**257**:435–41. <https://doi.org/10.1016/j.forsciint.2015.10.021>
595. Racz J, Csak R, Toth KT, Toth E, Rozman K, Gyarmathy VA. Veni, vidi, vici: the appearance and dominance of new psychoactive substances among new participants at the largest needle exchange program in Hungary between 2006 and 2014. *Drug Alcohol Depend* 2016;**158**:154–8. <https://doi.org/10.1016/j.drugalcdep.2015.10.034>
596. Pon R. A fatality involving 5-methoxy-*N,N*-diisopropyltryptamine ('Foxy') and cocaine. *Can Soc Forensic Sci J* 2008;**41**:165–70. <https://doi.org/10.1080/00085030.2008.10757173>
597. Pourmand A, Armstrong P, Mazer-Amirshahi M, Shokoohi H. The evolving high: new designer drugs of abuse. *Hum Exp Toxicol* 2014;**33**:993–9. <https://doi.org/10.1177/0960327113514100>
598. Pourmorteza M, Al Shathir M, Roy T, Byrd R. Expected and unexpected electrolyte disturbances with bath salt ingestion. *J Investig Med* 2015;**63**:343–4.
599. Prioleau C. Synthetic cathinones and the extent of their abuse in the United States. *Biol Psychiatry* 2012;**71**:105–15.
600. Prosser JM, Nelson LS. The toxicology of bath salts: a review of synthetic cathinones. *J Med Toxicol* 2012;**8**:33–42. <https://doi.org/10.1007/s13181-011-0193-z>
601. Psychoyos D, Vinod KY. Marijuana, Spice 'herbal high', and early neural development: implications for rescheduling and legalization. *Drug Test Anal* 2013;**5**:27–45. <https://doi.org/10.1002/dta.1390>
602. Ragone SP, Geller RJ, Lopez GP. A poison center's development of a media campaign to address trends of herbal incense abuse. *Clin Toxicol* 2010;**48**:649.
603. Ramsey J, Dargan PI, Smyllie M, Davies S, Button J, Holt DW, Wood DM. Buying 'legal' recreational drugs does not mean that you are not breaking the law. *QJM* 2010;**103**:777–83. <https://doi.org/10.1093/qjmed/hcq132>
604. Randolph SA. Synthetic drugs: bath salts and spice. *Workplace Health Saf* 2014;**62**:88. <https://doi.org/10.3928/21650799-20140121-06>

605. Rasimas JJ. 'Bath salts' and the return of serotonin syndrome. *J Clin Psychiatry* 2012;**73**:1126–7. <https://doi.org/10.4088/JCP.12com07965>
606. Regan L, Mitchelson M, Macdonald C. Mephedrone toxicity in a Scottish emergency department. *Emerg Med J* 2011;**28**:1055–8. <https://doi.org/10.1136/emj.2010.103093>
607. Reid MJ, Derry L, Thomas KV. Analysis of new classes of recreational drugs in sewage: synthetic cannabinoids and amphetamine-like substances. *Drug Test Anal* 2014;**6**:72–9. <https://doi.org/10.1002/dta.1461>
608. Remane D, Auwarter V, Werner R, Schermer J, Drobnik S, Mall G, et al. Fatal poisoning involving the synthetic cannabinoids JWH-122 and JWH-210. *Rechtsmedizin* 2012;**22**:286.
609. Rodgman CJ, Verrico CD, Worthy RB, Lewis EE. Inpatient detoxification from a synthetic cannabinoid and control of postdetoxification cravings with naltrexone. *Prim Care Companion CNS Disord* 2014;**16**. <https://doi.org/10.4088/PCC.13l01594>
610. Rojek S, Klys M, Maciów-Glab M, Kula K, Strona M. Cathinones derivatives-related deaths as exemplified by two fatal cases involving methcathinone with 4-methylmethcathinone and 4-methylethcathinone. *Drug Test Anal* 2014;**6**:770–7. <https://doi.org/10.1002/dta.1615>
611. Rojek S, Klys M, Strona M, Maciów M, Kula K. 'Legal highs' – toxicity in the clinical and medico-legal aspect as exemplified by suicide with bk-MBDB administration. *Forensic Sci Int* 2012;**222**:e1–6. <https://doi.org/10.1016/j.forsciint.2012.04.034>
612. Rominger A, Cumming P, Xiong G, Koller G, Förster S, Zwergal A, et al. Effects of acute detoxification of the herbal blend 'Spice Gold' on dopamine D2/3 receptor availability: a [18F] fallypride PET study. *Eur Neuropsychopharmacol* 2013;**23**:1606–10. <https://doi.org/10.1016/j.euroneuro.2013.01.009>
613. Reuter EL. *An Examination of Unintended Consequences and the Effectiveness of Bath Salts Criminalization*. Ann Arbor, MI: ProQuest Dissertation and Thesis Database; 2016.
614. Reuter P, Pardo B. Can new psychoactive substances be regulated effectively? An assessment of the British Psychoactive Substances Bill. *Addiction* 2017;**112**:25–31. <https://doi.org/10.1111/add.13439>
615. Rogers JS, Rehrer SJ, Hoot NR. Acetylfentanyl: an emerging drug of abuse. *J Emerg Med* 2016;**50**:433–6. <https://doi.org/10.1016/j.jemermed.2015.10.014>
616. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths – United States, 2000–2014. *MMWR Morb Mortal Wkly Rep* 2016;**64**:1378–82. <https://doi.org/10.15585/mmwr.mm6450a3>
617. Rychert M, Wilkins C. What products are considered psychoactive under New Zealand's legal market for new psychoactive substances (NPS, 'legal highs')? Implications for law enforcement and penalties. *Drug Test Anal* 2016;**8**:768–78. <https://doi.org/10.1002/dta.1943>
618. Rose RS, Cumpston KL, Stromberg PE, Wills BK. Severe poisoning following self-reported use of 25-I, a novel substituted amphetamine. *Clin Toxicol* 2012;**50**:707–8.
619. Rose SR, Poklis JL, Poklis A. A case of 25I-NBOMe (25-I) intoxication: a new potent 5-HT_{2A} agonist designer drug. *Clin Toxicol* 2013;**51**:174–7. <https://doi.org/10.3109/15563650.2013.772191>
620. Rosenbaum CD, Carreiro SP, Babu KM. Here today, gone tomorrow...and back again? A review of herbal marijuana alternatives (K2, Spice), synthetic cathinones (bath salts), kratom, *Salvia divinorum*, methoxetamine, and piperazines. *J Med Toxicol* 2012;**8**:15–32. <https://doi.org/10.1007/s13181-011-0202-2>
621. Rosenbaum CD, Scalzo AJ, Long C, Weber JA, Jenkins A, Lopez GP, et al. K2 & spice abusers: a case series of clinical and laboratory findings. *Clin Toxicol* 2011;**49**:528.

622. Rosenbaum CD, Ward JA, Boudreaux ED, Burstein S, Boyer EW. JWH-018, JWH-073, and spice. *Clin Toxicol* 2010;**48**:307.
623. Ross EA, Reisfield GM, Watson MC, Chronister CW, Goldberger BA. Psychoactive 'bath salts' intoxication with methylenedioxypropylvalerone. *Am J Med* 2012;**125**:854–8. <https://doi.org/10.1016/j.amjmed.2012.02.019>
624. Ross EA, Watson M, Goldberger B. 'Bath salts' intoxication. *N Engl J Med* 2011;**365**:967–8. <https://doi.org/10.1056/NEJMc1107097>
625. Russo R, Marks N, Morris K, King H, Gelvin A, Rooney R. Life-threatening necrotizing fasciitis due to 'bath salts' injection. *Orthopedics* 2012;**35**:e124–7. <https://doi.org/10.3928/01477447-20111122-36>
626. Rust KY, Baumgartner MR, Dally AM, Kraemer T. Prevalence of new psychoactive substances: a retrospective study in hair. *Drug Test Anal* 2012;**4**:402–8. <https://doi.org/10.1002/dta.1338>
627. Ryall G, Butler S. The great Irish head shop controversy. *Drugs (Abingdon Engl)* 2011;**18**:303–11. <https://doi.org/10.3109/09687637.2011.560911>
628. Ryan ML, Arnold T. The effectiveness of a state designer drug ban one year later. *Clin Toxicol* 2012;**50**:612.
629. Ryan ML, Arnold TC. From convenience stores to schedule I in less than 100 days. *Clin Toxicol* 2011;**49**:519–20.
630. Sacks J, Ray MJ, Williams S, Opatowsky MJ. Fatal toxic leukoencephalopathy secondary to overdose of a new psychoactive designer drug 2C-E ('Europa'). *Proc* 2012;**25**:374–6.
631. Sadeg N, Darie A, Vilamot B, Passamar M, Frances B, Belhadj-Tahar H. Case report of cathinone-like designer drug intoxication psychosis and addiction with serum identification. *Addict Disord Their Treat* 2014;**13**:38–43. <https://doi.org/10.1097/ADT.0b013e318285308d>
632. Saito T, Namera A, Miura N, Ohta S, Miyazaki S, Osawa M, et al. A fatal case of MAM-2201 poisoning. *Forensic Toxicol* 2013;**31**:333–7. <https://doi.org/10.1007/s11419-013-0190-9>
633. Salani DA, Zdanowicz MM. Synthetic cannabinoids: the dangers of spicing it up. *J Psychosoc Nurs Ment Health Serv* 2015;**53**:36–43. <https://doi.org/10.3928/02793695-20150422-01>
634. Sammler EM, Foley PL, Lauder GD, Wilson SJ, Goudie AR, O'Riordan JI. A harmless high? *Lancet* 2010;**376**:742. [https://doi.org/10.1016/S0140-6736\(10\)60891-4](https://doi.org/10.1016/S0140-6736(10)60891-4)
635. Sampson CS, Bedy SM, Carlisle T. Withdrawal seizures seen in the setting of synthetic cannabinoid abuse. *Am J Emerg Med* 2015;**33**:1712.e3. <https://doi.org/10.1016/j.ajem.2015.03.025>
636. Sarpong I, Jones F. A critical analysis of national policy relating to legal highs. *Nurs Stand* 2014;**28**:35–41. <https://doi.org/10.7748/ns.28.52.35.e8850>
637. Saglam O, Bahsi R, Akkoca Y, Filik L. Risperidone-induced hepatotoxicity in a patient addicted to synthetic cannabinoid. *Eur J Gastroenterol Hepatol* 2016;**28**:360–1. <https://doi.org/10.1097/MEG.0000000000000524>
638. Sande M. Characteristics of the use of 3-MMC and other new psychoactive drugs in Slovenia, and the perceived problems experienced by users. *Int J Drug Policy* 2016;**27**:65–73. <https://doi.org/10.1016/j.drugpo.2015.03.005>
639. Schifano F, Orsolini L, Papanti D, Corkery J. NPS: medical consequences associated with their intake. *Curr Top Behav Neurosci* 2017;**32**:351–80. https://doi.org/10.1007/7854_2016_15
640. Schifano F, Papanti GD, Orsolini L, Corkery JM. Novel psychoactive substances: the pharmacology of stimulants and hallucinogens. *Expert Rev Clin Pharmacol* 2016;**9**:943–54. <https://doi.org/10.1586/17512433.2016.1167597>

641. Sauer C, Hoffmann K, Schimmel U, Peters FT. Acute poisoning involving the pyrrolidinophenone-type designer drug 4'-methyl-alpha-pyrrolidinohexanophenone (MPHP). *Forensic Sci Int* 2011;**208**:e20–5. <https://doi.org/10.1016/j.forsciint.2011.02.026>
642. Schep LJ, Gee P, Tingle M, Galea S, Newcombe D. Regulating new psychoactive drugs: innovation leading to compromise. *BMJ* 2014;**349**:g5085. <https://doi.org/10.1136/bmj.g5085>
643. Schep LJ, Slaughter RJ, Hudson S, Place R, Watts M. Delayed seizure-like activity following analytically confirmed use of previously unreported synthetic cannabinoid analogues. *Hum Exp Toxicol* 2015;**34**:557–60. <https://doi.org/10.1177/0960327114550886>
644. Schep LJ, Slaughter RJ, Temple WA. Synthetic cannabinoid use in New Zealand: a brief evaluation of inquiries to the New Zealand National Poisons Centre. *N Z Med J* 2011;**124**:99–101.
645. Schep LJ, Slaughter RJ, Temple WA, Lambie BS, Gee P, Watts M, Gresham C. Synthetic cannabinoid use in New Zealand: a recent rebound. *N Z Med J* 2012;**125**:114–16.
646. Schifano F, Albanese A, Fergus S, Stair JL, Deluca P, Corazza O, et al. Mephedrone (4-methylmethcathinone; 'meow meow'): chemical, pharmacological and clinical issues. *Psychopharmacology* 2011;**214**:593–602. <https://doi.org/10.1007/s00213-010-2070-x>
647. Schneur AB, Baumbacher T. Convulsions associated with the use of a synthetic cannabinoid product. *J Med Toxicol* 2012;**8**:62–4. <https://doi.org/10.1007/s13181-011-0182-2>
648. Schneur AB, Cullen J, Ly BT. 'Spice' girls: synthetic cannabinoid intoxication. *J Emerg Med* 2011;**40**:296–9. <https://doi.org/10.1016/j.jemermed.2010.10.014>
649. Seely KA, Lapoint J, Moran JH, Fattore L. Spice drugs are more than harmless herbal blends: a review of the pharmacology and toxicology of synthetic cannabinoids. *Prog Neuropsychopharmacol Biol Psychiatry* 2012;**39**:234–43. <https://doi.org/10.1016/j.pnpbp.2012.04.017>
650. Seetohul LN, Maskell PD, De Paoli G, Pounder DJ. Deaths associated with new designer drug 5-IT. *BMJ* 2012;**345**:e5625. <https://doi.org/10.1136/bmj.e5625>
651. Seifert SA, Brazwell EM, Smeltzer C, Gibb J, Logan BK. Seizure and acute kidney injury associated with synthetic cannabinoid use. *Clin Toxicol* 2013;**51**:667.
652. Sein Anand J, Wiergowski M, Barwina M, Kaletha K. Accidental intoxication with high dose of methoxetamine (MXE) – a case report. *Prz Lek* 2012;**69**:609–10.
653. Sevinc MM, Kinaci E, Bayrak S, Yardimci AH, Cakar E, Bektas H. Extraordinary cause of acute gastric dilatation and hepatic portal venous gas: chronic use of synthetic cannabinoid. *World J Gastroenterol* 2015;**21**:10704–8. <https://doi.org/10.3748/wjg.v21.i37.10704>
654. Shanks KG, Winston D, Heidingsfelder J, Behonick G. Case reports of synthetic cannabinoid XLR-11 associated fatalities. *Forensic Sci Int* 2015;**252**:e6–9. <https://doi.org/10.1016/j.forsciint.2015.04.021>
655. Segrec N, Kastelic A, Pregelj P. Pentadone-induced acute psychosis in a patient with opioid addiction: a case report. *Heroin Addict Rel Cl* 2016;**18**:53–6.
656. Senta I, Krizman I, Ahel M, Terzic S. Multiresidual analysis of emerging amphetamine-like psychoactive substances in wastewater and river water. *J Chromatogr A* 2015;**1425**:204–12. <https://doi.org/10.1016/j.chroma.2015.11.043>
657. Seywright A, Torrance HJ, Wylie FM, McKeown DA, Lowe DJ, Stevenson R. Analysis and clinical findings of cases positive for the novel synthetic cannabinoid receptor agonist MDMB-CHMICA. *Clin Toxicol* 2016;**54**:632–7. <https://doi.org/10.1080/15563650.2016.1186805>
658. Shah B, Heaps T. Legal highs, lethal lows. *Acute Med* 2015;**14**:188–92.

659. Shanks KG, Behonick GS. Death after use of the synthetic cannabinoid 5F-AMB. *Forensic Sci Int* 2016;**262**:e21–4. <https://doi.org/10.1016/j.forsciint.2016.03.004>
660. Shanks KG, Clark W, Behonick G. Death associated with the use of the synthetic cannabinoid ADB-FUBINACA. *J Anal Toxicol* 2016;**40**:236–9. <https://doi.org/10.1093/jat/bkv142>
661. Sherif M, Radhakrishnan R, D'Souza DC, Ranganathan M. Human laboratory studies on cannabinoids and psychosis. *Biol Psychiatry* 2016;**79**:526–38. <https://doi.org/10.1016/j.biopsych.2016.01.011>
662. Siddiqi S, Verney C, Dargan P, Wood DM. Understanding the availability, prevalence of use, desired effects, acute toxicity and dependence potential of the novel opioid MT-45. *Clin Toxicol* 2015;**53**:54–9. <https://doi.org/10.3109/15563650.2014.983239>
663. Shelton M, Ramirez-Fort MK, Lee KC, Ladizinski B. Krokodil: from Russia with love. *JAMA Dermatol* 2015;**151**:32. <https://doi.org/10.1001/jamadermatol.2014.1025>
664. Sheridan J, Butler R. 'They're legal so they're safe, right?' What did the legal status of BZP-party pills mean to young people in New Zealand? *Int J Drug Policy* 2010;**21**:77–81. <https://doi.org/10.1016/j.drugpo.2009.02.002>
665. Sheridan J, Butler R, Wilkins C, Russell B. Legal piperazine-containing party pills – a new trend in substance misuse. *Drug Alcohol Rev* 2007;**26**:335–43. <https://doi.org/10.1080/09595230701255791>
666. Sherpa D, Paudel BM, Subedi BH, Chow RD. Synthetic cannabinoids: the multi-organ failure and metabolic derangements associated with getting high. *J Community Hosp Intern Med Perspect* 2015;**5**:27540. <https://doi.org/10.3402/jchimp.v5.27540>
667. Simmons J, Cookman L, Kang C, Skinner C. Three cases of 'spice' exposure. *Clin Toxicol* 2011;**49**:431–3. <https://doi.org/10.3109/15563650.2011.584316>
668. Simmons JR, Skinner CG, Williams J, Kang CS, Schwartz MD, Wills BK. Intoxication from smoking 'spice'. *Ann Emerg Med* 2011;**57**:187–8. <https://doi.org/10.1016/j.annemergmed.2010.08.039>
669. Simonato P, Corazza O, Santonastaso P, Corkery J, Deluca P, Davey Z, et al. Novel psychoactive substances as a novel challenge for health professionals: results from an Italian survey. *Hum Psychopharmacol* 2013;**28**:324–31. <https://doi.org/10.1002/hup.2300>
670. Simonsen KW, Edvardsen HM, Thelander G, Ojanperä I, Thordardottir S, Andersen LV, et al. Fatal poisoning in drug addicts in the Nordic countries in 2012. *Forensic Sci Int* 2015;**248**:172–80. <https://doi.org/10.1016/j.forsciint.2015.01.003>
671. Simu MI, Hudita C, Rosca MC, Dan IA. The mephedrone addiction phenomenon. *Int J Neuropsychopharmacol* 2010;**13**:56.
672. Singh S. Adolescent salvia substance abuse. *Addiction* 2007;**102**:823–4. <https://doi.org/10.1111/j.1360-0443.2007.01810.x>
673. Sivagnanam K, Chaudari D, Lopez P, Sutherland ME, Ramu VK. 'Bath salts' induced severe reversible cardiomyopathy. *Am J Case Rep* 2013;**14**:288–91. <https://doi.org/10.12659/AJCR.889381>
674. Skowronek R, Celiński R, Chowaniec C. 'Crocodile' – new dangerous designer drug of abuse from the East. *Clin Toxicol* 2012;**50**:269. <https://doi.org/10.3109/15563650.2012.660574>
675. Smith C, Cardile AP, Miller M. Bath salts as a 'legal high'. *Am J Med* 2011;**124**:e7–8. <https://doi.org/10.1016/j.amjmed.2011.03.014>

676. Smith CD, Robert S. 'Designer drugs': update on the management of novel psychoactive substance misuse in the acute care setting. *Clin Med* 2014;**14**:409–15. <https://doi.org/10.7861/clinmedicine.14-4-409>
677. Smith CD, Williams M, Shaikh M. Novel psychoactive substances: a novel clinical challenge. *BMJ Case Rep* 2013;**2013**:bcr2013200663. <https://doi.org/10.1136/bcr-2013-200663>
678. Smith DL, Roberts C. Synthetic marijuana use and development of catatonia in a 17-year-old male. *Minn Med* 2014;**97**:38.
679. Smith JP, Sutcliffe OB, Banks CE. An overview of recent developments in the analytical detection of new psychoactive substances (NPSs). *Analyst* 2015;**140**:4932–48. <https://doi.org/10.1039/c5an00797f>
680. Smith SK, Christian MR, Aks SE. Prolonged, severe agitation and rhabdomyolysis after intravenous injection of a synthetic cannabinoid. *Clin Toxicol* 2012;**50**:707.
681. Smollin C, Murray S, Gerona R. An unexpected finding of MDPPP in a patient with severe agitation and hallucinations. *Clin Toxicol* 2011;**49**:525–6.
682. Sinangil A, Celik V, Kockar A, Ecder T. Synthetic cannabinoid induced acute tubulointerstitial nephritis and uveitis syndrome: a case report and review of literature. *J Clin Diagn Res* 2016;**10**:OD31–OD2. <https://doi.org/10.7860/jcdr/2016/18762.7826>
683. Sofidiotou V, Dolianiti M, Basanou E, Kalostou A, Fountas K, Touloupaki V, et al. Drugs of abuse used by patients presenting to the emergency department over a one year period. *Clin Toxicol* 2016;**54**:400.
684. Soussan C, Kjellgren A. The users of novel psychoactive substances: online survey about their characteristics, attitudes and motivations. *Int J Drug Policy* 2016;**32**:77–84. <https://doi.org/10.1016/j.drugpo.2016.03.007>
685. Springs J. The psychotic couple – sharing drugs or delusions? *J S C Med Assoc* 2015;**110**:149–50.
686. Stachel N, Jacobsen-Bauer A, Skopp G. A methoxydiphenidine-impaired driver. *Int J Legal Med* 2016;**130**:405–9. <https://doi.org/10.1007/s00414-015-1280-5>
687. Solomon D, Grewal P, Taylor C, Solomon B. Managing misuse of novel psychoactive substances. *Nurs Times* 2014;**110**:12–15.
688. Sommerfeld K, Lukasik-Glebocka M, Nawrocka K. Designer drugs intoxications reported to the department of toxicology in Poznan in 2010. *Toxicol Lett* 2011;**205**:S94. <https://doi.org/10.1016/j.toxlet.2011.05.343>
689. Soussan C, Kjellgren A. Harm reduction and knowledge exchange—a qualitative analysis of drug-related Internet discussion forums. *Harm Reduct J* 2014;**11**:25. <https://doi.org/10.1186/1477-7517-11-25>
690. Soussan C, Kjellgren A. The flip side of 'Spice': the adverse effects of synthetic cannabinoids as discussed on a Swedish internet forum. *Nord Stud Alcohol Dr* 2014;**31**:207–19. <https://doi.org/10.2478/nsad-2014-0016>
691. Spaderna M, Addy PH, D'Souza DC. Spicing things up: synthetic cannabinoids. *Psychopharmacology* 2013;**228**:525–40. <https://doi.org/10.1007/s00213-013-3188-4>
692. Spengler E, LaBrecque D. A case of acute liver failure associated with synthetic cannabis use presidential poster. *Am J Gastroenterol* 2014;**109**:S358–9.
693. Spiller HA, Ryan ML, Weston RG, Jansen J. Clinical experience with and analytical confirmation of 'bath salts' and 'legal highs' (synthetic cathinones) in the United States. *Clin Toxicol* 2011;**49**:499–505. <https://doi.org/10.3109/15563650.2011.590812>

694. Spyker DA, Thomas S, Bateman DN, Thompson JP, Cooper G, Spears R, *et al.* International trends in designer amphetamine abuse in UK and US, 2009–2012. *Clin Toxicol* 2012;**50**:636–7.
695. Srisung W, Jamal F, Prabhakar S. Synthetic cannabinoids and acute kidney injury. *Proc* 2015;**28**:475–7.
696. Stevenson R, Tuddenham L. Novel psychoactive substance intoxication resulting in attempted murder. *J Forensic Leg Med* 2014;**25**:60–1. <https://doi.org/10.1016/j.jflm.2014.04.007>
697. Stirna A, Skaida S, Caune M. New psychoactive substances-herbal smoke mixtures. Prevalence and problems in Latvia. *Eur Psychiatry* 2013;**28**.
698. Stogner JM, Miller BL. Investigating the ‘bath salt’ panic: the rarity of synthetic cathinone use among students in the United States. *Drug Alcohol Rev* 2013;**32**:545–9. <https://doi.org/10.1111/dar.12055>
699. Stoica MV, Felthous AR. Acute psychosis induced by bath salts: a case report with clinical and forensic implications. *J Forensic Sci* 2013;**58**:530–3. <https://doi.org/10.1111/1556-4029.12038>
700. Streich HT, Rushton WF, Charlton NP. Death by spice: a case report of mortality following synthetic cannabinoid use. *Clin Toxicol* 2014;**52**:365.
701. Striebel JM, Pierre JM. Acute psychotic sequelae of ‘bath salts’. *Schizophr Res* 2011;**133**:259–60. <https://doi.org/10.1016/j.schres.2011.09.001>
702. Sumnall HR, Measham F, Brandt SD, Cole JC. Salvia divinorum use and phenomenology: results from an online survey. *J Psychopharmacol* 2011;**25**:1496–507. <https://doi.org/10.1177/0269881110385596>
703. Stanisiz J, Terry J, Zeidler J, Issenman R, Brill H. Unexplained ascites in an adolescent female: possible association with excessive ingestion of methylone. *Can J Gastroenterol Hepatol* 2016;**2016**:4792898.
704. Stanley JL, Mogford DV, Lawrence RJ, Lawrie SM. Use of novel psychoactive substances by inpatients on general adult psychiatric wards. *BMJ Open* 2016;**6**:e009430. <https://doi.org/10.1136/bmjopen-2015-009430>
705. Stevens A, Fortson R, Measham F, Sumnall H. Legally flawed, scientifically problematic, potentially harmful: the UK Psychoactive Substance Bill. *Int J Drug Policy* 2015;**26**:1167–70. <https://doi.org/10.1016/j.drugpo.2015.10.005>
706. Stich R, Geith S, Romanek K, Asfalk V, Eyer F. Pneumomediastinum after intentional injection of MDPV and cannabinoids into the jugular vein. *Clin Toxicol* 2016;**54**:486.
707. Stogner JM, Khey DN, Agnich LE, Miller BL. They were getting high on what? Evaluating novel psychoactive drug knowledge among practitioners. *Am J Crim Justice* 2016;**41**:97–111. <https://doi.org/10.1007/s12103-015-9327-1>
708. Sutherland R, Peacock A, Whittaker E, Roxburgh A, Lenton S, Matthews A, *et al.* New psychoactive substance use among regular psychostimulant users in Australia, 2010–2015. *Drug Alcohol Depend* 2016;**161**:110–18. <https://doi.org/10.1016/j.drugalcdep.2016.01.024>
709. Sweeney B, Talebi S, Toro D, Gonzalez K, Menoscal JP, Shaw R, Hassen GW. Hyperthermia and severe rhabdomyolysis from synthetic cannabinoids. *Am J Emerg Med* 2016;**34**:121.e1–2. <https://doi.org/10.1016/j.ajem.2015.05.052>
710. Tait RJ, Caldicott D, Mountain D, Hill SL, Lenton S. A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment. *Clin Toxicol* 2016;**54**:1–13. <https://doi.org/10.3109/15563650.2015.1110590>

711. Takase I, Koizumi T, Fujimoto I, Yanai A, Fujimiya T. An autopsy case of acetyl fentanyl intoxication caused by insufflation of 'designer drugs'. *Leg Med* 2016;**21**:38–44. <https://doi.org/10.1016/j.legalmed.2016.05.006>
712. Sun HQ, Bao YP, Zhou SJ, Meng SQ, Lu L. The new pattern of drug abuse in China. *Curr Opin Psychiatry* 2014;**27**:251–5. <https://doi.org/10.1097/YCO.0000000000000073>
713. Sun X, Dey SK. Synthetic cannabinoids and potential reproductive consequences. *Life Sci* 2014;**97**:72–7. <https://doi.org/10.1016/j.lfs.2013.06.018>
714. Suzuki J, Dekker MA, Valenti ES, Arbelo Cruz FA, Correa AM, Poklis JL, *et al.* Toxicities associated with NBOMe ingestion – a novel class of potent hallucinogens: a review of the literature. *Psychosomatics* 2015;**56**:129–39. <https://doi.org/10.1016/j.psych.2014.11.002>
715. Sykutera M, Cychowska M, Bloch-Boguslawska E. A fatal case of pentedrone and α -Pyrrolidinovalerophenone poisoning. *J Anal Toxicol* 2015;**39**:324–9. <https://doi.org/10.1093/jat/bkv011>
716. Szily E, Bitter I. Designer drugs in psychiatric practice – a review of the literature and the recent situation in Hungary. *Neuropsychopharmacol Hung* 2013;**15**:223–31.
717. Takematsu M, Hoffman RS, Nelson LS, Schechter JM, Moran JH, Wiener SW. 'WTF': a case of acute cerebral ischemia following synthetic cannabinoid inhalation. *Clin Toxicol (Phila)* 2014;**52**:973–5. <https://doi.org/10.3109/15563650.2014.958614>
718. Tang MH, Ching CK, Tsui MS, Chu FK, Mak TW. Two cases of severe intoxication associated with analytically confirmed use of the novel psychoactive substances 25B-NBOMe and 25C-NBOMe. *Clin Toxicol (Phila)* 2014;**52**:561–5. <https://doi.org/10.3109/15563650.2014.909932>
719. Tarján A, Dudás M, Gyarmathy VA, Rusvai E, Tresó B, Csohán Á. emerging risks due to new injecting patterns in Hungary during austerity times. *Subst Use Misuse* 2015;**50**:848–58. <https://doi.org/10.3109/10826084.2015.978672>
720. Tekulve K, Alexander A, Tormoehlen L. Seizures associated with synthetic cathinone exposures in the pediatric population. *Pediatr Neurol* 2014;**51**:67–70. <https://doi.org/10.1016/j.pediatrneurol.2014.03.003>
721. Tellioglu T, Celebi F. Synthetic marijuana: a recent turmoil in substance abuse. *Bull Clin Psychopharmacol* 2014;**24**:396–404. <https://doi.org/10.5455/bcp.20141120022005>
722. Terry SM. Bath salt abuse: more than just hot water. *J Emerg Nurs* 2014;**40**:88–91. <https://doi.org/10.1016/j.jen.2013.05.013>
723. Thekkemuriyi DV, John SG, Pillai U. 'Krokodil' – a designer drug from across the Atlantic, with serious consequences. *Am J Med* 2014;**127**:e1–2. <https://doi.org/10.1016/j.amjmed.2013.09.030>
724. Theron L, Jansen K, Miles J. Benzylpiperazine-based party pills' impact on the Auckland City Hospital Emergency Department Overdose Database (2002–2004) compared with ecstasy (MDMA or methylene dioxymethamphetamine), gamma hydroxybutyrate (GHB), amphetamines, cocaine, and alcohol. *N Z Med J* 2007;**120**:U2416.
725. Thomas S, Bliss S, Malik M. Suicidal ideation and self-harm following K2 use. *J Okla State Med Assoc* 2012;**105**:430–3.
726. Thornton MD, Baum CR. Bath salts and other emerging toxins. *Pediatr Emerg Care* 2014;**30**:47–52. <https://doi.org/10.1097/PEC.0000000000000069>
727. Thornton SL, Akpunonu P, Glauner K, Hoehn KS, Gerona R. Unintentional pediatric exposure to a synthetic cannabinoid (AB-PINACA) resulting in coma and intubation. *Ann Emerg Med* 2015;**66**:343–4. <https://doi.org/10.1016/j.annemergmed.2015.05.021>

728. Thornton SL, Gerona RR, Tomaszewski CA. Psychosis from a bath salt product containing flephedrone and MDPV with serum, urine, and product quantification. *J Med Toxicol* 2012;**8**:310–13. <https://doi.org/10.1007/s13181-012-0232-4>
729. Thornton SL, Lo J, Clark RF, Wu AH, Gerona RR. Simultaneous detection of multiple designer drugs in serum, urine, and CSF in a patient with prolonged psychosis. *Clin Toxicol* 2012;**50**:1165–8. <https://doi.org/10.3109/15563650.2012.744996>
730. Thornton SL, Wood C, Friesen MW, Gerona RR. Synthetic cannabinoid use associated with acute kidney injury. *Clin Toxicol* 2013;**51**:189–90. <https://doi.org/10.3109/15563650.2013.770870>
731. Toescu SM. Mephedrone: when science and policy fell out. *Ment Health Subst Use* 2012;**5**:197–205. <https://doi.org/10.1080/17523281.2012.679293>
732. Tofighi B, Lee JD. Internet highs – seizures after consumption of synthetic cannabinoids purchased online. *J Addict Med* 2012;**6**:240–1. <https://doi.org/10.1097/ADM.0b013e3182619004>
733. Topeff JM, Ellsworth H, Willhite LA, Bangh SA, Edwards EM, Cole JB. A case series of symptomatic patients, including one fatality, following 2C-E exposure. *Clin Toxicol* 2011;**49**:526.
734. Torrance H, Cooper G. The detection of mephedrone (4-methylmethcathinone) in 4 fatalities in Scotland. *Forensic Sci Int* 2010;**202**:e62–3. <https://doi.org/10.1016/j.forsciint.2010.07.014>
735. Toth AR, Kovacs K, Arok Z, Varga T, Kereszty E, Institoris L. The role of stimulant designer drug consumption in three fatal cases in south-east Hungary in 2011. *Rom J Leg Med* 2013;**21**:275–80. <https://doi.org/10.4323/rjlm.2013.275>
736. Trecki J, Gerona RR, Schwartz MD. Synthetic cannabinoid-related illnesses and deaths. *N Engl J Med* 2015;**373**:103–7. <https://doi.org/10.1056/NEJMp1505328>
737. Troy JD. New ‘legal’ highs: kratom and methoxetamine. *Current Psychiatry* 2013;**12**:E1–2.
738. Tse R, Kodur S, Squires B, Collins N. Sudden cardiac death complicating acute myocardial infarction following synthetic cannabinoid use. *Intern Med J* 2014;**44**:934–6. <https://doi.org/10.1111/imj.12521>
739. Tung CK, Chiang TP, Lam M. Acute mental disturbance caused by synthetic cannabinoid: a potential emerging substance of abuse in Hong Kong. *East Asian Arch Psychiatry* 2012;**22**:31–3.
740. Turcant A, Boels D, Helfer AG, Ferec S, Bretaudeau-Deguigne M, Lelièvre B, et al. Acute combined poisoning with the new designer drug 4-methyl-N-ethyl- cathinone (4-MEC) and gammabutyrolactone (GBL): a case report with different analytical approaches for identification of some metabolites. *Toxicologie Analytique et Clinique* 2014;**26**:119–27. <https://doi.org/10.1016/j.toxac.2014.07.001>
741. Thurtle N, Dargan PI, Hunter LJ, Lovett C, White JA, Wood DM. A comparison of recreational drug use amongst sexual health clinic users in London with existing prevalence data. *Int J STD AIDS* 2016;**27**:1309–16. <https://doi.org/10.1177/0956462415616056>
742. Togari T, Inoue Y, Takaku Y, Abe S, Hosokawa R, Itagaki T, et al. Recreational drug use and related social factors among HIV-positive men in Japan. *AIDS Care* 2016;**28**:932–40. <https://doi.org/10.1080/09540121.2016.1140888>
743. Tscharke BJ, Chen C, Gerber JP, White JM. Temporal trends in drug use in Adelaide, South Australia by wastewater analysis. *Sci Total Environ* 2016;**565**:384–91. <https://doi.org/10.1016/j.scitotenv.2016.04.183>
744. Tuv SS, Bergh MS, Vindenes V, Karinen R. Methiopropamine in blood samples from drivers suspected of being under the influence of drugs. *Traffic Inj Prev* 2016;**17**:1–4. <https://doi.org/10.1080/15389588.2015.1036157>

745. Tyndall JA, Gerona R, De Portu G, Trecki J, Elie MC, Lucas J, *et al.* An outbreak of acute delirium from exposure to the synthetic cannabinoid AB-CHMINACA. *Clin Toxicol* 2015;**53**:950–6. <https://doi.org/10.3109/15563650.2015.1100306>
746. Tyrkkö E, Andersson M, Kronstrand R. The toxicology of new psychoactive substances: synthetic cathinones and phenylethylamines. *Ther Drug Monit* 2016;**38**:190–216. <https://doi.org/10.1097/FTD.0000000000000263>
747. Umebachi R, Aoki H, Sugita M, Taira T, Wakai S, Saito T, *et al.* Clinical characteristics of alpha-pyrrolidinovalerophenone (alpha-PVP) poisoning. *Clin Toxicol (Phila)* 2016;**54**:563–7. <https://doi.org/10.3109/15563650.2016.1166508>
748. Tuv SS, Krabseth H, Karinen R, Olsen KM, Oiestad EL, Vindenes V. Prevalence of synthetic cannabinoids in blood samples from Norwegian drivers suspected of impaired driving during a seven weeks period. *Accid Anal Prev* 2014;**62**:26–31. <https://doi.org/10.1016/j.aap.2013.09.009>
749. Ukaigwe A, Karmacharya P, Donato A. A gut gone to pot: a case of cannabinoid hyperemesis syndrome due to K2, a synthetic cannabinoid. *Case Rep Emerg Med* 2014;**2014**:167098. <https://doi.org/10.1155/2014/167098>
750. Umemura Y, Andrew T, Jacobs V, Giustini A, Lewis L, Hanowell J, *et al.* Fatal outcome of status epilepticus, hyperthermia, rhabdomyolysis, multi-organ failure, and cerebral edema after 25I-NBOMe ingestion. *Neurology* 2014;**82**:P1.342. www.neurology.org/content/82/10_Supplement/P1.342 (accessed 29 June 2016).
751. Uosukainen H, Tacke U, Winstock AR. Self-reported prevalence of dependence of MDMA compared to cocaine, mephedrone and ketamine among a sample of recreational poly-drug users. *Int J Drug Policy* 2015;**26**:78–83. <https://doi.org/10.1016/j.drugpo.2014.07.004>
752. Ustundag MF, Ozhan Ibis E, Yucel A, Ozcan H. Synthetic cannabis-induced mania. *Case Rep Psychiatry* 2015;**2015**:310930. <https://doi.org/10.1155/2015/310930>
753. Vakkalanka P, Hill CM, Holstege CP. Synthetic cathinones in the global media and United States poison control centers. *Clin Toxicol* 2013;**51**:694–5.
754. Valente MJ, Guedes de Pinho P, de Lourdes Bastos M, Carvalho F, Carvalho M. Khat and synthetic cathinones: a review. *Arch Toxicol* 2014;**88**:15–45. <https://doi.org/10.1007/s00204-013-1163-9>
755. van Amsterdam J, Brunt T, van den Brink W. The adverse health effects of synthetic cannabinoids with emphasis on psychosis-like effects. *J Psychopharmacol* 2015;**29**:254–63. <https://doi.org/10.1177/0269881114565142>
756. van Amsterdam J, Nutt D, van den Brink W. Generic legislation of new psychoactive drugs. *J Psychopharmacol* 2013;**27**:317–24. <https://doi.org/10.1177/0269881112474525>
757. van Amsterdam JG, Nabben T, Keiman D, Haanschoten G, Korf D. Exploring the attractiveness of new psychoactive substances (NPS) among experienced drug users. *J Psychoactive Drugs* 2015;**47**:177–81. <https://doi.org/10.1080/02791072.2015.1048840>
758. Van der Veer N, Friday J. Persistent psychosis following the use of Spice. *Schizophr Res* 2011;**130**:285–6. <https://doi.org/10.1016/j.schres.2011.04.022>
759. Van Buskirk J, Roxburgh A, Bruno R, Naicker S, Lenton S, Sutherland R, *et al.* Characterising dark net marketplace purchasers in a sample of regular psychostimulant users. *Int J Drug Policy* 2016;**35**:32–7. <https://doi.org/10.1016/j.drugpo.2016.01.010>
760. Van Hout MC. An Internet study of user's experiences of the synthetic cathinone 4-Methylethcathinone (4-MEC). *J Psychoactive Drugs* 2014;**46**:273–86. <https://doi.org/10.1080/02791072.2014.934979>

761. Van Hout MC, Brennan R. Plant food for thought: a qualitative study of mephedrone use in Ireland. *Drugs (Abingdon Engl)* 2011;**18**:371–81. <https://doi.org/10.3109/09687637.2010.537713>
762. Van Hout MC, Brennan R. 'Heads held high': an exploratory study of legal highs in pre-legislation Ireland. *J Ethn Subst Abuse* 2011;**10**:256–72. <https://doi.org/10.1080/15332640.2011.600210>
763. Van Hout MC, Brennan R. Curiosity killed M-cat: a post-legislative study on mephedrone use in Ireland. *Drugs (Abingdon Engl)* 2012;**19**:156–62. <https://doi.org/10.3109/09687637.2011.617796>
764. Van Vrancken MJ, Benavides R, Wians FH. Identification of designer drug 2C-E (4-ethyl-2, 5-dimethoxy-phenethylamine) in urine following a drug overdose. *Proc* 2013;**26**:58–61.
765. Vandrey R, Dunn KE, Fry JA, Girling ER. A survey study to characterize use of Spice products (synthetic cannabinoids). *Drug Alcohol Depend* 2012;**120**:238–41. <https://doi.org/10.1016/j.drugalcdep.2011.07.011>
766. Vandrey R, Johnson MW, Johnson PS, Khalil MA. Novel drugs of abuse: a snapshot of an evolving marketplace. *Adolesc Psychiatry* 2013;**3**:123–34. <https://doi.org/10.2174/2210676611303020003>
767. Vanna D, Dalai P, Azar A, Knohl S. Recurrent reversible kidney injury with bath salt intoxication: the agonizing memory of ecstasy. *Am J Kidney Dis* 2013;**61**:A97. <https://doi.org/10.1053/j.ajkd.2013.02.333>
768. Vardakou I, Pistos C, Spiliopoulou Ch. Spice drugs as a new trend: mode of action, identification and legislation. *Toxicol Lett* 2010;**197**:157–62. <https://doi.org/10.1016/j.toxlet.2010.06.002>
769. Vardakou I, Pistos C, Spiliopoulou Ch. Drugs for youth via Internet and the example of mephedrone. *Toxicol Lett* 2011;**201**:191–5. <https://doi.org/10.1016/j.toxlet.2010.12.014>
770. Vasile RD, Baconi D, Barca M, Ciobanu AM, Balalau C. Emergency room admission in polydrug consumers: one year survey in Romania. *Farmacía* 2013;**61**:551–7.
771. Vento AE, Martinotti G, Cinosi E, Lupi M, Acciavatti T, Carrus D, *et al*. Substance use in the club scene of Rome: a pilot study. *Biomed Res Int* 2014;**2014**:617546. <https://doi.org/10.1155/2014/617546>
772. Vevelstad M, Øiestad EL, Middelkoop G, Hasvold I, Lilleng P, Delaveris GJ, *et al*. The PMMA epidemic in Norway: comparison of fatal and non-fatal intoxications. *Forensic Sci Int* 2012;**219**:151–7. <https://doi.org/10.1016/j.forsciint.2011.12.014>
773. Vohra R, Seefeld A, Cantrell FL, Clark RF. Salvia divinorum: exposures reported to a statewide poison control system over 10 years. *J Emerg Med* 2011;**40**:643–50. <https://doi.org/10.1016/j.jemermed.2009.05.019>
774. Vorce SP, Knittel JL, Holler JM, Magluilo J, Levine B, Berran P, Bosy TZ. A fatality involving AH-7921. *J Anal Toxicol* 2014;**38**:226–30. <https://doi.org/10.1093/jat/bku011>
775. Wagner KD, Armenta RF, Roth AM, Maxwell JC, Cuevas-Mota J, Garfein RS. Use of synthetic cathinones and cannabimimetics among injection drug users in San Diego, California. *Drug Alcohol Depend* 2014;**141**:99–106. <https://doi.org/10.1016/j.drugalcdep.2014.05.007>
776. Wahl M, Theobald J. Synthetic drugs smoked out: outcome of a unique public health partnership. *Clin Toxicol* 2013;**51**:700–1.
777. Wakeman S. *For an Embodied Sociology of Drug Use: Mephedrone and 'Corporeal Pleasure'*. Chester: University of Chester Press; 2013.
778. Walker D, Neighbors C, Walton T, Pierce A, Mbilinyi L, Kaysen D, Roffman R. Spicing up the military: use and effects of synthetic cannabis in substance abusing army personnel. *Addict Behav* 2014;**39**:1139–44. <https://doi.org/10.1016/j.addbeh.2014.02.018>

779. Walterscheid JP, Phillips GT, Lopez AE, Gonsoulin ML, Chen HH, Sanchez LA. Pathological findings in 2 cases of fatal 25I-NBOMe toxicity. *Am J Forensic Med Pathol* 2014;**35**:20–5. <https://doi.org/10.1097/PAF.0000000000000082>
780. Warrick B, Hill M, Lehr B, Mowry J, Gummin D, Anderson D, et al. A review of bath salt exposures reported to six regional poison centers. *Clin Toxicol* 2011;**49**:567.
781. Warrick BJ, Hill M, Hekman K, Christensen R, Goetz R, Casavant MJ, et al. A 9-state analysis of designer stimulant, 'bath salt,' hospital visits reported to poison control centers. *Ann Emerg Med* 2013;**62**:244–51. <https://doi.org/10.1016/j.annemergmed.2012.12.017>
782. Von Der Haar J, Talebi S, Ghobadi F, Singh S, Chirurji R, Rajeswari P, et al. Synthetic cannabinoids and their effects on the cardiovascular system. *J Emerg Med* 2016;**50**:258–62. <https://doi.org/10.1016/j.jemermed.2015.10.009>
783. Waugh J, Najafi J, Hawkins L, Hill SL, Eddleston M, Vale JA, et al. Epidemiology and clinical features of toxicity following recreational use of synthetic cannabinoid receptor agonists: a report from the United Kingdom National Poisons Information Service. *Clin Toxicol (Phila)* 2016;**54**:512–18. <https://doi.org/10.3109/15563650.2016.1171329>
784. Welter-Luedeke J, Maurer HH. New psychoactive substances: chemistry, pharmacology, metabolism, and detectability of amphetamine derivatives with modified ring systems. *Ther Drug Monit* 2016;**38**:4–11. <https://doi.org/10.1097/FTD.0000000000000240>
785. Westin AA, Frost J, Brede WR, Gundersen PO, Einvik S, Aarset H, Slørdal L. Sudden cardiac death following use of the synthetic cannabinoid MDMB-CHMICA. *J Anal Toxicol* 2016;**40**:86–7. <https://doi.org/10.1093/jat/bkv110>
786. White CM. Mephedrone and 3,4-Methylenedioxypropylvalerone (MDPV): synthetic cathinones with serious health implications. *J Clin Pharmacol* 2016;**56**:1319–25. <https://doi.org/10.1002/jcph.742>
787. Wasunna B, Thomas E, Morgan S. Development of legal highs. *J Psychiat Intensive Care* 2015;**11**:128–37. <https://doi.org/10.1017/S1742646415000011>
788. Weaver MF, Hopper JA, Gunderson EW. Designer drugs 2015: assessment and management. *Addict Sci Clin Pract* 2015;**10**:8. <https://doi.org/10.1186/s13722-015-0024-7>
789. Wells DL, Ott CA. The 'new' marijuana. *Ann Pharmacother* 2011;**45**:414–17. <https://doi.org/10.1345/aph.1P580>
790. Werner RB, Chowdhury N, Smalligan RD. When adding spice can threaten life. *J Gen Intern Med* 2013;**28**:S422.
791. Wheatley N, Thompson JP. Mephedrone – a new 'legal' online drug of abuse. Do we know anything about its safety? *Clin Toxicol* 2010;**48**:305.
792. Wieland DM, Halter MJ, Levine C. Bath salts: they are not what you think. *J Psychosoc Nurs Ment Health Serv* 2012;**50**:17–21. <https://doi.org/10.3928/02793695-20120120-01>
793. Wikström M, Thelander G, Nyström I, Kronstrand R. Two fatal intoxications with the new designer drug methedrone (4-methoxymethcathinone). *J Anal Toxicol* 2010;**34**:594–8. <https://doi.org/10.1093/jat/34.9.594>
794. Wilkins C. Recent developments with the establishment of a regulated legal market for new psychoactive substances ('legal highs') in New Zealand. *Drug Alcohol Rev* 2014;**33**:678–80. <https://doi.org/10.1111/dar.12203>
795. Wilkins C. The interim regulated legal market for NPS ('legal high') products in New Zealand: the impact of new retail restrictions and product licensing. *Drug Test Anal* 2014;**6**:868–75. <https://doi.org/10.1002/dta.1643>

796. Wilkins C, Sheridan J, Adams P, Russell B, Ram S, Newcombe D. The new psychoactive substances regime in New Zealand: a different approach to regulation. *J Psychopharmacol* 2013;**27**:584–9. <https://doi.org/10.1177/0269881113491441>
797. Wilson B, Tavakoli H, DeCecchis D, Mahadev V. Synthetic cannabinoids, synthetic cathinones, and other emerging drugs of abuse. *Psychiatric Annals* 2013;**43**:558–64. <https://doi.org/10.3928/00485713-20131206-08>
798. Wiley JL, Marusich JA, Huffman JW, Balster RL, Thomas BF. Hijacking of basic research: the case of synthetic cannabinoids. *Methods Rep RTI Press* 2011;**2011**:17971. <https://doi.org/10.3768/rtipress.2011.op.0007.1111>
799. Wilkins C, Parker K, Prasad J, Jawalkar S. Do police arrestees substitute legal highs for other drugs? *Int J Drug Policy* 2016;**31**:74–9. <https://doi.org/10.1016/j.drugpo.2016.01.006>
800. Wilkins C, Prasad J, Wong KC, Rychert M, Graydon-Guy T. An exploratory study of the health harms and utilisation of health services of frequent legal high users under the interim regulated legal high market in central Auckland. *N Z Med J* 2016;**129**:51–8.
801. Wood DM, Ceronie B, Dargan PI. Healthcare professionals are less confident in managing acute toxicity related to the use of new psychoactive substances (NPS) compared with classical recreational drugs. *QJM* 2016;**109**:527–9. <https://doi.org/10.1093/qjmed/hcv208>
802. Wood DM, Dargan PI. Using internet snapshot surveys to enhance our understanding of the availability of the novel psychoactive substance alpha-methyltryptamine (AMT). *Subst Use Misuse* 2014;**49**. <https://doi.org/10.3109/10826084.2013.808224>
803. Wood DM, Dines AM, Heyerdahl F, Yates C, Giraudon I, Paasma R, et al. Review of European-Drug Emergencies Network (Euro-DEN) training package for non-specialist workers to assess acute recreational drug and new psychoactive substance toxicity in night-time economy environments. *Drugs (Abingdon Engl)* 2016;**23**:73–7. <https://doi.org/10.3109/09687637.2015.1081379>
804. Wood DM, Dines AM, Yates C, Heyerdahl F, Giraudon I, Sedefov R, et al. Pattern of acute toxicity related to the use of the novel psychoactive substance methedrone (4-methoxymethcathinone, 4-MeOMC). *Clin Toxicol* 2016;**54**:382–3.
805. Wright TH, Harris C. Twenty-one cases involving alpha-pyrrolidinovalerophenone (α -PVP). *J Anal Toxicol* 2016;**40**:396–402. <https://doi.org/10.1093/jat/bkw029>
806. Wu LT, Woody GE, Yang C, Li JH, Blazer DG. Recent national trends in Salvia divinorum use and substance-use disorders among recent and former Salvia divinorum users compared with nonusers. *Subst Abuse Rehabil* 2011;**2011**:53–68. <https://doi.org/10.2147/SAR.S17192>
807. Wypior M, Sobieraj A, Salomon-Perzynski A, Dyrda W, Krzyżowska K, Matusiak A, et al. Are suicidal thoughts in adolescents dependent on substance abuse? *Eur Psychiatry* 2016;**33**:S606–7. <https://doi.org/10.1016/j.eurpsy.2016.01.2270>
808. Yamamoto T, Rao S, Walker C, Kicman A, Wood DM, Dargan PI. Chest pain associated with recreational use of cocaine and mephedrone: should we be asking patients about use? *Clin Toxicol* 2016;**54**:401.
809. Young MM. A rapidly changing recreational drug market: findings from the Canadian Community Epidemiology network on drug use. *Drug Alcohol Depend* 2015;**156**:e243. <https://doi.org/10.1016/j.drugalcdep.2015.07.655>
810. Young S, Shoreibah MG, Kodali S. Synthetic drug causing a real problem. *Gastroenterology* 2016;**150**:S1123. [http://dx.doi.org/10.1016/S0016-5085\(16\)33789-1](http://dx.doi.org/10.1016/S0016-5085(16)33789-1) (accessed 29 June 2016).

811. Zaleta S, Kumar P, Miller S. Chest pain, troponin rise, and ST-elevation in an adolescent boy following the use of the synthetic cannabis product K2. *Ann Pediatr Cardiol* 2016;**9**:79–81. <https://doi.org/10.4103/0974-2069.171400>
812. Zanda MT, Fadda P, Chiamulera C, Fratta W, Fattore L. Methoxetamine, a novel psychoactive substance with serious adverse pharmacological effects: a review of case reports and preclinical findings. *Behav Pharmacol* 2016;**28**:28. <https://doi.org/10.1097/fbp.0000000000000241>
813. Zarifi C, Vyas S. Spice-Y kidney failure. *Am J Kidney Dis* 2016;**67**:A117. <https://doi.org/10.1053/j.ajkd.2016.03.402>
814. Zaurova M, Hoffman RS, Vlahov D, Manini AF. Clinical effects of synthetic cannabinoid receptor agonists compared with marijuana in emergency department patients with acute drug overdose. *J Med Toxicol* 2016;**2**:2. <https://doi.org/10.1007/s13181-016-0558-4>
815. Zawilska JB, Andrzejczak D. Next generation of novel psychoactive substances on the horizon – a complex problem to face. *Drug Alcohol Depend* 2015;**157**:1–17. <https://doi.org/10.1016/j.drugalcdep.2015.09.030>
816. Zheng CY, Minniti CP, Chaitowitz MH. Sickle cell crisis complicated by synthetic cannabinoid abuse: a case report. *Hemoglobin* 2016;**40**:220–2. <https://doi.org/10.3109/03630269.2016.1149077>
817. Winder GS, Stern N, Hosanagar A. Are ‘bath salts’ the next generation of stimulant abuse? *J Subst Abuse Treat* 2013;**44**:42–5. <https://doi.org/10.1016/j.jsat.2012.02.003>
818. Winstock A, Mitcheson L, Marsden J. Mephedrone: still available and twice the price. *Lancet* 2010;**376**:1537. [https://doi.org/10.1016/S0140-6736\(10\)62021-1](https://doi.org/10.1016/S0140-6736(10)62021-1)
819. Winstock AR, Barratt MJ. Synthetic cannabis: a comparison of patterns of use and effect profile with natural cannabis in a large global sample. *Drug Alcohol Depend* 2013;**131**:106–11. <https://doi.org/10.1016/j.drugalcdep.2012.12.011>
820. Winstock AR, Mitcheson LR, Deluca P, Davey Z, Corazza O, Schifano F. Mephedrone, new kid for the chop? *Addiction* 2011;**106**:154–61. <https://doi.org/10.1111/j.1360-0443.2010.03130.x>
821. Winstock AR, Ramsey JD. Legal highs and the challenges for policy makers. *Addiction* 2010;**105**:1685–7. <https://doi.org/10.1111/j.1360-0443.2010.03163.x>
822. Wodak AD. New psychoactive substances: reducing the harm caused by untested drugs and an unregulated market. *Med J Aust* 2014;**201**:310–11. <https://doi.org/10.5694/mja14.01138>
823. Wong ML, Holt RI. The potential dangers of mephedrone in people with diabetes: a case report. *Drug Test Anal* 2011;**3**:464–5. <https://doi.org/10.1002/dta.316>
824. Woo TM, Hanley JR. ‘How high do they look?’: identification and treatment of common ingestions in adolescents. *J Pediatr Health Care* 2013;**27**:135–44. <https://doi.org/10.1016/j.pedhc.2012.12.002>
825. Wood DM, Dargan PI. Mephedrone (4-methylmethcathinone): what is new in our understanding of its use and toxicity. *Prog Neuropsychopharmacol Biol Psychiatry* 2012;**39**:227–33. <https://doi.org/10.1016/j.pnpbp.2012.04.020>
826. Wood DM, Dines AM, Heyerdahl F, Yates C, Giraudon I, Hovda KE, *et al*. The cathinones are the most commonly reported novel psychoactive substances (NPS) associated with emergency department presentations with acute drug toxicity reported to the European Drug Emergencies Network (Euro-DEN). *Clin Toxicol* 2015;**53**:355–6.
827. Wood DM, Greene SL, Dargan PI. Five-year trends in self-reported recreational drugs associated with presentation to a UK emergency department with suspected drug-related toxicity. *Eur J Emerg Med* 2013;**20**:263–7. <https://doi.org/10.1097/MEJ.0b013e3283573115>

828. Wood DM, Hill SL, Thomas SH, Dargan PI. Using poisons information service data to assess the acute harms associated with novel psychoactive substances. *Drug Test Anal* 2014;**6**:850–60. <https://doi.org/10.1002/dta.1671>
829. Wood DM, Looker JJ, Shaikh L, Button J, Puchnarewicz M, Davies S, *et al.* Delayed onset of seizures and toxicity associated with recreational use of Bromo-dragonFLY. *J Med Toxicol* 2009;**5**:226–9. <https://doi.org/10.1007/BF03178273>
830. Wood DM, Sedefov R, Cunningham A, Dargan PI. Prevalence of use and acute toxicity associated with the use of NBOMe drugs. *Clin Toxicol* 2015;**53**:85–92. <https://doi.org/10.3109/15563650.2015.1004179>
831. Wood KE. Exposure to bath salts and synthetic tetrahydrocannabinol from 2009 to 2012 in the United States. *J Pediatr* 2013;**163**:213–16. <https://doi.org/10.1016/j.jpeds.2012.12.056>
832. Wood DM, Dargan PI. Mephedrone: a novel synthetic cathinone – a case series of sympathomimetic toxicity associated with its use. *Clin Toxicol* 2010;**48**:307.
833. Wood DM, Dargan PI. Understanding how data triangulation identifies acute toxicity of novel psychoactive drugs. *J Med Toxicol* 2012;**8**:300–3. <https://doi.org/10.1007/s13181-012-0241-3>
834. Wood DM, Dargan PI. Use and acute toxicity associated with the novel psychoactive substances diphenylprolinol (D2PM) and desoxypipradrol (2-DPMP). *Clin Toxicol* 2012;**50**:727–32. <https://doi.org/10.3109/15563650.2012.716158>
835. Wood DM, Davies S, Cummins A, Button J, Holt DW, Ramsey J, *et al.* Energy-1 ('NRG-1'): don't believe what the newspapers say about it being legal. *Emerg Med J* 2011;**28**:1068–70. <https://doi.org/10.1136/emj.07.2010.3184rep>
836. Wood DM, Davies S, Greene SL, Button J, Holt DW, Ramsey J, Dargan PI. Case series of individuals with analytically confirmed acute mephedrone toxicity. *Clin Toxicol* 2010;**48**:924–7. <https://doi.org/10.3109/15563650.2010.531021>
837. Wood DM, Davies S, Puchnarewicz M, Johnston A, Dargan PI. Methoxetamine: a ketamine analogue associated with both ketamine-like dissociative effects and sympathomimetic toxicity. *Clin Toxicol* 2012;**50**:342.
838. Wood DM, Greene SL, Dargan PI. Plant food and bath salts – how harmful is mephedrone? *Clin Toxicol* 2010;**48**:616.
839. Wood DM, Greene SL, Dargan PI. Control of mephedrone (4-methylmethcathinone) in the UK appears effective in reducing presentations to the emergency department with acute toxicity related to its use. *Clin Toxicol* 2011;**49**:522–3.
840. Wood DM, Greene SL, Dargan PI. Clinical pattern of toxicity associated with the novel synthetic cathinone mephedrone. *Emerg Med J* 2011;**28**:280–2. <https://doi.org/10.1136/emj.2010.092288>
841. Wood DM, Greene SL, Dargan PI. Five-year trends in recreational drugs associated with presentation to the emergency department with acute toxicity/harm. *Clin Toxicol* 2012;**50**:342–3.
842. Wood DM, Hunter L, Measham F, Dargan PI. Limited use of novel psychoactive substances in South London nightclubs. *QJM* 2012;**105**:959–64. <https://doi.org/10.1093/qjmed/hcs107>
843. Wood DM, Measham F, Dargan PI. 'Our favourite drug': prevalence of use and preference for mephedrone in the London night-time economy 1 year after control. *J Subst Use* 2012;**17**:91–7. <https://doi.org/10.3109/14659891.2012.661025>
844. Wood DM, Puchnarewicz M, Johnston A, Dargan PI. A case series of individuals with analytically confirmed acute diphenyl-2-pyrrolidinemethanol (D2PM) toxicity. *Eur J Clin Pharmacol* 2012;**68**:349–53. <https://doi.org/10.1007/s00228-011-1142-0>

845. Wright TH, Cline-Parhamovich K, Lajoie D, Parsons L, Dunn M, Ferslew KE. Deaths involving methylenedioxypropylamphetamine (MDPV) in Upper East Tennessee. *J Forensic Sci* 2013;**58**:1558–62. <https://doi.org/10.1111/1556-4029.12260>
846. Yamamoto T, Kawsar A, Ramsey J, Collignon U, Dargan PI, Wood DM. Detection of novel psychoactive substances through analysis of recreational drug samples obtained in the emergency department. *Clin Toxicol* 2014;**52**:361–2.
847. Yamamoto T, Kawsar A, Ramsey J, Dargan PI, Wood DM. Monitoring trends in recreational drug use from the analysis of the contents of amnesty bins in gay dance clubs. *QJM* 2013;**106**:1111–17. <https://doi.org/10.1093/qjmed/hct183>
848. Yargic I. Synthetic cannabinoids: more dangerous than marijuana. *Bulletin of Clinical Psychopharmacology* 2013;**23**:S18.
849. Yeakel JK, Logan BK. Blood synthetic cannabinoid concentrations in cases of suspected impaired driving. *J Anal Toxicol* 2013;**37**:547–51. <https://doi.org/10.1093/jat/bkt065>
850. Yen M, Berger RE, Roberts J, Ganetsky M. Middle cerebral artery stroke associated with use of synthetic cannabinoid K2. *Clin Toxicol* 2012;**50**:673–4.
851. Young AC, Schwarz ES, Velez LI, Gardner M. Two cases of disseminated intravascular coagulation due to 'bath salts' resulting in fatalities, with laboratory confirmation. *Am J Emerg Med* 2013;**31**:445.e3–5. <https://doi.org/10.1016/j.ajem.2012.05.032>
852. Young MM, Dubeau C, Corazza O. Detecting a signal in the noise: monitoring the global spread of novel psychoactive substances using media and other open-source information. *Hum Psychopharmacol* 2015;**30**:319–26. <https://doi.org/10.1002/hup.2477>
853. Young MM, Dubeau C, Diedrich K, Corazza O. Detecting a signal in the noise: results of a pilot project to monitor the global spread of new drugs by monitoring media. *Drug Alcohol Depend* 2015;**146**:e29–e30. <https://doi.org/10.1016/j.drugalcdep.2014.09.760>
854. Yuhico L. Unexplained muscle breakdown: could this be yet another effect of a new designer drug? *Crit Care Med* 2012;**40**:323.
855. Zaitis K, Katagi M, Kamata T, Kamata H, Shima N, Tsuchihashi H, *et al.* Determination of a newly encountered designer drug 'p-methoxyethylamphetamine' and its metabolites in human urine and blood. *Forensic Sci Int* 2008;**177**:77–84. <https://doi.org/10.1016/j.forsciint.2007.11.001>
856. Zaldivar F, Lopez F, Garcia-Montes JM, Molina A. Self-reported consumption of alcohol and other drugs in a Spanish university population. *Elec J Res Educ Psychol* 2011;**9**:113–31.
857. Zamengo L, Frison G, Bettin C, Sciarrone R. Understanding the risks associated with the use of new psychoactive substances (NPS): high variability of active ingredients concentration, mislabelled preparations, multiple psychoactive substances in single products. *Toxicol Lett* 2014;**229**:220–8. <https://doi.org/10.1016/j.toxlet.2014.06.012>
858. Zawilska JB. 'Legal highs' – new players in the old drama. *Curr Drug Abuse Rev* 2011;**4**:122–30. <https://doi.org/10.2174/1874473711104020122>
859. Zawilska JB. 'Legal highs' – an emerging epidemic of novel psychoactive substances. *Int Rev Neurobiol* 2015;**120**:273–300. <https://doi.org/10.1016/bs.irm.2015.02.009>
860. Zawilska JB, Wojcieszak J. Designer cathinones – an emerging class of novel recreational drugs. *Forensic Sci Int* 2013;**231**:42–53. <https://doi.org/10.1016/j.forsciint.2013.04.015>
861. Zawilska JB, Wojcieszak J. Spice/K2 drugs – more than innocent substitutes for marijuana. *Int J Neuropsychopharmacol* 2014;**17**:509–25. <https://doi.org/10.1017/S1461145713001247>

862. Zimmermann US, Winkelmann PR, Pilhatsch M, Nees JA, Spanagel R, Schulz K. Withdrawal phenomena and dependence syndrome after the consumption of 'spice gold'. *Dtsch Arztebl Int* 2009; **106**:464–7. <https://doi.org/10.3238/arztebl.2009.0464>
863. Legal Highs UK. *UK Legal Highs Forum*. URL: legalhighsforum.com (accessed 29 June 2016).
864. Bluelight. *Bluelight*. URL: <http://bluelight.org/vb/content/?s=2ef95547c5bf7c4f121e6aacca61dbfe> (accessed 29 June 2016).
865. Peterfi A, Major M, Dunay MA, Horvarth GCH. *NPS Users in Drug Rehabilitation Services*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
866. Phoenix Futures. 'Use Your Head, Don't Lose It!' *How Phoenix Futures is Tackling NPS in Prisons*. London: Phoenix Futures URL: [www.phoenix-futures.org.uk/sites/default/files/files/How%20Phoenix%20is%20tackling%20NPS%20in%20Prisons\(1\).pdf](http://www.phoenix-futures.org.uk/sites/default/files/files/How%20Phoenix%20is%20tackling%20NPS%20in%20Prisons(1).pdf) (accessed 29 June 2016).
867. Public Health Wales. *Harm Reduction Database Wales: Needle and Syringe Provision 2014–2015*. Cardiff: Public Health Wales; 2015.
868. Prilutskaya M. *Impact of Novel Psychoactive Substance on Opioid Withdrawal Duration*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
869. Public Health England. *Adult Substance Misuse Statistics from the National Drug Treatment Monitoring System (NDTMS): 1 April 2014 to 31 March 2015*. London: Public Health England; 2015.
870. Public Health England. *New Psychoactive Substances: A Toolkit for Substance Misuse Commissioners*. London: Public Health England; 2014.
871. Public Health Action Support Team. *New Psychoactive Substances 'Legal Highs'*. Suffolk, VA: Suffolk City Council; 2015.
872. Public Health Wales. *PHILTRE Annual Report 2014–2015*. Cardiff: Public Health Wales; 2015.
873. Robertson L. *2012/13 Scottish Crime and Justice Survey: Drug Use*. Edinburgh: The Scottish Government; 2014.
874. Roche J, Huke V. *Novel Psychoactive Substance Use, Prescription Drug Abuse and Internet Drug Purchasing in Eating Disorders*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
875. Abdulrahim D, Bowden-Jones O, NEPTUNE. *Guidance on the Clinical Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances*. London: NEPTUNE; 2015.
876. Baker S. *An Examination of the Reasons That Prisoners Use Spice (Synthetic Cannabinoids)*. Cambridge: University of Cambridge; 2015.
877. Barber S. *The Psychoactive Substances Bill 2015*. London: House of Commons Library; 2015.
878. Barnsdale L, Gordon R, Graham L, Walker D, Elliott V, Graham B. *The National Drug-Related Deaths Database (Scotland) Report: Analysis of Deaths Occurring In 2014*. Edinburgh: Information Services Division and NHS National Service Scotland; 2016.
879. Barnsdale L, Gordon R, McAuley A. *The National Drug-Related Deaths Database (Scotland) Report: Analysis of Deaths Occurring in 2013*. Edinburgh: Information Services Division and NHS National Services Scotland; 2015.
880. Benjamin DM. *Synthetic Cannabinoids Cause Adverse Neuropsychiatric Symptoms Via 5-Ht2a Receptors*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.

881. Bourne A, Reid D, Hickson F, Torres-Rueda S, Steinberg P, Weatherburn P. 'Chemsex' and harm reduction need among gay men in South London. *Int J Drug Policy* 2015;**26**:1171–6. <https://doi.org/10.1016/j.drugpo.2015.07.013>
882. Bowden-Jones O, Fitch C, Hilton C, Lewis J, Ofori-Attah G. *One New Drug a Week: Why Novel Psychoactive Substances and Club Drugs Need a Different Response from UK Treatment Providers*. London: Faculty of Addictions Psychiatry, Royal College of Psychiatrists; 2014.
883. Brennan R, Van Hout MC. Miaow miaow: a review of the new psychoactive drug mephedrone. *Drugs Alcohol Today* 2012;**12**:241–53. <https://doi.org/10.1108/17459261211286654>
884. Brookman F. *The Links Between Mephedrone Use, Violence and Other Harms in South Wales*. Pontypridd: Centre for Criminology, University of South Wales; 2014.
885. Brunt T, Niesnik RJM. *Popularity of Legal Highs Depends on the National Illicit Drug Market Situation*. Amsterdam: Drug Information and Monitoring System, Netherlands Institute of Mental Health and Addiction; 2012.
886. Van Hout MC, Bingham T. 'A costly turn on': patterns of use and perceived consequences of mephedrone based head shop products amongst Irish injectors. *Int J Drug Policy* 2012;**23**:188–97. <https://doi.org/10.1016/j.drugpo.2012.01.008>
887. Bersani G. *NPS-Induced Changes in the Phenomenology Of Psychiatric Disorders*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.
888. Calzada JN, Hernandez RR, Cebollada SD, Murillo EC, Guillen SM, Dufol AF. *Acute Poisoning by DOC (2,5-dimethoxy- 4-chloroamphetamine): Report of 6 Cases Presenting Together at the Emergency Department*. 35th International Congress of the European Association of Poisons Centres and Clinical Toxicologists, EAPCCT 2015 St Julian's Malta, 2015.
889. Centers for Disease Control and Prevention. Notes from the field: increase in reported adverse health effects related to synthetic cannabinoid use – United States, January–May 2015. *MMWR Surveill Summ* 2015;**64**:618–19.
890. Centre for Social Justice. *Drugs in Prison*. London: Centre for Social Justice; 2015.
891. Changing Lives. *Novel Psychoactive Substance Use Amongst Clients Accessing Changing Lives Services in Newcastle upon Tyne*. Newcastle upon Tyne: Changing Lives; 2014.
892. Chiappini S, Claridge H, Corkery JM, Goodair C, Loi B, Schifano F. *Methoxetamine-Related Deaths in the UK: An Overview*. London: International Centre for Drug Policy, St George's, University of London; 2015.
893. Chung H, Lee J, Kim E. Trends of novel psychoactive substances and their fatal cases. *Forensic Toxicol* 2016;**34**:1–11. <https://doi.org/10.1007/s11419-015-0286-5>
894. Claridge H, Goodair C. *Drug-Related Deaths in England, Northern Ireland, the Channel Islands and the Isle of Man: January–December 2013*. London: St George's, University of London; 2015.
895. Corazza O, Assi S, Schifano F. From 'Special K' to 'Special M': the evolution of the recreational use of ketamine and methoxetamine. *CNS Neurosci Ther* 2013;**19**:454–60. <https://doi.org/10.1111/cns.12063>
896. Corazza O, Assi S, Trincas G, Trincas G, Simonat, P-L, Davey Z, et al. Novel drugs, novel solutions: exploring the potential of technological tools for prevention of drug abuse. *Italian J Addict* 2011;**1**:25–30.
897. Craig CL, Loeffler GH. The ketamine analog methoxetamine: a new designer drug to threaten military readiness. *Mil Med* 2014;**179**:1149–57. <https://doi.org/10.7205/MILMED-D-13-00470>
898. CREW. *NPS at CREW Annual Report*. Edinburgh: CREW; 2016.

899. Csorba J. *Mapping of the New Psychoactive Substances*. The International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
900. D'Agostino T. *Service User Consultation, Mephedrone Manual and Off the Concrete*. London: TD Consultancy. URL: <http://tonydagostino.co.uk> (accessed 29 June 2016).
901. Davey Z. *Mephedrone: Exploring Reasons for Use and User Typologies Using a Mixed Methods Approach*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
902. Davey Z, Schifano F, Corazza O, Deluca P, Psychonaut Web Mapping Group. e-Psychonauts: conducting research in online drug forum communities. *J Ment Health* 2012;**21**:386–94. <https://doi.org/10.3109/09638237.2012.682265>
903. Demetrovics Z, Kapitany-Foveny M. *NPS in Hungary: A Historical Overview*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
904. Department of Health Northern Ireland. *All Ireland Drug Prevalence Survey 2014/15*. Belfast: Department of Health Northern Ireland; 2015.
905. DrugScope. *Not for Human Consumption: An Update and Amended Status Report on New Psychoactive Substances and Club Drugs in the UK 2015*. URL: www.drugwise.org.uk/wp-content/uploads/not-for-human-consumption.pdf (accessed 29 June 2016).
906. EMCDDA. *2014 National report (2013 data) to the EMCDDA by the REitox National Focal Point: United Kingdom New Developments and Trends*. London: EMCDDA; 2014.
907. EMCDDA. *Perspectives on Drugs: Synthetic Cannabinoids in Europe*. Lisbon: EMCDDA; 2015.
908. EMCDDA. *Perspectives on Drugs: Injection of Synthetic Cathinones*. Lisbon: EMCDDA; 2015.
909. EMCDDA. *New Psychoactive Substances in Europe: An Update from the EU Early Warning System March 2015*. Lisbon: EMCDDA; 2015.
910. EMCDDA. *Perspectives on Drugs: Legal Approaches to Controlling New Psychoactive Substances*. Lisbon: EMCDDA; 2015.
911. EMCDDA. *EU Drug Market Report: An In-Depth Analysis*. Lisbon: EMCDDA; 2016.
912. EMCDDA. *Health Responses to New Psychoactive Substances*. Lisbon: EMCDDA; 2016.
913. erowid.org. *EROWID: Documenting the Complex Relationship Between Humans and Psychoactives*. URL: www.erowid.org/ (accessed 29 June 2016).
914. Europe Against Drugs (EURAD). *Novel Psychoactive Substances: Issues for Policy Makers*. Brussels: EURAD; 2012.
915. European Commission. *Young People and Drugs Report*. Brussels: European Commission; 2014.
916. Farré M, Papaseit E, Pérez-Mañá C, Pujadas M, Fonseca F, Torrens M, et al. *Human Pharmacology of Mephedrone: A Dose-Finding Pilot Study*. Washington, DC: National Institute on Drug Abuse; 2014. URL: www.drugabuse.gov/international/abstracts/human-pharmacology-mephedrone-dose-finding-pilot-study (accessed 29 June 2016).
917. Farré M, Pérez-Mañá C, Mateus J, Pujadas M, Fonseca F, Torrens M, et al. *Abuse Liability Evaluation of Mephedrone in Humans*. Washington, DC: NIDA; 2015. URL: www.drugabuse.gov/international/abstracts/abuse-liability-evaluation-mephedrone-in-humans (accessed 29 June 2016).
918. Fletcher E, Tasker S, Easton P, Denvir L. *New Psychoactive Substances Needs Assessment for Tayside, 2014*. Dundee: NHS Tayside; 2014.

919. Fraser F. *New Psychoactive Substances – Evidence Review*. Edinburgh: The Scottish Government Social Research; 2014.
920. Gilani F. Legal highs: novel psychoactive substances. *InnovAiT* 2015;**8**:717–24. <https://doi.org/10.1177/1755738015612509>
921. Gillies A. *Closing Evidence Gaps on the Prevalence and Harms of New Psychoactive Substances in Scotland*. Edinburgh: Justice Analytical Services, Scottish Government; 2015.
922. Gillies A. *Mapping Current and Potential Sources of Routine Data Capture on New Psychoactive Substances in Scotland*. Edinburgh: Justice Analytical Services, Scottish Government; 2015.
923. González D, Torrens M, Farré M. Acute effects of the novel psychoactive drug 2C-B on emotions. *Biomed Res Int* 2015;**2015**:643878. <https://doi.org/10.1155/2015/643878>
924. Grumann C, Hermanns-Clausen M, Kithinji J, Angerer V, Auwarter V. *Accidental Intoxication with 25I-NBOMe*. Freiburg: University of Freiburg; 2015.
925. HSCIC. *Smoking, Drinking, and Drug Use Among Young People in England in 2014*. London: HSCIC; 2015.
926. Hegazi A, Lee MJ, Whittaker W, Green S, Simms R, Cutts R, et al. Chemsex and the city: sexualised substance use in gay bisexual and other men who have sex with men attending sexual health clinics. *Int J STD AIDS* 2017;**28**:362–6. <https://doi.org/10.1177/0956462416651229>
927. Hermanns-Clausen M, Kneisel S, Auwarter V. *Acute Intoxications by Herbal Blends Containing Synthetic Cannabinoids*. 2012 International Congress of the European Association of Poisons Centres and Clinical Toxicologists, EAPCCT 2012, London, 2012.
928. Home Office. *New Psychoactive Substances Review: Report from the Expert Panel*. London: Home Office; 2014.
929. Home Office. *Annual Report on the Home Office Forensic Early Warning System (FEWS): A System to Identify New Psychoactive Substances (NPS) in the UK*. London: Home Office; 2015.
930. Home Office. *New Psychoactive Substances (NPS) Resource Pack for Informal Educators and Practitioners*. London: Home Office, 2015.
931. Homeless Link. *NPS/Legal Highs Survey Results*. Manchester: Homeless Link; 2016.
932. Imbert L, Boucher A, Delhome G, Cueto T, Boudinaud M, Maublanc J, et al. Analytical findings of an acute intoxication after inhalation of methoxetamine. *J Anal Toxicol* 2014;**38**:410–15. <https://doi.org/10.1093/jat/bku052>
933. Isbister GK, Poklis A, Poklis JL, Grice J. Beware of blotting paper hallucinogens: severe toxicity with NBOMes. *Med J Aust* 2015;**203**:266–7e.1.
934. Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE, Miech RA. *Monitoring the Future National Survey Results on Drug Use, 1975–2014: Volume 2, College Students and Adults Ages 19–55*. Ann Arbor, MI: Institute for Social Research, University of Michigan; 2015.
935. Johnston LD, O'Malley PM, Miech RA, Bachman JG, Schulenberg JE. *Monitoring the Future National Survey Results on Drug Use, 1975–2015: Overview, Key Findings on Adolescent Drug Use*. Ann Arbor, MI: Institute for Social Research, University of Michigan; 2016.
936. Kassai S, Racz J. *How the Users of Synthetic Cannabinoid Products Organize their Experiences? An Interpretative Phenomenological Analysis*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.
937. Kelleher C, Christie R, Lalor R, Fox J, Bowden M, O'Donnell C. *An Overview of New Psychoactive Substances and the Outlets Supplying Them*. Dublin: National Advisory Committee on Drugs; 2011.

938. Keller E. *Forensic Case of Novel Psychoactive Substances*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
939. Kihara R, Day E. Transient psychotic episodes following recreational use of NRG-3. *Progress in Neurology and Psychiatry* 2014; May/June 2014:14–18. <https://doi.org/10.1002/pnp.331>
940. McElrath K, Van Hout MC. A preference for mephedrone: drug markets, drugs of choice, and the emerging 'legal high' scene. *J Drug Issues* 2011;**41**:487–507. <https://doi.org/10.1177/002204261104100403>
941. MNCAP. *Substance Misuse Treatment – Emerging Needs Analysis*. URL: www.leicester.gov.uk/media/177757/substance-misuse-treatment-emerging-needs-analysis-june-2014.pdf (accessed 29 June 2016).
942. Moore K. *Benzodiazepines Online: Reflecting on the Contemporary Challenges for Users, the Medical Profession, and Drug Services in the UK*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.
943. Measham F, Moore K, Welch Z. *Emerging Drug Trends in Lancashire: Night Club Surveys Phase Three Report*. Lancaster: Department of Applied Social Science, Lancaster University; 2012.
944. Monteiro MS, Bastos Mde L, Guedes de Pinho P, Carvalho M. Update on 1-benzylpiperazine (BZP) party pills. *Arch Toxicol* 2013;**87**:929–47. <https://doi.org/10.1007/s00204-013-1057-x>
945. King LA. New phenethylamines in Europe. *Drug Test Anal* 2014;**6**:808–18. <https://doi.org/10.1002/dta.1570>
946. King LA. Legal controls on cannabimimetics: an international dilemma? *Drug Test Anal* 2014;**6**:80–7. <https://doi.org/10.1002/dta.1510>
947. Kjellgren A, Jonsson K. Methoxetamine (MXE) – a phenomenological study of experiences induced by a 'legal high' from the internet. *J Psychoactive Drugs* 2013;**45**:276–86. <https://doi.org/10.1080/02791072.2013.803647>
948. Knoy JL, Peterson BL, Couper FJ. Suspected impaired driving case involving α -pyrrolidinovalerophenone, methylone and ethylone. *J Anal Toxicol* 2014;**38**:615–17. <https://doi.org/10.1093/jat/bku073>
949. Kriikku P. *Novel Psychoactive Substances in Cause-of-Death Investigations*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
950. Kriikku P, Rintatalo J, Pihlainen K, Hurme J, Ojanperä I. The effect of banning MDPV on the incidence of MDPV-positive findings among users of illegal drugs and on court decisions in traffic cases in Finland. *Int J Legal Med* 2015;**129**:741–9. <https://doi.org/10.1007/s00414-015-1184-4>
951. Lally J, El-Higaya E, Nisar Z, Bainbridge E, Hallahan B. Prevalence study of head shop drug usage in mental health services. *Psychiatrist* 2013;**37**:44–8. <https://doi.org/10.1192/pb.bp.111.038315>
952. Loeffler G, Craig C. Methoxetamine misuse and toxicity. *J Stud Alcohol Drugs* 2013;**74**:816–17. <https://doi.org/10.15288/jsad.2013.74.816>
953. Logan B. *Case Reports of Designer Opioids in Postmortem Forensic Toxicology Casework*. Fourth International Conference of Novel Psychoactive Substances, Budapest, 30–31 May 2016.
954. Low L, Cheok C. *New Psychoactive Substances – High Index of Suspicion Needed in Emergency Services*. Singapore: Central Narcotics Bureau. URL: www.nams.sg/resources/info_for_healthcare_professionals/Pages/NAMS-Studies.aspx (accessed 19 June 2016).
955. Martinotti G. *Use of Novel Psychoactive Substances and Induced Psychiatric Symptoms: Outcomes from the Eivissa Project*. Fourth International Conference of Novel Psychoactive Substances, Budapest, 30–31 May 2016.

956. National Assembly of Wales. *Inquiry into New Psychoactive Substances*. Cardiff: National Assembly of Wales; 2015.
957. Center for Substance Abuse Research National Drug Early Warning System (NDEWS). *Sentinel Community Site Profiles 2015: Atlanta Metro*. College Par, MD: NDEWS Coordinating Center; 2015.
958. National Records of Scotland. *Drug-Related Deaths in Scotland in 2014*. Edinburgh: National Records of Scotland; 2016.
959. NHS Lothian Substance Misuse Directorate Harm Reduction Team. *Test for Change: New Psychoactive Substances*. Lothian: NHS Lothian Substance Misuse Directorate Harm Reduction Team; 2015.
960. NHS National Services Scotland. *Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS): Drug Use Among 13 and 15 Year Olds in Scotland 2013*. Edinburgh: NHS National Services Scotland; 2014.
961. Northamptonshire City Council. *Health and Wellbeing Children's Services Joint Strategic Needs Assessment of Children and Young People in Northamptonshire*. Northampton: Northamptonshire City Council; 2016.
962. Brighton and Hove City Council. Not specified. *Brighton and Hove: NPS/Legal High/Club Drugs Information Sources*. Brighton and Hove: Brighton and Hove City Council; 2016.
963. Office for National Statistics. *Drug Misuse: Findings from the 2014/15 Crime Survey for England and Wales*. London: Office for National Statistics; 2015.
964. Office for National Statistics. *Deaths Related to Drug Poisoning in England and Wales: 2014 Registrations*. London: Office for National Statistics; 2015.
965. Office for National Statistics. *Deaths Involving Legal Highs in England and Wales: Between 2004 and 2013*. London: Office for National Statistics; 2016.
966. Paksi B. *The Prevalence of New Psychoactive Substances in Hungary – Based on a General Population Survey Dealing with Addiction Related Problems (OLAAP 2015)*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
967. Papaseit E, Perez-Mana C, Menoyo E, Perez M, Gibert C, Pujadas M, et al. Pharmacology of mephedrone in humans: a pilot dose-finding study. *Basic Clin Pharmacol Toxicol* 2013;**113**:19.
968. Sacco LN, Finklea K. *Synthetic Drugs: Overview and Issues For Congress*. Washington, DC: Congressional Research Service; 2016.
969. Substance Abuse and Mental Health Services Administration (SAMHSA). *The Dawn Report: Drug-related Emergency Department Visits Involving Synthetic Cannabinoids*. Rockville, MD: SAMHSA; 2012.
970. Substance Abuse and Mental Health Services Administration (SAMHSA). *Spice, Bath Salts, and Behavioral Health*. Rockville, MD: SAMHSA; 2014.
971. Sami M, Piggott K, Coysh C, Fialho A. Psychosis, psychedelic substance misuse and head injury: a case report and 23 year follow-up. *Brain injury* 2015;**29**:1383–6. <https://doi.org/10.3109/02699052.2015.1046491>
972. Santacroce R. *Living Limitless: Knowledge and Use of Cognitive Enhancers in a Sample of University Students In Italy*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
973. Sedefov R, Griffiths P. *How NPS Changed the Way we Understand and Respond to Drugs?* Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.

974. Deligianni E. *Global Survey on the Preference and Use of Ketamine and Novel Psychoactive Substances (NPS)*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
975. Shafi A, Gallagher P, Stewart N. *Psychoactive Substances and Mental Health Services: The Unknown Unknowns*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.
976. Sheridan J, Dong CY, Butler R, Barnes J. The impact of New Zealand's 2008 prohibition of piperazine-based party pills on young people's substance use: results of a longitudinal, web-based study. *Int J Drug Policy* 2013;**24**:412–22. <https://doi.org/10.1016/j.drugpo.2013.02.002>
977. Simonato P. *NPS and Psychopathology: Novel Compounds and Patients*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
978. Smyth BP, James P, Cullen W, Darker C. 'So prohibition can work?' Changes in use of novel psychoactive substances among adolescents attending a drug and alcohol treatment service following a legislative ban. *Int J Drug Policy* 2015;**26**:887–9. <https://doi.org/10.1016/j.drugpo.2015.05.021>
979. Stephenson G, Richardson A. *New Psychoactive Substances in England: A Review of the Evidence*. London: Home Office; 2014.
980. Tarjan A. *Impact of Increasing NPS Injecting Combined with Weakening Responses: Infections and Risk Behaviours*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
981. Tettey J, Crean C. New psychoactive substances: catalysing a shift in forensic science practice? *Philos Trans R Soc Lond, B, Biol Sci* 2015;**370**:20140265. <https://doi.org/10.1098/rstb.2014.0265>
982. United Nations Office on Drugs and Crime. *The Challenge of New Psychoactive Substances*. Vienna: United Nations Office on Drugs and Crime; 2013.
983. United Nations Office on Drugs and Crime. *NPS Emergence, Challenges and Trends – The Global Perspective*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
984. United Nations Office on Drugs and Crime. *2014 Global Synthetic Drugs Assessment: Amphetamine-Type Stimulants and New Psychoactive Substances*. Vienna: United Nations Office on Drugs and Crime; 2014.
985. Van Hout MC, Hearne E. 'Word of mouse': indigenous harm reduction and online consumerism of the synthetic compound methoxphenidine. *J Psychoactive Drugs* 2015;**47**:30–41. <https://doi.org/10.1080/02791072.2014.974002>
986. Van Hout MC, Brennan R. 'Bump and grind': an exploratory study of mephedrone users' perceptions of sexuality and sexual risk. *Drugs and Alcohol Today* 2011;**11**:93–103. <https://doi.org/10.1108/17459261111174046>
987. Van Hout MC, Hearne E. 'Plant or poison': a netnographic study of recreational use of 1,3-dimethylamylamine (DMAA). *Int J Drug Policy* 2015;**26**:1279–81. <https://doi.org/10.1016/j.drugpo.2015.04.002>
988. Van Hout MC, Hearne E. User experiences of development of dependence on the synthetic cannabinoids, 5f-AKB48 and 5f-PB-22, and subsequent withdrawal syndromes. *Int J Ment Health Addict* 2016:1–15. <https://doi.org/10.1007/s11469-016-9650-x>
989. Van Hout MC, Hearne E. *A Phenomenological Study of Dependent User Experiences of Withdrawal from Herbal Smoking Mixtures*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.

990. Van Hout MC, Bingham T. 'Surfing the Silk Road': a study of users' experiences. *Int J Drug Policy* 2013;**24**:524–9. <https://doi.org/10.1016/j.drugpo.2013.08.011>
991. Van Hout MC, Bingham T. 'Silk Road', the virtual drug marketplace: a single case study of user experiences. *Int J Drug Policy* 2013;**24**:385–91. <https://doi.org/10.1016/j.drugpo.2013.01.005>
992. Wallis L. *Diffusion of New Psychoactive Substances: Understanding Population Motives, Harms and Intervention Needs*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.
993. Weinstein A. *The Effects of Synthetic Cannabinoids on Executive Function and Related Brain Activity in fMRI*. Fourth International Conference on Novel Psychoactive Substances, Budapest, 30–31 May 2016.
994. Werse B. *Stoners 2.0 and Experimental Psychonauts – An Online Survey on Legal Highs Use in Germany*. Frankfurt: Goethe-Universität Frankfurt am Main; 2012.
995. Werse B. *Risks and Harms of NPS from the User's Perspective and Regional Differences in Prevalence: Social Research Results from Germany*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.
996. Wikström M, Thelander G, Dahlgren M, Kronstrand R. An accidental fatal intoxication with methoxetamine. *J Anal Toxicol* 2013;**37**:43–6. <https://doi.org/10.1093/jat/bks086>
997. Wilkins C, Sweetsur P. The impact of the prohibition of benzylpiperazine (BZP) 'legal highs' on the prevalence of BZP, new legal highs and other drug use in New Zealand. *Drug Alcohol Depend* 2013;**127**:72–80. <https://doi.org/10.1016/j.drugalcdep.2012.06.014>
998. Wilkins C. *Did the Legal Market for Synthetic Cannabinoids Displace the Illegal Market for Cannabid in New Zealand*. Fourth International Conference on Novel Psychoactive Substance, Budapest, 30–31 May 2016.
999. Williams MM, Taylor PJ, Page CB, Martin JH. Clinical research in synthetic cannabinoids – do we need a national approach? *Med J Aust* 2014;**201**:317–9. <https://doi.org/10.5694/mja13.11020>
1000. Winstock A, Wilkins C. *Legal Highs: The Challenge of New Psychoactive Substances*. London: International Drug Policy Consortium; 2011.
1001. Winstock AR, Lawn W, Deluca P, Borschmann R. Methoxetamine: an early report on the motivations for use, effect profile and prevalence of use in a UK clubbing sample. *Drug Alcohol Rev* 2016;**35**:212–7. <https://doi.org/10.1111/dar.12259>
1002. Wish ED, Billing AS, Artigiani EE. *Community Drug Early Warning System: The CDEWS-2 Replication Study*. Washington, DC: Office of National Drug Control Policy; 2015.
1003. Wiszejko-Wierzbička D. *Typology and Motives of Use of New Psychoactive Substances Based on Survey and Online Forum Analysis Within the Project I-TREND*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.
1004. Wood DM, Measham F, Dargan PI. Was controlling methoxetamine under the UK temporary class drug order legislation effective in reducing its use in a high-drug using population? *Clin Toxicol* 2013;**51**:663–4.
1005. Worcestershire Health and Wellbeing Board. *Worcestershire Health and Social Care Substance Misuse Needs Assessment March 2014*. Worcester: Worcestershire County Council; 2014.
1006. Young MM, Wilkins C. *Proposal for an International Knowledge Exchange Network on Novel Psychoactive Substances*. Fourth International Novel Psychoactive Substances Conference, Budapest, 30–31 May 2016.

1007. Zawilska JB. Methoxetamine – a novel recreational drug with potent hallucinogenic properties. *Toxicol Lett* 2014;**230**:402–7. <https://doi.org/10.1016/j.toxlet.2014.08.011>
1008. Storti M, Wilson M. *New Psychoactive Substances and Their Risk to Patient Safety*. Melbourne, VIC: The Royal Melbourne Hospital; 2015.
1009. Robertson L. *2014/15 Scottish Crime and Justice Survey: Drug Use*. Edinburgh: National Statistics Scotland; 2016.
1010. World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*. 2011. URL: www.who.int/classifications/icd/ICD10Volume2_en_2010.pdf (accessed 29 June 2016).
1011. Wallis L. *Diffusion of New Psychoactive Substances: Understanding Population Motives, Harms and Intervention Needs*. Liverpool: Liverpool John Moores University; 2016.
1012. Loeffler G, Craig C. The effect of legal bans on poison control center contacts regarding 'legal highs'. *Addiction* 2013;**108**:1348–9. <https://doi.org/10.1111/add.12194>
1013. Ministry of Health. *Psychoactive Substances Act 2013*. Wellington: Ministry of Health; 2013.
1014. Great Britain. *Misuse of Drugs Act 1971 (Temporary Class Drug) Order*. London: The Stationery Office; 2015.
1015. Government of Ireland. *Misuse of Drugs Act 1977 (Controlled Drugs) (Declaration) Order 2010*. Dublin: Government of Ireland; 2010.
1016. EMCDDA. *European Drug Report. Trends and Developments*. Lisbon: EMCDDA; 2015.
1017. ACMD. *Consideration of the Novel Psychoactive Substances ('Legal Highs')*. London: ACMD; 2011.
1018. The New Psychoactive Substances Review Expert Panel. *New Psychoactive Substances Review Report of the Expert Panel*. London: Home Office; 2014.
1019. EMCDDA-Europol. *Annual Report on the Implementation of Council Decision 2005/387/JHA. Annex 2: New Psychoactive Substances Reported to the EMCDDA and Europol for the First Time in 2008 Under the Terms of Council Decision, 005/387/JHA.2008*. URL: www.emcdda.europa.eu/attachements.cfm/att_77263_EN_EMCCDDA-Europol_Annual_Report_Art10_2008.pdf (accessed 21 May 2012).
1020. Lader D. *Drug Misuse: Findings from the 2014/15 Crime Survey for England and Wales. Statistical Bulletin 03/15*. London: Home Office; 2015.
1021. ACMD. *Letter to Home Secretary, Dated 25th October 2011*. London: ACMD; 2011.
1022. Babor T, Caetano R, Casswell S, Edwards G, Giesbrecht N, Graham K, et al. *Alcohol: No Ordinary Commodity – Research and Public Policy*. Oxford: Oxford University Press; 2010. <https://doi.org/10.1093/acprof:oso/9780199551149.001.0001>
1023. Babor TF, Robaina K, Jernigan D. The influence of industry actions on the availability of alcoholic beverages in the African region. *Addiction* 2015;**110**:561–71. <https://doi.org/10.1111/add.12832>
1024. Babor T, Caulkins J, Edwards G, Fischer B, Foxcroft D, Humphreys K, et al. *Drug Policy and the Public Good*. Oxford: Oxford University Press; 2010.
1025. Beaglehole R, Bonita R, Yach D, Mackay J, Reddy KS. A tobacco-free world: a call to action to phase out the sale of tobacco products by 2040. *Lancet* 2015;**385**:1011–18. [https://doi.org/10.1016/S0140-6736\(15\)60133-7](https://doi.org/10.1016/S0140-6736(15)60133-7)

1026. Strang J, Babor T, Caulkins J, Fischer B, Foxcroft D, Humphreys K. Drug policy and the public good: evidence for effective interventions. *Lancet* 2012;**379**:71–83. [https://doi.org/10.1016/S0140-6736\(11\)61674-7](https://doi.org/10.1016/S0140-6736(11)61674-7)
1027. MacCoun R, Reuter P. Evaluating alternative cannabis regimes. *Br J Psychiatry* 2001;**178**:123–8. <https://doi.org/10.1192/bjp.178.2.123>
1028. Hawken A, Caulkins J, Kilmer B, Kleiman M. Quasi-legal cannabis in Colorado and Washington: local and national implications. *Addiction* 2013;**108**:837–8. <https://doi.org/10.1111/add.12156>
1029. Room R. Legalizing a market for cannabis for pleasure: Colorado, Washington, Uruguay and beyond. *Addiction* 2014;**109**:345–51. <https://doi.org/10.1111/add.12355>
1030. Kim HS, Hall KE, Genco EK, Van Dyke M, Barker E, Monte AA. Marijuana tourism and emergency department visits in Colorado. *N Engl J Med* 2016;**374**:797–8. <https://doi.org/10.1056/NEJMc1515009>
1031. Berridge V. Drug policy: should the law take a back seat? *Lancet* 1996;**347**:301–5. [https://doi.org/10.1016/S0140-6736\(96\)90471-7](https://doi.org/10.1016/S0140-6736(96)90471-7)
1032. Reuter P, Caulkins JP. Redefining the goals of national drug policy: recommendations from a working group. *Am J Public Health* 1995;**85**:1059–63. https://doi.org/10.2105/AJPH.85.8_Pt_1.1059
1033. Caulkins JP, Reuter P. Setting goals for drug policy: harm reduction or use reduction? *Addiction* 1997;**92**:1143–50. <https://doi.org/10.1111/j.1360-0443.1997.tb03673.x>
1034. Pacula RL, Kilmer B, Wagenaar AC, Chaloupka FJ, Caulkins JP. Developing public health regulations for marijuana: lessons from alcohol and tobacco. *Am J Public Health* 2014;**104**:1021–8. <https://doi.org/10.2105/AJPH.2013.301766>
1035. Berridge V. *Demons: Our Changing Attitudes to Alcohol, Tobacco and Drugs*. Oxford: Oxford University Press; 2013.
1036. Davies SC, Winpenny E, Ball S, Fowler T, Rubin J, Nolte E. For debate: a new wave in public health improvement. *Lancet* 2014;**384**:1889–95. [https://doi.org/10.1016/S0140-6736\(13\)62341-7](https://doi.org/10.1016/S0140-6736(13)62341-7)
1037. Hamlin C. The History and Development of Public Health in Developed Countries. In Abdool Karim Q, Tan CC, Detels R, Guildford M, editors. *Oxford Textbook of Global Public Health*. Oxford: Oxford University Press; 2015. <https://doi.org/10.1093/med/9780199661756.003.0002>
1038. Hanlon P, Carlisle S, Hannah M, Reilly D, Lyon A. Making the case for a ‘fifth wave’ in public health. *Public Health* 2011;**125**:30–6. <https://doi.org/10.1016/j.puhe.2010.09.004>
1039. Beaglehole R, Bonita R, Horton R, Adams O, McKee M. Public health in the new era: improving health through collective action. *Lancet* 2004;**363**:2084–6. [https://doi.org/10.1016/S0140-6736\(04\)16461-1](https://doi.org/10.1016/S0140-6736(04)16461-1)
1040. Detels R, Tan CC. The Scope and Concerns of Public Health. In Abdool Karim Q, Tan CC, Detels R, Gulliford M, editors. *Oxford Textbook of Global Public Health*. Oxford: Oxford University Press; 2015. <https://doi.org/10.1093/med/9780199661756.003.0001>
1041. Rose G. Sick individuals and sick populations. *Int J Epidemiol* 1985;**14**:32–8. <https://doi.org/10.1093/ije/14.1.32>
1042. Rose G. *The Strategy of Preventive Medicine*. Oxford: Oxford University Press; 1992.
1043. Mehta N, Croudace T, Davies SC. Public mental health: evidenced-based priorities. *Lancet* 2015;**385**:1472–5. [https://doi.org/10.1016/S0140-6736\(14\)61400-8](https://doi.org/10.1016/S0140-6736(14)61400-8)

1044. Levin K, Cashore B, Bernstein S, Auld G. Overcoming the tragedy of super wicked problems: constraining our future selves to ameliorate global climate change. *Policy Sci* 2012;**45**:123–52. <https://doi.org/10.1007/s11077-012-9151-0>
1045. Centers for Disease Control and Prevention. *CDC Policy on Climate and Health*. 2014. URL: www.cdc.gov/climateandhealth/policy.htm (accessed 29 June 2016).
1046. Hess JJ, Eidson M, Tlumak JE, Raab KK, Lubet G. An evidence-based public health approach to climate change adaptation. *Environ Health Perspect* 2014;**122**:1177–786. <https://doi.org/10.1289/ehp.1307396>
1047. Sallis JF, Owen N, Fisher EB. Ecological Models of Health Behavior. In Glanz K, Rimer BK, Viswanath K, editors. *Health Behavior and Health Education: Theory, Research and Practice*. 4th edn. San Francisco, CA: Jossey-Bass; 2008.
1048. Schneider M, Stokols D. Multilevel Theories of Behavior Change: A Social Ecological Framework. In Shumaker SA, Ockene JK, Riekert KA, editors. *The Handbook of Health Behavior Change*. New York, NY: Springer Publishing Company; 2009.
1049. Bronfenbrenner U. Ecological Systems Theory. In Vasta R, ed. *Six Theories of Child Development: Revised Formulations and Current Issues*. London: Jessica Kingsley; 1992.
1050. Gluckman P, Nishtar S, Armstrong T. Ending childhood obesity: a multidimensional challenge. *Lancet* 2015;**385**:1048–50. [https://doi.org/10.1016/S0140-6736\(15\)60509-8](https://doi.org/10.1016/S0140-6736(15)60509-8)
1051. World Health Organization. *Draft Final Report of the Commission on Ending Childhood Obesity*. Geneva: World Health Organization; 2015.
1052. Strang J. Opiates: are there under-utilized and unexplored areas of prevention? *Addiction* 1994;**89**:1511–16. <https://doi.org/10.1111/j.1360-0443.1994.tb03751.x>
1053. Laslett AM, Room R, Ferris J, Wilkinson C, Livingston M, Mugavin J. Surveying the range and magnitude of alcohol's harm to others in Australia. *Addiction* 2011;**106**:1603–11. <https://doi.org/10.1111/j.1360-0443.2011.03445.x>
1054. Room R, Ferris J, Laslett AM, Livingston M, Mugavin J, Wilkinson C. The drinker's effect on the social environment: a conceptual framework for studying alcohol's harm to others. *Int J Environ Res Public Health* 2010;**7**:1855–71. <https://doi.org/10.3390/ijerph7041855>
1055. Gordon L, Tinsley L, Godfrey C, Parrott S. The Economic and Social Costs of Class A Drug Use in England and Wales, 2003/04. In Singleton N, Murray R, Tinsley L, editors. *Measuring Different Aspects of Problem Drug Use: Methodological Developments*. Home Office Online Report 16/06; 2006. pp. 41–5.
1056. Frohlich KL, Potvin L. Transcending the known in public health practice: the inequality paradox: the population approach and vulnerable populations. *Am J Public Health* 2008;**98**:216–21. <https://doi.org/10.2105/AJPH.2007.114777>
1057. Singer M. *Drugging the Poor: Legal and Illegal Drugs and Social Inequality*. Long Grove, IL: Waveland Press; 2008.
1058. Orford J. *Power, Powerlessness and Addiction*. Cambridge: Cambridge University Press; 2013. <https://doi.org/10.1017/CBO9781139540971>
1059. Mackenbach JP, Kulhánová I, Bopp M, Borrell C, Deboosere P, Kovács K, et al. Inequalities in Alcohol-Related Mortality in 17 European Countries: A Retrospective Analysis of Mortality Registers. *PLOS Med* 2015;**12**:e1001909. <https://doi.org/10.1371/journal.pmed.1001909>
1060. Dorling H, Cook A, Ollerhead L, Westmore M. The NIHR Public Health Research Programme: responding to local authority research needs in the United Kingdom. *Health Res Policy Syst* 2015;**13**:77. <https://doi.org/10.1186/s12961-015-0068-x>

1061. Edwards G. Problems and Dependence: The History of Two Dimensions. In Edwards G, Lader M, Drummond DC, editors. *The Nature of Alcohol and Drug Related Problems*. Oxford: Oxford Medical Publications; 1992.
1062. Rehm J, Marmet S, Anderson P, Gual A, Kraus L, Nutt DJ, *et al*. Defining substance use disorders: do we really need more than heavy use? *Alcohol Alcohol* 2013;**48**:633–40. <https://doi.org/10.1093/alcalc/agt127>
1063. Cunningham JA, McCambridge J. Is alcohol dependence best viewed as a chronic relapsing disorder? *Addiction* 2012;**107**:6–12. <https://doi.org/10.1111/j.1360-0443.2011.03583.x>
1064. Babor TF, Stenius K, Romelsjo A. Alcohol and drug treatment systems in public health perspective: mediators and moderators of population effects. *Int J Methods Psychiatr Res* 2008;**17**(Suppl. 1):50–9. <https://doi.org/10.1002/mpr.249>
1065. McNeely J, Cleland CM, Strauss SM, Palamar JJ, Rotrosen J, Saitz R. Validation of Self-Administered Single-Item Screening Questions (SISQs) for Unhealthy Alcohol and Drug Use in Primary Care Patients. *J Gen Intern Med* 2015;**30**:1757–64. <https://doi.org/10.1007/s11606-015-3391-6>
1066. Home Office. *Tables for 'Drug Misuse; Findings from the 2013 to 2014 CSEW'*. London: Home Office; 2014.
1067. Baggio S, Studer J, Mohler-Kuo M, Daepfen JB, Gmel G. Profiles of drug users in Switzerland and effects of early-onset intensive use of alcohol, tobacco and cannabis on other illicit drug use. *Swiss Med Wkly* 2013;**143**:w13805. <https://doi.org/10.4414/smw.2013.13805>
1068. Catalano RF, Fagan AA, Gavin LE, Greenberg MT, Irwin CE, Ross DA, Shek DT. Worldwide application of prevention science in adolescent health. *Lancet* 2012;**379**:1653–64. [https://doi.org/10.1016/S0140-6736\(12\)60238-4](https://doi.org/10.1016/S0140-6736(12)60238-4)
1069. Livingston M. Trends in non-drinking among Australian adolescents. *Addiction* 2014;**109**:922–9. <https://doi.org/10.1111/add.12524>
1070. Budney AJ, Sargent JD, Lee DC. Vaping cannabis (marijuana): parallel concerns to e-cigs? *Addiction* 2015;**110**:1699–704. <https://doi.org/10.1111/add.13036>
1071. Wall DS, Williams ML. Policing cybercrime: networked and social media technologies and the challenges for policing. *Policing Soc* 2013;**23**:409–12. <https://doi.org/10.1080/10439463.2013.780222>

Appendix 1 Novel psychoactive substances electronic database literature search (original search: 16 November 2015; updated search: 29 June 2016)

We searched the EMBASE, MEDLINE, PsycINFO and Science Citation Index databases and a total of 13,772 records were identified. These were imported into bibliographic software and deduplicated, leaving a total of 9165 records.

EMBASE (via Ovid)

Date range searched: 1980 to 2015 Week 46.

1. exp designer drug/
2. psychotropic agent/
3. substance abuse/
4. 2 and 3
5. (designer adj (drug\$ or stimulat\$ or amphetamine\$)).ti,ab.
6. legal high\$.ti,ab.
7. ((club or street) adj drug\$).ti,ab.
8. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive drug\$).ti,ab.
9. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive agent\$).ti,ab.
10. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive substance\$).ti,ab.
11. ((new or novel or emerg) adj (cannabinoid\$ or phenethylamine\$ or arylalkylamine\$ or cathinone\$ or opioid\$ or benzodiazepine\$ or piperidine\$ or pyrrolidine\$ or piperazine\$ or arylcyclohexylamine\$ or aminoindane\$ or tryptamine\$)).ti,ab.
12. (synthetic adj (cannabinoid\$ or phenethylamine\$ or arylalkylamine\$ or cathinone\$ or opioid\$ or benzodiazepine\$ or piperidine\$ or pyrrolidine\$ or piperazine\$ or arylcyclohexylamine\$ or aminoindane\$ or tryptamin)).ti,ab.
13. (psychotropic adj (drug\$ or substance\$ or agent\$)).ti,ab.
14. 13 and 3
15. ((psychotropic adj2 (drug\$ or substance\$ or agent\$)) and (abuse or misuse)).ti,ab.
16. (herbal adj (blend\$ or high\$ or incense\$)).ti,ab.
17. (party pill\$ or research chemical\$ or smoking mixture\$).ti,ab.
18. 1 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 14 or 15 or 16 or 17
19. benzylpiperazine\$.ti,ab.
20. cannabimimetic\$.ti,ab.
21. diclazepam.ti,ab.
22. gamma butyrolact\$.ti,ab.
23. mephedrone.ti,ab.
24. methiopropamine.ti,ab.
25. methoxetamine.ti,ab.
26. naphyrone.ti,ab.
27. 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28. substance abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
29. 27 and 28
30. BZP.ti,ab.
31. MPVD.ti,ab.

32. NRG-1.ti,ab.
33. MDAI.ti,ab.
34. 25i-NBOMe.ti,ab.
35. 30 or 31 or 32 or 33 or 34
36. Substance abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
37. 35 and 36
38. (Annihilation or Armageddon).ti,ab.
39. (bamboo or bathsalt\$ or bath salt\$ or benzofury or benzo fury or berry bomb or black mamba or bromo-dragonfly or bullet or bumpin).ti,ab.
40. (charly sheen or cherry bomb or chillout or china white or ching or c-liquid or clockwork orange).ti,ab.
41. (disco biscuits or doves ultra).ti,ab.
42. (exodus damnation or exodus nightshade).ti,ab.
43. focus.ti,ab.
44. (gogaine or green beans).ti,ab.
45. (happy joker blueberry or happy joker juice fruit or happy rasta or head trip or hipster or hooter).ti,ab.
46. insane joker.ti,ab.
47. jammin joker.ti,ab.
48. (K2 or king joker or kronic).ti,ab.
49. lotus.ti,ab.
50. (Mexecat or mcat or m-cat or mind melt).ti,ab.
51. (pandora\$ box or pink panthers or plant feeder\$ or plant food\$ or pond cleaner\$ or psyclone).ti,ab.
52. (salvia or sensate or sexy v or spice or super lemon haze or synthacaine).ti,ab.
53. timeless.ti,ab.
54. voodoo.ti,ab.
55. (White MM or white widow or wicked).ti,ab.
56. 38 or 39 or 40 or 41 or 42 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55
57. Substance abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
58. 56 and 57
59. 18 or 29 or 37 or 58
60. exp animals/ not humans/
61. 59 not 60
62. limit 61 to yr="2006 -Current"

MEDLINE (via Ovid)

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)

Date range searched: 1946 to present.

1. exp designer drug/
2. psychotropic drugs/
3. drug abuse/
4. 2 and 3
5. (designer adj (drug\$ or stimulat\$ or amphetamine\$)).ti,ab.
6. legal high\$.ti,ab.
7. ((club or street) adj drug\$).ti,ab.
8. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive drug\$).ti,ab.
9. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive agent\$).ti,ab.
10. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive substance\$).ti,ab.
11. ((new or novel or emerg) adj (cannabinoid\$ or phenethylamine\$ or arylalkylamaine\$ or cathinone\$ or opioid\$ or benzodiazepine\$ or piperidine\$ or pyrrolidine\$ or piperazine\$ or arylcyclohexylamine\$ or aminoindane\$ or tryptamine\$)).ti,ab.

12. (synthetic adj (cannabinoid\$ or phenethylamine\$ or arylalkylamine\$ or cathinone\$ or opioid\$ or benzodiazepine\$ or piperidine\$ or pyrrolidine\$ or piperazine\$ or arylcyclohexylamine\$ or aminoindane\$ or tryptamin)).ti,ab.
13. (psychotropic adj (drug\$ or substance\$ or agent\$)).ti,ab.
14. 13 and 3
15. ((psychotropic adj2 (drug\$ or substance\$ or agent\$)) and (abuse or misuse)).ti,ab.
16. (herbal adj (blend\$ or high\$ or incense\$)).ti,ab.
17. (party pill\$ or research chemical\$ or smoking mixture\$).ti,ab.
18. 1 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 14 or 15 or 16 or 17
19. benzylpiperazine\$.ti,ab.
20. cannabimimetic\$.ti,ab.
21. diclazepam.ti,ab.
22. gamma butyrolact\$.ti,ab.
23. mephedrone.ti,ab.
24. methiopropamine.ti,ab.
25. methoxetamine.ti,ab.
26. naphyrone.ti,ab.
27. 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28. Drug abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
29. 27 and 28
30. BZP.ti,ab.
31. MPVD.ti,ab.
32. NRG-1.ti,ab.
33. MDAI.ti,ab.
34. 25i-NBOMe.ti,ab.
35. 30 or 31 or 32 or 33 or 34
36. Drug abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
37. 35 and 36
38. (Annihilation or Armageddon).ti,ab.
39. (bamboo or bathsalt\$ or bath salt\$ or benzofury or benzo fury or berry bomb or black mamba or bromo-dragonfly or bullet or bumpin).ti,ab.
40. (charly sheen or cherry bomb or chillout or china white or ching or c-liquid or clockwork orange).ti,ab.
41. (disco biscuits or doves ultra).ti,ab.
42. (exodus damnation or exodus nightshade).ti,ab.
43. focus.ti,ab.
44. (gogaine or green beans).ti,ab.
45. (happy joker blueberry or happy joker juice fruit or happy rasta or head trip or hipster or hooter).ti,ab.
46. insane joker.ti,ab.
47. jammin joker.ti,ab.
48. (K2 or king joker or kronic).ti,ab.
49. lotus.ti,ab.
50. (Mexecat or mcat or m-cat or mind melt).ti,ab.
51. (pandora\$ box or pink panthers or plant feeder\$ or plant food\$ or pond cleaner\$ or psyclone).ti,ab.
52. (salvia or sensate or sexy v or spice or super lemon haze or synthacaine).ti,ab.
53. timeless.ti,ab.
54. voodoo.ti,ab.
55. (White MM or white widow or wicked).ti,ab.
56. 38 or 39 or 40 or 41 or 42 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55
57. Drug abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
58. 56 and 57
59. 18 or 29 or 37 or 58

60. exp animals/ not humans/
61. 59 not 60
62. limit 61 to yr="2006 -Current"

PsycINFO (via Ovid)

Date range searched: 1987 to November Week 2 2015.

1. prescription drugs/
2. neuroleptic drugs/
3. drug abuse/
4. (1 or 2) and 3
5. (designer adj (drug\$ or stimulat\$ or amphetamine\$)).ti,ab.
6. legal high\$.ti,ab.
7. ((club or street) adj drug\$).ti,ab.
8. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive drug\$).ti,ab.
9. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive agent\$).ti,ab.
10. ((new or novel or emerg\$ or illicit\$ or illegal) adj psychoactive substance\$).ti,ab.
11. ((new or novel or emerg) adj (cannabinoid\$ or phenethylamine\$ or arylalkylamine\$ or cathinone\$ or opioid\$ or benzodiazepine\$ or piperidine\$ or pyrrolidine\$ or piperazine\$ or arylcyclohexylamine\$ or aminoindane\$ or tryptamine\$)).ti,ab.
12. (synthetic adj (cannabinoid\$ or phenethylamine\$ or arylalkylamine\$ or cathinone\$ or opioid\$ or benzodiazepine\$ or piperidine\$ or pyrrolidine\$ or piperazine\$ or arylcyclohexylamine\$ or aminoindane\$ or tryptamin)).ti,ab.
13. (psychotropic adj (drug\$ or substance\$ or agent\$)).ti,ab.
14. 13 and 3
15. ((psychotropic adj2 (drug\$ or substance\$ or agent\$)) and (abuse or misuse)).ti,ab.
16. (herbal adj (blend\$ or high\$ or incense\$)).ti,ab.
17. (party pill\$ or research chemical\$ or smoking mixture\$).ti,ab.
18. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 14 or 15 or 16 or 17
19. benzylpiperazine\$.ti,ab.
20. cannabimimetic\$.ti,ab.
21. diclazepam.ti,ab.
22. gamma butyrolact\$.ti,ab.
23. mephedrone.ti,ab.
24. methiopropamine.ti,ab.
25. methoxetamine.ti,ab.
26. naphyrone.ti,ab.
27. 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28. Drug abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
29. 27 and 28
30. BZP.ti,ab.
31. MPVD.ti,ab.
32. NRG-1.ti,ab.
33. MDAI.ti,ab.
34. 25i-NBOMe.ti,ab.
35. 30 or 31 or 32 or 33 or 34
36. Drug abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
37. 35 and 36
38. (Annihilation or Armageddon).ti,ab.
39. (bamboo or bathsalt\$ or bath salt\$ or benzofury or benzo fury or berry bomb or black mamba or bromo-dragonfly or bullet or bumpin).ti,ab.
40. (charly sheen or cherry bomb or chillout or china white or ching or c-liquid or clockwork orange).ti,ab.
41. (disco biscuits or doves ultra).ti,ab.

42. (exodus damnation or exodus nightshade).ti,ab.
43. focus.ti,ab.
44. (gogaine or green beans).ti,ab.
45. (happy joker blueberry or happy joker juice fruit or happy rasta or head trip or hipster or hooter).ti,ab.
46. insane joker.ti,ab.
47. jammin joker.ti,ab.
48. (K2 or king joker or kronic).ti,ab.
49. lotus.ti,ab.
50. (Mexecat or mcat or m-cat or mind melt).ti,ab.
51. (pandora\$ box or pink panthers or plant feeder\$ or plant food\$ or pond cleaner\$ or psyclone).ti,ab.
52. (salvia or sensate or sexy v or spice or super lemon haze or synthacaine).ti,ab.
53. timeless.ti,ab.
54. voodoo.ti,ab.
55. (White MM or white widow or wicked).ti,ab.
56. 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55
57. Drug abuse/ or (drug abuse or "drug use" or drug misuse).ti,ab.
58. 56 and 57
59. 18 or 29 or 37 or 58
60. exp human males/
61. exp human females/
62. 60 or 61
63. exp animals/
64. 63 not 62
65. 59 not 64 (2345)

Science Citation Index (via Web of Science)

-
- #12 #11 OR #9 OR #7 *DocType=All document types; Language=All languages;*
- #11 #10 AND #6 *DocType=All document types; Language=All languages;*
- #10 TS=(Annihilation or Armageddon or bamboo or bathsalt* or "bath salt*" or benzofury or "benzo fury" or "berry bomb" or "black mamba" or bromo-dragonfly or bullet or bumpin or "charly sheen" or "cherry bomb" or chillout or "china white" or ching or c-liquid or "clockwork orange" or "disco biscuits" or "doves ultra" or "exodus damnation" or "exodus nightshade" or focus) OR TS=(gogaine or "green beans" or 'happy joker blueberry' or 'happy joker juice fruit' or 'happy rasta' or 'head trip' or hipster or hooter or 'insane joker' or 'jammin joker' or K2 or 'king joker' or kronic or lotus or mexecat or mcat or m-cat or 'mind melt') OR TS=('pandora* box' or 'pink panthers' or 'plant feeder*' or 'plant food*' or 'pond cleaner*' or psyclone or salvia or sensate or 'sexy v' or spice or 'super lemon haze' or synthacaine or timeless or voodoo or 'white MM' or 'white widow' or wicked) *DocType = All document types; Language = All languages;*
- #9 #8 AND #6 *DocType=All document types; Language=All languages;*
- #8 TS=(benzylpiperazine* or cannabimimetic* or diclazepam or "gamma butyrolact*" or mephedrone or methiopropamine or methoxetamine or naphyrone) OR TS = (BZP or MPVD or NRG-1 or MDAI or 25i-NBOMe) *DocType = All document types; Language = All languages;*
- #7 #6 AND #5 *DocType=All document types; Language=All languages;*
- #6 TS=("drug abuse" or "drug use" or "drug misuse") *DocType=All document types; Language=All languages;*
- #5 #4 OR #3 OR #2 OR #1 *DocType=All document types; Language=All languages;*
- #4 TS=(herbal NEAR (blend* or high* or incense*)) OR TS=(("party pill*" or "research chemical*" or "smoking mixture*")) *DocType=All document types; Language=All languages;*
- #3 TS=((psychotropic NEAR (drug* or substance* or agent*))) *DocType=All document types; Language=All languages;*
-

-
- #2 TS=("legal high*") OR TS=((club or street) NEAR drug*) OR TS=((new or novel or emerg* or illicit* or illegal) NEAR "psychoactive drug*")
- OR TS=((new or novel or emerg* or illicit* or illegal) NEAR "psychoactive agent*") OR
- TS=((new or novel or emerg* or illicit* or illegal) NEAR "psychoactive substance*") OR
- TS=((new or novel or emerg*) NEAR (cannabinoid* or phenethylamine* or arylalkylamine* or cathinone* or opioid*
- or benzodiazepine* or piperidine* or pyrrolidine* or piperazine* or arylcyclohexylamine* or aminoindane* or tryptamine*)) OR
- TS=(synthetic NEAR (cannabinoid* or phenethylamine* or arylalkylamine* or cathinone* or opioid* or benzodiazepine* or
- piperidine* or pyrrolidine* or piperazine* or arylcyclohexylamine* or aminoindane* or tryptamin)) *DocType = All document types; Language = All languages;*
- #1 TS=((designer NEAR (drug* or stimulat* or amphetamine*))) *DocType=All document types; Language=All languages;*
-

Appendix 2 Legal high brand/trade names included in the electronic searches

Name	Global weekends (see www.globalweekends.co.uk)	Ice headshop (see www.iceheadshop.co.uk/)	Legal Highs World (see https://legalhighsworld.wordpress.com/)
Annihilation	✓	✓	✓
Armageddon	✓	✓	✓
Bamboo	✓	✓	✓
Berry bomb	✓	✓	✓
Black mamba	✓	✓	✓
Bullet	✓	✓	✓
Bumpin	✓	✓	✓
Charly sheen	✓	✓	✓
Cherry bomb	✓	✓	✓
Chillout	✓	✓	✓
China white	✓	✓	✓
Ching	✓	✓	✓
C-liquid	✓	✓	✓
Clockwork orange	✓	✓	✓
Diclozepam	✓	✓	✓
Disco biscuits	✓	✓	✓
Doves ultra	✓	✓	✓
Exodus damnation	✓	✓	✓
Exodus nightshade	✓	✓	✓
Focus	✓	✓	✓
Gogaine	✓	✓	✓
Green beans	✓	✓	✓
Happy joker blueberry/ juicy fruit	✓	✓	✓
Happy rasta	✓	✓	✓
Head trip	✓	✓	✓
Hipster	✓	✓	✓
Hooter	✓	✓	✓
Insane joker	✓	✓	✓
Jammin' joker	✓	✓	✓
K2	✓	✓	✓
King joker	✓	✓	✓
Kronic	✓	✓	✓

Name	Global weekends (see www.globalweekends.co.uk)	Ice headshop (see www.iceheadshop.co.uk/)	Legal Highs World (see https://legalhighsworld.wordpress.com/)
Lotus	✓	✓	✓
Methiopropamine	✓	✓	✓
Mexecat/Mcat/ M-cat	✓	✓	✓
Mind melt	✓	✓	✓
Pandora's box	✓	✓	✓
Pink panthers	✓	✓	✓
Psychone	✓	✓	✓
Salvia	✓	✓	
Sensate	✓	✓	✓
Sexy V	✓	✓	✓
Spice	✓	✓	✓
Super lemon haze	✓	✓	✓
Synthacaine	✓	✓	✓
Timeless	✓	✓	✓
Voodoo	✓	✓	✓
Voodoo gold	✓	✓	✓
White MM	✓	✓	✓
White widow	✓	✓	✓
Wicked	✓	✓	✓

A decorative graphic consisting of numerous thin, parallel green lines that curve from the left side of the page towards the right, creating a sense of movement and depth.

**EME
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