

Can new psychoactive substances be regulated effectively? An assessment of the British Psychoactive Substances Bill

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ABSTRACT

The regulation of new psychoactive substances (NPS) has confounded governments throughout the western world. In 2014 the UK government convened an NPS Review Expert Panel to consider a range of approaches. Ultimately the Panel recommended that the government ban all new psychoactive drugs and allow only psychoactive substances specifically exempted, such as alcohol, tobacco and those allowed as medicines. The government introduced the Psychoactive Substances Bill (PSB) in response to that recommendation. Passed in 2016, the Bill has attracted a torrent of criticism from scientists and experts. The Bill could be improved with revision, but the problems of the total ban, as envisioned by the PSB, with respect to the NPS, may be inherent: (1) defining psychoactivity is conceptually fraught, with great consequence for the scope of the prohibition; (2) operationalizing psychoactivity as a usable concept for legal control purposes is extremely difficult, perhaps impossible; and (3) the detachment of penalties for violating a total ban from establishing the harmfulness of a substance is normatively troubling. Given the uncertainties about the effects of a total ban, it is appropriate at this time for other governments to assess more fully the nature of the NPS problem, and the potential control approaches.

Keywords Headshops, legal highs, new psychoactive substances, Psychoactive Substances Act, psychoactivity, regulation, substitution effect.

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INTRODUCTION

New psychoactive substances (NPS) have been a source of growing frustration for governments throughout the western world, including that of the United Kingdom [1,2]. NPS have generated essentially reactive policy, requiring the invocation of a complicated process to ban the next substance flowing out of clandestine laboratories in response to the previous set of prohibitive regulations. No government looks good in that role, apparently off-guard and transparently unable to anticipate what will come along next. The improving technological capabilities in China and India, increased communication and trade via the internet and the ability to produce new substances in small laboratories have all contributed to an increase in the number of different NPS flowing into western nations [3,4].

Facing this onslaught, the temptation for the government is then to turn to a blanket prohibition. No

psychoactive substances may be produced, marketed or consumed except those that have already been permitted explicitly, such as alcohol, tobacco, caffeine, scheduled medicines and perhaps a small number of mildly harmful substances already in common use. All ambiguity captured in the phrase 'legal highs' is eliminated. This approach is a marked departure from conventional drug control laws, which prohibit only substances that are listed. It is the approach already taken, with minor but important variations, by Ireland (the pioneer), Poland and Romania [5,6].

In 2016 the United Kingdom passed legislation which imposes a blanket ban, in response to the recommendation of the New Psychoactive Substances Review Expert Panel (hereafter the Panel), a 12-member government-appointed committee of drug policy experts. The Panel was tasked principally by the Home Secretary to analyse the nature of the NPS problem, review current legislative responses

and propose a set of recommendations to the Home Office and other administrative bodies [7].

The PSB has attracted strident critiques from leading scientists. For example, 40 prominent scientific and policy figures, including Colin Blakemore, Lord Ramsbotham and David Nutt, signed a letter that called the bill ‘very poorly drafted, unethical in principle, unenforceable in practice, and likely to constitute a real danger to the health and well-being of our nation’s citizens’ [8]. In a series of unusually critical letters to the Home Secretary, the Advisory Council on the Misuse of Drugs (ACMD) has expressed considerable unhappiness with the PSB [9–11]. There has been a notable lack of support for the PSB from any part of the expert community.

What went wrong, given that the government claims that it was simply following the recommendation of a well-qualified Panel? The Panel included five government officials (four from enforcement agencies), two academics and three from the non-governmental organization (NGO) sector; three members were also members of the ACMD. In fact, the Panel’s recommendation was, as one of its members (the chair of the ACMD) described it, ‘a little bit woolly’. Arguably, the Panel failed to articulate the necessary details to establish a meaningful and reasonable blanket ban. The entire set of recommendations proposed to effectuate a blanket ban comprised of two paragraphs. Neglecting details such as the Panel’s emphasis on prohibiting just ‘novel substances’ allowed the government to follow its instincts to simplify the task by reflexively extending barriers to recreational drug use, what Stevens & Measham [12] see as another turn of ‘the drug policy ratchet’.

Is a total ban in fact the best approach to the NPS problem in the United Kingdom or other wealthy countries? None of the five options considered by the Panel, based on models tried in other countries, is very satisfying. As so often in drug policy, it is a question of choosing the problem rather than the solution [13]. The total ban has some advantages over the alternatives in terms of the nature of the problem it shapes. However, so little is known about its feasibility and consequences that we caution against sweeping laws until more effort is made to assess all the alternatives. The 6 months available to the Panel was far too short for the task assigned. However, given the prominence of the United Kingdom in drug policy affairs internationally, the choice made by the United Kingdom is likely to reverberate throughout the world.

This paper starts by identifying the components of the NPS problem, emphasizing the need to go beyond the numbers of new substances detected each year and instead focus on the harms. The following section then discusses policy options, with a brief analysis of some relevant experiences; the concept of a total ban is discussed in more detail. The penultimate section describes the details of the PSB and its major problems. The final section offers some

general reflections on the NPS policy problem in the United Kingdom.

DEFINING THE PROBLEM

The number of NPS detected in Europe has been a growing concern for governments since 2005. Approximately 16 NPS were reported in 2005 compared with just over 100 in 2014 [14]. Although the problem appears to be increasing rapidly, there is less to these numbers than meets the eye. Most NPS fall into just two categories (cannabimimetics and cathinones) [14] and, as competing substances, any one drug’s success would drive most of the others out of the market.

Rather than appealing to the larger drug market, NPS serve three distinct niches, as follows.

- 1 Those skirting the law; the new substance produces similar effects to one that is banned and, because it is not yet being prohibited itself, can be sold and consumed without criminal legal threat.
- 2 Those seeking a new drug similar to an existing drug but not easily detected in random drug tests. The growth of work-place testing [15,16] makes this an increasingly important market niche. Prisoners also use synthetic cannabinoids to avoid detection [17,18]. Note that it is not necessarily an issue of legality; a cannabimimetic that is not included in the drug-testing procedures is helpful to the user even if it has been banned.
- 3 Those seeking a new and attractive experience. Arguably, this was the case for ecstasy during the 1970s and 1980s [19,20]; unlike other stimulants such as cocaine, it provided users with a unique entactogenic experience.

It is impossible at present to give any sense of the relative size of these three niches, although we suspect that the third niche is considerably smaller than the other two.

For policy analysis the three should be kept distinct, as they are driven by different dynamics. For example, the third niche is not affected by the law as to what is banned but by the skill of chemists and the curiosity of some drug users. Conversely, the first is shaped entirely by the law so that many NPS follow a samsaric cycle of birth, death and rebirth. That is, after arriving in a market, governments attempt to prohibit them, which sometimes necessitates their molecular reincarnation to circumvent the latest control. Therefore, the drugs that are produced are a function of what the government has prohibited.

NPS account for a small share of total drug-related harms in the United Kingdom [7,21]. For example, in 2013 a total of 60 deaths involved the use of NPS or recently controlled novel substances in England and Wales, compared to 1640 involving illegal drugs [21]. NPS-related treatment admissions in 2013–14 totaled 1641 of a total

of more than 69 000 [7]. Nonetheless, NPS collectively represent a potential major threat for at least two distinct, almost complementary, reasons. First, a new substance could be highly successful in the market. That is, an NPS might turn out to have the combination of features that made cocaine such a threat to public health; the first 20 or so experiences are attractive, but for many users the drug turns out to be addictive and long-term dependence has dangerous behavioral and health consequences, especially if used with other intoxicants such as alcohol. Secondly, an NPS might turn out to be a dangerous failure; harmful to users in those early experiences but, tried by enough users before the market, nudged by public health authority warnings, transmits the message of danger effectively. The experience of Jamaica Ginger during Alcohol Prohibition in the United States provides a good analogy [22,23]: more than 35 000 users experienced long-term paralysis as the result of consuming a variant of alcohol combined with tricresyl phosphate, a neurotoxin, designed to deceive prohibition inspectors testing for denaturing additives intended to discourage drinking. Both the long-term success and the short-term dangerous failure represent serious potential harms.

Adding another drug to the available mix of drugs consumed by those seeking some recreational intoxicant other than alcohol may alter the harms related to total psychoactive substance use. One view, with a common-sense ring to it, is that the more drugs on offer, the more drug-taking will occur [24]. Moreover, it adds to the possible dangers arising from polydrug use [25,26]. One corollary to the dangers perhaps also includes harmful drug interactions [27]. Other observers, however, emphasize the possibility of substitution of NPS existing for more dangerous drugs [28,29]. Both statements may be true; on one hand, NPS may lead to higher prevalence or more frequent and intense use, but on the other hand lead at the same time to an overall reduction in harms as a consequence of some substitution for more harmful drugs [29,30]. Some observers have

speculated that mephedrone may have substituted for a more dangerous drug (e.g. cocaine) and produced fewer adverse consequences at the population level. For other drugs, the harms are certainly exacerbated. Substitution is a major conceptual issue for drug control, although it turns out to be hard to operationalize.

THE REGULATORY AND LEGAL ALTERNATIVES

Governments around the world have attempted various solutions to the NPS problem, with depressing results. The Panel classified the approaches into five groups (See Table 1).

The first three approaches, which cover almost all countries apart from New Zealand, aim to prohibit the production and use of new non-therapeutic psychoactive substances. The contemporary New Zealand approach, classified by the Panel as Regulatory, is the one that has attracted the most attention perhaps because it is the only one, apart from the total ban, in which the government is not purely reactive [31–35].

In New Zealand, the use of a particular NPS known as BZP (a piperazine) became widespread in the early 2000s. The government granted the drug limited restricted status as a Class D substance under the Misuse of Drugs Act in 2005. Substances in this class were thought to be of low harm and thus restricted to adults and regulations were placed on manufacturers and distributors. Granting such legal status coincided with the drug's increased popularity; a 2007 survey found that almost one in seven individuals aged 16–64 years had used it in the last month. Its harms were later established by public health officials and the drug was consequently prohibited in 2008 [36]. The NZ government then made a fundamental change in law, shifting the burden of proof of harm from the government to the producer. Thus, in 2012 the Psychoactive Substances Act was proposed under which an NPS could be

Table 1 Different legal approaches to NPS.

<i>Approach</i>	<i>Definition</i>	<i>Examples</i>
Analogue approach	Control based on chemical similarity or intended psychoactive effects to substances already controlled by law	United States Federal Analogue Act
Neurochemical approach	Control different groupings of substances regardless of chemical variation that have a specific neuropharmacological effect on brain	Cannabimimetic agents under the United States Synthetic Drug Abuse Prevention Act
General prohibition	Prohibit supply, import and export of any psychoactive substance that is not exempted	Irish Psychoactive Substances Act
Full regulatory approach	Through detailed regulations, permit and regulate sale of limited class of NPS that are proven to be of low risk	New Zealand Psychoactive Substances Act
Restricted availability approach	Restrict NPS to limited points of sale, labeling, age, etc. until harms are established	New Zealand Class D substances under Misuse of Drugs Act

NPS = New psychoactive substances.

distributed legally if the manufacturer showed that it was 'low risk' [32].

However, the government failed to define 'low risk'. It is in fact challenging both conceptually and empirically to do so. The government identified six distinct components to consider (i.e. the 'toxicological effects', 'risk to public health', 'potential to cause death', 'potential to create dependence', 'likelihood of misuse' and 'appeal to vulnerable populations'), at least three of which go well beyond conventional drug testing requirements. New Zealand's restrictions on animal testing and the prohibitive cost of other forms of testing relative to the size of the market for a nation of 4.2 million complicate this even further [31,32]. These difficulties seem to have overwhelmed the political and regulatory establishment: more than 2 years after the Psychoactive Substances Act passed, New Zealand has yet to establish meaningful regulations to govern the market. No products are legally available for sale under this law.

Another possible approach to controlling NPS is through laws that regulate medicines and other products marketed and sold in pharmacies; this falls under Restricted Availability. Such laws are designed to protect consumers from products that make fraudulent claims or pose a modest to severe health risk to the user. In many jurisdictions the utilization of medicines laws would provide stringent controls on marketing and distribution. For example, the sale of many over-the-counter cold remedies has been restricted in recent years to prevent illicit manufacture of methamphetamines [37,38]. The advantages of using such regulation are twofold. Classifying an NPS as a medicine and withholding market authorization is an agile and proportional response [39]. It requires only administrative action, and no health assessment is needed. Additionally this would avoid criminalizing use-related acts and place less onerous criminal sanctions on those supplying unauthorized medicines. According to several accounts, Austria was successful in rapidly ending the open sale of Spice using this approach [5,39].

Attractive as this option seems, it rests on legerdemain, if not downright deception. Although some products may be sold as health supplements, NPS are not offered as medicines; their implicit claim is to provide pleasure. On this basis the European Court of Justice ruled that member states could not use medicine laws to prohibit NPS [40]. It is perhaps a case of reaching the wrong conclusion through the right reasons, but this option is no longer available to the United Kingdom or to any member state of the European Union.

TOTAL PROHIBITION

We turn now to the Panel's preferred option, as enshrined in the PSB—total prohibition. Given that Ireland has had a

total ban in place for 5 years, its experience should provide useful guidance. Only a few outcome indicators are available. The Panel reported evidence that headshops in Ireland had disappeared, that there were few on-line sites domiciled in that country and that the numbers of individuals being treated for NPS dependence or abuse had declined from 2011 to 2012 [7]. Against that, a small general population survey (Eurobarometer) found that 22% of 15–24-year-olds reported using NPS, compared to a European average of 8%. Unfortunately, there is no systematic evaluation yet available, a point emphasized by the ACMD Chair [41].

One advantage of the total ban that has gone unnoticed by many experts is that if successful it should reduce the number of NPS introduced in a given period. The ACMD chair noted that in just a 5-year period there have been three rounds of synthetic cannabinoids introduced to the UK market, the second and third rounds being responses to the government's scheduling of the specific type of cannabinoid in question, under the 1971 Misuse of Drugs Act, of the previous round. Each successive round was more potent than the previous [41]. If every new substance poses a risk of being dangerous or popular, then from that viewpoint the total ban lowers risk.

Under a total ban the government is no longer simply reactive. The existing process for assessing an NPS under the Misuse of Drugs Act (MDA) in Britain is time-consuming and requires an almost ritual, rather than expert, judgment by the ACMD on new substances. The government must make a decision at a time when there are minimal data on the harms of the drug or its potential for substitution; see, for example, the ACMD Report on Naphyrone [42]. If it is possible to develop clear and legally operational definitions, the total ban ought to reduce the cost of managing the NPS problem [43]. Any non-exempted psychoactive substance—be it pill or powder—is illegal *per se*; authorities need not confirm its molecular composition against a list of scheduled chemicals.

A total ban should eliminate headshops. However, the Panel was ambivalent on this issue, citing on one hand the relatively responsible behavior of headshops to limit sales to adults, and on the other hand the relatively easier access they provided *vis-à-vis* the illicit market and the legitimacy conferred on the substances that they did sell. The same ambivalence is reflected in ACMD statements (e.g. parliamentary testimony of the chair [41]).

In considering the limitations of the total ban, we return to the three distinct market niches for NPS: evading prohibition, fooling drug tests and seeking new sources of pleasure. The total ban reduces only the first of these. NPS producers will still have the other two markets as a source of demand.

THE PSB AND ITS CRITICS

Under the PSB all psychoactive substances except those on a list of exempted substances (including alcohol, tobacco, foodstuffs and substances subject to control under the MDA) are prohibited. The criticism has been focused on three issues; the Bill's overly broad and confusing definition of psychoactivity and its narrow scope of exempted substances, the difficulty of operationalizing psychoactivity for enforcement purposes and the failure to distinguish dangerous and low-harm NPS in punishing offenders.

Defining psychoactivity

Can psychoactivity be defined in a conceptually clear way? This fundamental problem has been raised by many of the critics, including the ACMD in its dialogue with the Home Office [9–11]. The PSB's definition of a psychoactive substance as one which 'affects a person's mental function or emotional state' by stimulating or depressing the central nervous system [44] is overly broad. It implies that any substance, other than those exempted, has at least the risk of causing harm. Not only does it include new substances about which next to nothing is known, but also some substances which are known to be of minimal to moderate harm. Although most NPS seek to imitate existing prohibited substances, critics have pointed out the PSB goes well beyond such substances. For example, much has been made of the fact that 'laughing gas' (nitrous oxide), far from being a new psychoactive substance (having been discovered in the 18th century), would be banned, even though the ACMD did not believe that its harms warranted scheduling under the Misuse of Drugs Act [41]. Until Parliament intervened at the very last minute (February 2016), Poppers (alkyl nitrates) were among the banned substances, even though just 4 years earlier the ACMD concluded that Poppers are 'not seen to be capable of having 'harmful effects' sufficient to constitute a societal problem' [45].

The ACMD has recommended that the PSB be amended to define a psychoactive substance as:

Any compound, which is capable of producing a pharmacological response on the central nervous system or which produces a chemical response *in vitro*, identical or pharmacologically similar to substances controlled under the Misuse of Drugs Act 1971 [11].

This proposed definition would align the policy goals of the bill with more established principles. It grounds the bill in existing law (the MDA), narrows its scope and relates it to harmfulness (with its reference to already controlled substances). In short, it would put forward a more reasonable and grounded blanket ban. However, there are many problems concealed in terms as simple as 'similar to', an

issue raised by the Home Secretary in her response to the ADMD [45]. 'The devil is in the details' is an overused aphorism, but that does not make it untrue.

Operationalizing psychoactivity

The Bill does not establish any mechanism to measure psychoactivity. The ACMD noted that:

Psychoactivity in humans cannot be *definitively* established in many cases in a way that would definitely stand up in a court of law where a high threshold of evidence is required. There is currently no way to define psychoactivity through a biochemical test, therefore there is no guarantee of *proving* psychoactivity in a court of law. The only definitive way of determining psychoactivity is via human experience, which is usually not documented [10].

The definition above proposed by the ACMD would seemingly require continued harm assessments of new substances in order to determine whether a substance affects the human brain in any meaningfully psychoactive manner. Determining psychoactivity is complex, as it depends upon a whole host of factors. There is a theoretical prediction based on a substance's chemical composition. If a drug is thought to be psychoactive, researchers often test it on animals. However, we do not truly know all the effects—good or bad—until after a period of human experimentation. It turns out that some substances may have pharmacological effects on the brain different from what experts would predict in the laboratory. For example, Stevens *et al.* (2015) discuss salvia, a plant that once ingested provides a dissociative hallucinogenic effect [46]. The principal psychotropic molecule in salvia, salvinorin A, is an opioid agonist, yet the drug's subjective effect is not analgesic but serotogenic [47]. Further, Stevens *et al.* (2015) point out that animal testing is inconclusive as laboratory animals do not self-administer the drug, which may indicate lack of abuse potential.

Detaching penalties from harm

The PSB not only imposes a total ban; it also creates severe criminal penalties for a wide variety of offenses. Although the Bill excludes criminal penalties for personal possession, it establishes criminal offenses for individuals who import such substances for consumption or share with friends. A small but not insignificant portion of the NPS market in developed countries takes place via the internet. In effect, an individual acting alone or with a group of friends could face civil and criminal penalties of up to 7 years in prison. This could lead to abuses in the law and a misapplication of justice.

Stevens *et al.* (2015) point out that the PSB's criminal clauses contradict the existing legal regime in which maximum sentences reflect the dangerousness of the drug; marijuana offenses lead to a lesser penalty than heroin offenses. Under the PSB judges cannot impose a common sense approach in sentencing, as they will have little if any evidence on the harms of the specific drug involved in the case.

CONCLUDING THOUGHTS

This paper is concerned with the regulation of new psychoactive substances. These three simple words turn out to form a conceptual thicket. There is no possibility, say British government lawyers, of establishing what is 'new' (or even the Panel counterpart 'novel') in a legally meaningful way. Defining and determining psychoactivity is challenging. Even 'substance' is in question; must it be a synthesized compound, as the ACMD advises? If even the nature of what is to be regulated is so uncertain, it is no wonder that regulatory choices are difficult.

Critics of the PSB point out its many shortcomings, but few quarrel with the principle of the total ban [48]. An important attraction of the total ban is its apparent simplicity. That turns out to be deceptive, as discussed above. For example, if the penalties for violations of a total ban are to be proportional to the harm of the substance involved, then it may be necessary to conduct an expensive and time-consuming testing program to show what are the harms associated with each specific substance. The complications of a total ban are not simply a matter of drafting, but are inherent in the concept itself. Moreover, the ban raises troubling civil liberty issues associated with the enforcement of a ban that can bring many individuals into the net of potentially harsh criminal sanctions.

It is hard to foresee the effects of such a broad law. Little thought has been given to how the total ban will affect the behavior of producers, distributors and users. Alternative options, including the use of the civil penalties or cease and desist orders, for first and second offenses are more measured approaches. The Panel, with just 6 months to complete its work, did not have the opportunity to explore these options in depth. The experiences of nations that have tried this option have not been studied seriously for purposes of learning what can go wrong or how to improve the design; for example, with respect to the exemption process. Given Britain's prominence in global discussions of drug policy and the strength of its research community, there will be intense interest in learning from Britain's leap into the troubling unknown.

Declaration of interests

None.

References

1. Dargan P., Wood D., editors. *Novel Psychoactive Substances: Classification, Pharmacology and Toxicology*. 1st edition. London/Waltham, MA: Academic Press; 2013.
2. King L. A., Kicman A. T. A brief history of 'new psychoactive substances'. *Drug Test Anal* 2011; 3: 401–3.
3. 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.
4. Griffiths P., Sedefov R., Gallegos A., Lopez D. How globalization and market innovation challenge how we think about and respond to drug use: 'Spice', a case study. *Addiction* 2010; 105: 951–3.
5. Hughes B., Winstock A. R. Controlling new drugs under marketing regulations. *Addiction* 2012; 107: 1894–9.
6. van Amsterdam J., Nutt D., van den Brink W. Generic legislation of new psychoactive drugs. *J Psychopharmacol* 2013; 27: 317–24.
7. Home Office. *New psychoactive substances review: report of the expert panel* [internet]. London: Home Office; 2014 Oct [cited 2 April 2015], p. 84 (Drug misuse and dependency). Available at: <https://www.gov.uk/government/publications/new-psychoactive-substances-review-report-of-the-expert-panel> (accessed 2 April 2016).
8. Ramsbotham L., Nutt D., Blakemore C., Williams R., Drummond C. Open letter to Prime Minister [internet]. 2015 [cited 23 September 2015]. Available at: <http://2015.breakingconvention.co.uk/open-letter/> (accessed 2 April 2016).
9. Advisory Council on the Misuse of Drugs (ACMD). *ACMD letter to the Home Secretary: Psychoactive Substances Bill* [internet]. 2015 [cited 22 September 2015]. Available at: <https://www.gov.uk/government/publications/acmd-letter-to-the-home-secretary-psychoactive-substances-bill> (accessed 2 April 2016).
10. Advisory Council on the Misuse of Drugs (ACMD). *ACMD letter to the Home Secretary: Psychoactive Substances Bill* [internet]. 2015 [cited 22 September 2015]. Available at: <https://www.gov.uk/government/publications/acmd-letter-to-the-home-secretary-psychoactive-substances-bill-13-july-2015> (accessed 2 April 2016).
11. Advisory Council on the Misuse of Drugs (ACMD). *ACMD report on definitions for the Psychoactive Substances Bill* [internet]. 2015 [cited September 2015]. Available at: <https://www.gov.uk/government/publications/acmd-report-on-definitions-for-the-psychoactive-substances-bill> (accessed 2 April 2016).
12. Stevens A., Measham F. The 'drug policy ratchet': why do sanctions for new psychoactive drugs typically only go up? *Addiction* 2014; 109: 1226–32.
13. Kleiman M. *Against excess: drug policy for results*. BasicBooks; 1992, p. 508.
14. Evans-Brown M., Gallegos A., Francis W., Christie R., Cunningham A., Sekula J. *et al.* *New psychoactive substances in Europe an update from the EU Early Warning System*. March 2015 [internet]. Luxembourg: Publications Office; 2015 [cited September 24]. Available at: <http://dx.publications.europa.eu/10.2810/372415> (accessed 2 April 2016).
15. Ironmonger J. Workplace drug testing 'on the rise', say providers [internet]. BBC News [cited 24 September 2015]. Available at: <http://www.bbc.com/news/uk-29465755> (accessed 2 April 2016).

16. Gunderson E. W., Haughey H. M., Ait-Daoud N., Joshi A. S., Hart C. L. A survey of synthetic cannabinoid consumption by current cannabis users. *Subst Abuse* 2014; **35**: 184–9.
17. Featherstone S. Spike Nation. New York Times [internet]. 8 July 2015 [cited 8 October 2015]. Available at: <http://www.nytimes.com/2015/07/12/magazine/spike-nation.html> (accessed 2 April 2016).
18. Brown S. Synthetic cannabis causing serious health problems in English prisons. *Guardian* [internet]. 15 May 2014 [cited 8 October 2015]. Available at: <http://www.theguardian.com/society/2014/may/15/synthetic-cannabis-serious-health-problems-english-prisons> (accessed 2 April 2016).
19. Savlov M. Countdown to Ecstasy: A New Drug for a New Millennium. *Austin Chronicle* [internet]. 9 June 2000 [cited 8 October 2015]. Available at <http://www.austinchronicle.com/music/2000-06-09/77529/> (accessed 2 April 2016).
20. Aleksander I. Molly: Pure, but Not So Simple. *New York Times* [internet]. 21 June 2013 [cited 8 October 2015]. Available at: <http://www.nytimes.com/2013/06/23/fashion/molly-pure-but-not-so-simple.html> (accessed 2 April 2016).
21. Office for National Statistics. Deaths related to drug poisoning [internet]. Office for National Statistics. 8 October 2013 [cited 8 October 2015]. Available at: <http://www.ons.gov.uk/ons/rel/subnational-health3/deaths-related-to-drug-poisoning-england-and-wales-2013/stb-deaths-related-to-drug-poisoning-in-england-and-wales-2013.html> (accessed 2 April 2016).
22. Parascandola J. The Public Health Service and Jamaica ginger paralysis in the 1930s. *Public Health Rep* 1995; **110**: 361–3.
23. Morgan J. P., Penovich P. Jamaica ginger paralysis. Forty-seven-year follow-up. *Arch Neurol* 1978; **35**: 530–2.
24. Volkow N. D., Baler R. D., Compton W. M., Weiss S. R. Adverse health effects of marijuana use. *N Engl J Med* 2014; **370**: 2219–27.
25. McCabe S., Cranford J., Morales M., Young A. Simultaneous and concurrent polydrug use of alcohol and prescription drugs: prevalence, correlates, and consequences. *J Stud Alcohol* 2006; **67**: 529–37.
26. Smith G. W., Farrell M., Bunting B. P., Houston J. E., Shevlin M. Patterns of polydrug use in Great Britain: findings from a national household population survey. *Drug Alcohol Depend* 2011; **113**: 222–8.
27. Jones C. M., McAninch J. K. Emergency department visits and overdose deaths from combined use of opioids and benzodiazepines. *Am J Prev Med* 2015; **49**: 493–501.
28. Nutt D. Perverse effects of the precautionary principle: how banning mephedrone has unexpected implications for pharmaceutical discovery. *Ther Adv Psychopharmacol* 2011; **1**: 35–6.
29. Measham E., Moore K., Newcombe R., Smith Z. Tweaking, bombing, dabbing and stockpiling: the emergence of mephedrone and the perversity of prohibition. *Drugs Alcohol Today* 2010; **10**: 14–21.
30. Moore K., Dargan P. I., Wood D. M., 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.
31. Bretteville-Jensen A. L. The New Zealand Psychoactive Substances Act (PSA): a policy breakthrough or just a symbolic act? *ADD Addict* 2014; **109**: 1590–1.
32. 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.
33. Diemen L. New psychoactive substances: issues about the new approach from New Zealand government. *Addiction* 2014; **109**: 1588–9.
34. Sumnall H. R. The New Zealand new psychoactive substances regime—a step in the right direction, but questions still remain. *J Psychopharmacol (Oxf)* 2013; **27**: 1076–8.
35. 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.
36. Ministry of Health. Drug Use in New Zealand: key results of the 2007/08 New Zealand Alcohol and Drug Use Survey [internet]. Ministry of Health NZ. 2010 [cited 8 October 2015]. Available at: <http://www.health.govt.nz/publication/drug-use-new-zealand-key-results-2007-08-new-zealand-alcohol-and-drug-use-survey> (accessed 2 April 2016).
37. Cunningham J. K., Callaghan R. C., Tong D., Liu L.-M., Li H.-Y., Lattyak W. J. Changing over-the-counter ephedrine and pseudoephedrine products to prescription only: impacts on methamphetamine clandestine laboratory seizures. *Drug Alcohol Depend* 2012; **126**: 55–64.
38. McBride D. C., Terry-McElrath Y. M., Chriqui J. E., O'Connor J. C., VanderWaal C. J., Mattson K. L. State methamphetamine precursor policies and changes in small toxic lab methamphetamine production. *J Drug Issues* 2011; **41**: 253–81.
39. Winstock A., Wilkins C. 'Legal Highs': The Challenge of New Psychoactive Substances [internet]. Rochester, NY: Social Science Research Network; October 2011 (cited 13 October 2015). Report no.: ID 2184359. Available at: <http://papers.ssrn.com/abstract=2184359> (accessed 2 April 2016).
40. European Court of Justice. Joined Cases C-358/13 and C 181/14 [internet]. 2014. Available at: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C_2014.315.01.0019.01.ENG (accessed 2 April 2016).
41. Iversen L. Oral evidence: psychoactive substances, HC 361. Sect. Home Affairs Committee House of Commons, London, UK, 15 September 2015.
42. Advisory Council on the Misuse of Drugs (ACMD). Naphyrone Report (2010) [Internet]. July 2010 [cited 2 April 2015]. (ACMD drug-specific reports). Available at: <https://www.gov.uk/government/publications/advisory-council-on-the-misuse-of-drugs-naphyrone-report-2010> (accessed 2 April 2016).
43. Home Office. Creation of a blanket ban on new psychoactive substances in the UK [internet]. London; May 2015. Report no.: HO0187. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/433151/NPSGBImpactAssessment.pdf (accessed 2 April 2016).
44. UK Parliament. Psychoactive Substances Bill [internet]. 2015. Available at: http://www.publications.parliament.uk/pa/bills/cbill/2015-2016/0063/cbill_2015-20160063_en_1.htm (accessed 2 April 2016).
45. Advisory Council on the Misuse of Drugs (ACMD). Consideration of the Novel Psychoactive Substances ('Legal Highs'). 2011. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/119139/acmdnps2011.pdf (accessed 2 April 2016).
46. Stevens A., Fortson R., Measham E., Sumnall H. Legally flawed, scientifically problematic, potentially harmful: The UK Psychoactive Substance Bill. *Int J Drug Policy* 2015; **26**: 1167–70.
47. MacLean K. A., Johnson M. W., Reissig C. J., Prinszano T. E., Griffiths R. R. Dose-related effects of salvinorin A in humans: dissociative, hallucinogenic, and memory effects. *Psychopharmacology (Berl)* 2012; **226**: 381–92.
48. Scott M. T. May wants to ban pleasure. 2 June 2015 [cited 8 October 2015]. Available at: <http://www.telegraph.co.uk/news/general-election-2015/politics-blog/11645354/Theresa-May-wants-to-ban-pleasure.html> (accessed 2 April 2016).