Mephedrone, new kid for the chop?

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ABSTRACT

Aims  Mephedrone (4-methylmethcathinone) is a novel synthetic stimulant drug that has recently become popular in the United Kingdom and elsewhere in Europe. It has a short history of human consumption and little is known about its prevalence and pattern of use. This study aimed to obtain preliminary data on its use and effects among dance drug users in the United Kingdom.

Design  Cross-sectional anonymous online survey of mephedrone recruited as part of a larger study exploring patterns of drug use among those associated with the dance music scene.

Setting  UK-based dance music and clubbing website.

Participants  A total of 947 ever users of mephedrone recruited as part of a wider study on dance drug use patterns.

Measurements  Assessment of demographics, ever and current drug use and patterns and selected effects following use of mephedrone.

Findings  A total of 947 (41.3%) of 2295 participants reported ever having used mephedrone. Mephedrone was the sixth most frequently used drug in the last month after tobacco, alcohol, cannabis, cocaine and 3,4-methylenedioxymethamphetamine (MDMA). Users were typically younger (P < 0.001) and male (P < 0.01); 15.1% reported using weekly or more frequently; 49.5% reported using between 0.5 and 1 g during a typical session; 69.5% reported that intranasal use was the most common route of use. Intranasal use was associated with increased abuse liability: 54.6% of those who have also used cocaine reported that the quality of the high obtained with mephedrone was better, with those using intranasally being significantly more likely than those who took the drug orally to report that mephedrone was more addictive (P < 0.02) and more risky (P < 0.02) than cocaine. Route of use was unrelated to any stimulant-related adverse effect apart from palpitations (P < 0.005).

Conclusions  Mephedrone appears to be used primarily intranasally and to have comparable abuse potential to cocaine, with more than half those who use both reporting that mephedrone gives a better quality high.

Keywords  Cathinones, internet, legal highs, mephedrone, stimulants.

INTRODUCTION

Mephedrone [4-methylmethcathinone, or 1-(4-methylphenyl)-2-methylaminopropan-1-one] is a phenethylamine and cathinone derivative with a relatively short history of human consumption which has rapidly become known by a number of marketable pseudonyms. These include 4-MMC, MMCat, Meow/Miaow Miaow, Bubbles, Meph, Rush, Drone and Plant Feeder. Sharing psychoactive properties of cocaine, amphetamines and methylenedioxymethamphetamine (MDMA), first evidence of its use appeared in online fora in at least 2007 [1]. Its appearance and widespread availability followed in the wake of recent legislation in the United Kingdom controlling piperazines [such as benzylpiperazine (BZP)], γ-butyrolactone (GBL) and a large number of cannabinoid agonists in December 2009. Mephedrone is one of a number of cathinones that are beta keto analogues of amphetamine; others include methylone (beta keto MDMA) and flephedrone (4-fluoromethcathinone). It should not be confused with methedrone (4-methoxymethcathinone, bk-PMMA), an analogue of para-methoxy-amphetamine (PMA), or methadone.

At the time of conducting this study, mephedrone was not legislated for under the Misuse of Drugs Act 1971 and was available legally in the United Kingdom and in most of Europe (it was already a controlled substance in
Sweden, Norway, Denmark, the Netherlands, Finland, Croatia and Estonia) using either drug control or medicines legislation. However, on 16 April 2010, 5 months after the study research period, mephedrone was classified by the UK government as a Class B drug under the Misuse of Drugs Act. At the time of writing it is currently the focus of European risk assessment by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) which will result in a risk assessment report by the end of August 2010.

Mephedrone is usually sold as a white crystalline powder with a light yellow hue, or as capsules, and widely available to purchase over the internet. Its marketing as ‘plant feeder’, ‘bath salts’, ‘research chemicals’, ‘not for human consumption’ and the absence of published studies on its pharmacology meant that mephedrone and related products fell outside the definition of a medicinal product and were thus not covered under the Medicines Act 1968. To avoid bringing unwanted attention from regulators, packages were also devoid of harm reduction advice or information on dosing, precautions, contraindications and associated risks [2]. Common modalities of intake are through snorting intranasally (insufflation) or by oral ingestion by either swallowing capsules, ‘bombing’ (wrapping mephedrone powder in cigarette papers and swallowing) or dissolving it in liquid [1,3]. Less common methods may include rectal administration and intravenous use [1].

The growth in interest and use of mephedrone, particularly in the United Kingdom, has been rapid. Google Insights for Search shows a steep increase in mephedrone-related searches since June 2009 [4]. Mainstream media and scientific advisory groups found it on their radar following a series of alleged fatalities and non-fatal overdoses in various European countries. There have been 10 or more reported fatalities in Europe in which mephedrone has been found in the post-mortem toxicology samples. However, apart from two confirmed deaths (one in the United Kingdom, one in Sweden), for the remaining cases the extent to which mephedrone was involved is not clear. Purported cases have involved seeing mephedrone taken as part of polydrug use (e.g. alcohol, ketamine, cannabis) and/or have reported uncertainty over the actual substance taken (i.e. mephedrone, methedrone or methadone) and in at least one case an unconfirmed coroner’s report gave the cause of death as cardiac arrest and bronchopneumonia [5–11]. Matters will become clearer once the relevant coronial inquests have been concluded. Some of the uncertainty in its involvement comes from the fact that it is not currently detectable on routine drug screens, although on some immunoassays it may show cross-reactivity with methamphetamine. Recent work has, however, permitted identification of mephedrone and other cathinones and their metabolites by gas chromatography-mass spectrometry (GC-MS) techniques [12].

To date there is very limited information available in the scientific literature regarding mephedrone use and associated risks, long-term side effects and toxicity, and there have been laboratory studies on the pharmacokinetics and pharmacodynamics in humans. What is known comes from analysis and monitoring of online fora and discussions, other online resources such as YouTube videos, single case reports and small-scale focus groups [1,3,10,12–15]. According to analysis of online sources carried out by the European Psychonaut Web Mapping Project, mephedrone may have significant abuse liability, with binges and redosing in a single session being common [1]. Analysis of websites also suggests that use results in typical stimulant-like consequences (e.g. anorexia, insomnia, teeth grinding and sweating), which is confirmed by later studies involving focus groups [1,3,10]. In some cases use has also been associated with visual and auditory hallucinations [1,3,10]. A recent case series of 15 presentations to an emergency department in London suggests that mephedrone may result in excessive sympathomimetic stimulation with agitation, tachycardia, systolic hypertension and seizures [15]. The median lethal dose (LD50) of mephedrone is not known.

This paper presents data from 947 ever users of mephedrone recruited as part of a larger study on club drug use, and is the first to provide detailed information on patterns of use, abuse liability and the incidence of adverse effects associated with the use of mephedrone.

**METHOD**

**Survey details**

An online cross-sectional survey was developed in line with previous work conducted by the researchers [16–18]. Utilizing a previously established collaboration with a dance music publication called MixMag, our research questionnaire was given a high profile and promoted through their associated website http://www.dontstayin.com (the survey is available to view at http://www.menincarter.net/mixmag/; also archived at http://www.webcitation.org/5ri0vOdJN) [16,19]. An online survey was considered a credible vehicle to use for opportunistic research that provided inexpensive and rapid access to large numbers of a sentinel drug-using population [16]. When judged against traditional epidemiological criteria for a good public health surveillance system this method has significant limitations, not least because it recruits from a self-nominating population that is relatively poorly characterized. In addition it relies upon self-reported experiences with a substance whose
true composition is uncertain. However, whatever the shortcomings of this approach, their imperfections are a major improvement on media anecdotes and precipitant often inaccurate public authority assumptions. Early on in a drug’s use history it can be difficult to conduct better studies. The results are thus an imperfect but useful way of scoping the possible size of the public health threat that new drugs of abuse comprise in a sample of regular recreational drug users with a history of experimentation with a wide range of similar recreational drugs. Previous studies by our group support the validity and reliability of such an approach in the early identification of new drugs [e.g. 4-methylthioamphetamine (4-MTA) [17]] and serial drug trends [19]. For further information about the utility, validity and limitations of the current methodology please see Winstock et al. and McCambridge et al. [16,17,19,20]. Ethical approval was received from the Joint South London and Maudsley and Institute of Psychiatry National Health Service (NHS) Research Ethics Committee.

In addition to basic demographics and prevalence of life-time and recent use of a large number of substances, four key measures of use were considered here for mephedrone: life-time use prevalence (ever used), age of first use, last 12-month use and frequency of use over this time, and prevalence and extent of current use within the last month (frequency and number of days used). Questions were also asked about the incidence of a range of stimulant-related physiological effects including excessive sweating, palpitations, nausea, headache, increased sex drive and cold blue fingers. Respondents were also asked to compare the effects of mephedrone to cocaine on four parameters: addictiveness, quality of high, duration of high and related risk.

### RESULTS

The survey went online on 17 November 2009, and as of 30 November a total of 2700 responses had been received, of which 2295 were from UK respondents; 65.3% of the UK respondents were male. The mean age of the whole sample was 25.0 years [standard deviation (SD) = 6.7] (male: mean = 25.2 years, SD = 6.9; female: mean = 24.6 years, SD = 6.4). The group were experienced polydrug users and mephedrone was the sixth most common drug used in the last month after alcohol (97%), tobacco (72%), cannabis (54.4%), MDMA (53.1%) and cocaine (47.4%). A total of 41.3% (n = 947) reported ever having used mephedrone (see Table 1), with 38.7% (n = 890) reporting use within the last 12 months and 33.2% (n = 762) reporting last month use. By comparison, the experience of the group with methylene and MDPV was much less, with respective ever use figures being 10.8% and 1.9%; last 12-month use figure 10% and 1.4%; and last month use figure 7.3%, 0.7%.

Of mephedrone users, 69.3% were male with an average age of 23.8 years (SD = 6.93, P < 0.001) and younger (t(2088) = 8.02, P < 0.005) and younger (t(2088) = 6.93, P < 0.001) compared to the whole UK sample.

A total of 137 users (15.1%) reported consuming mephedrone weekly or more often, 15.2% every 2 weeks, but the majority monthly or less often (69.7%). Those who reported use in the last month reported using, on

<table>
<thead>
<tr>
<th>Drugs ever useda</th>
<th>Total UK responses (n)b</th>
<th>Proportion of UK respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>2256</td>
<td>98.6</td>
</tr>
<tr>
<td>Ecstasy (pills)</td>
<td>2048</td>
<td>89.5</td>
</tr>
<tr>
<td>Tobacco</td>
<td>2047</td>
<td>89.4</td>
</tr>
<tr>
<td>Cannabis (grass)</td>
<td>1966</td>
<td>85.9</td>
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<tr>
<td>Cocaine (powder)</td>
<td>1916</td>
<td>84.6</td>
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<tr>
<td>Cannabis (resin)</td>
<td>1928</td>
<td>84.2</td>
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<tr>
<td>Cannabis (skunk)</td>
<td>1908</td>
<td>83.4</td>
</tr>
<tr>
<td>Ecstasy (powder)</td>
<td>1814</td>
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<td>Speed/amphetamine (powder)</td>
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<td>Isopropyl nitrite (poppers)</td>
<td>1547</td>
<td>67.6</td>
</tr>
<tr>
<td>Ketamine</td>
<td>1512</td>
<td>66.1</td>
</tr>
<tr>
<td>Nitrous oxide (balloons)</td>
<td>1364</td>
<td>59.6</td>
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<td>Magic mushrooms</td>
<td>1229</td>
<td>53.7</td>
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<td>Amphetamine (base)</td>
<td>1174</td>
<td>51.3</td>
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<td>Benzodiazepines/Temazepam/Valium</td>
<td>962</td>
<td>42.0</td>
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<td>LSD (trips)</td>
<td>960</td>
<td>41.9</td>
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<tr>
<td>Mephedrone</td>
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<tr>
<td>Legal high party pills (other)</td>
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<td>29.2</td>
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<tr>
<td>Salvia divinorum</td>
<td>658</td>
<td>28.7</td>
</tr>
<tr>
<td>BZP legal high party pills</td>
<td>593</td>
<td>25.9</td>
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<tr>
<td>Viagra</td>
<td>519</td>
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<tr>
<td>2CB</td>
<td>403</td>
<td>17.6</td>
</tr>
<tr>
<td>GHB</td>
<td>349</td>
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<tr>
<td>Crack</td>
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<tr>
<td>Spice/Magic/Warrior smoking blend</td>
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<td>12.6</td>
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<tr>
<td>2CI</td>
<td>257</td>
<td>11.2</td>
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<tr>
<td>Methylene</td>
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<tr>
<td>Ritalin</td>
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<td>Heroin</td>
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<td>GBL</td>
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<tr>
<td>Mephedrone (ice/crytal meth)</td>
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<td>Steroids</td>
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<tr>
<td>Blue Mystic (2C-T-7)</td>
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<td>2.4</td>
</tr>
<tr>
<td>MDPV</td>
<td>44</td>
<td>1.9</td>
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</tbody>
</table>

aRespondents were able to give more than one response. bTotal n = 2289 (six respondents did not answer). 2CB: 2,5-dimethoxy-4-bromophenethylamine; BZP: benzylpiperazine; GBL: γ-hydroxybutyric acid; LSD: lysergic acid diethylamide; MDPV: methylenedioxypyrovalerone; 2CI: 2,5-dimethoxy-4-iodophenethylamine.
average, 4.3 days (SD = 4.67) of the last 30, with 13.9% reporting use on 10 or more days in the last 30, 3.4% reporting use on more than 20 days and 0.4% reporting use on 30 days.

Almost half of respondents (49.5%, n = 443) reported using between 0.5 g and 1 g of mephedrone in a typical session, with 22.3% reporting more than 1 g.

There is a significant interaction ($F_{(5,884)} = 42.48, P < 0.001$) between average amount of use and frequency of use over the last 12 months, with those who reported using more frequently consuming more in a typical session.

The most common route of use was by snorting (65.9%, n = 624). No one reported intravenous use. Intranasal use was significantly more likely among women (76.2%, n = 208) than men (67.2%, n = 413) ($\chi^2 (1, n = 887) = 7.34, P < 0.01$). The amount used in a typical session was significantly larger for those who snorted the drug (mean = 0.97 g, SD = 0.91) compared to those who used the drug orally (mean = 0.74 g, SD = 0.64) ($F_{(6883)} = 3.63, P < 0.001$). Number of days used per month was significantly more for those who snorted the drug (mean = 4.85 days, SD = 5.11) compared to those who used the drug orally (mean = 3.12 days, SD = 3.01) ($F_{(1716)} = 20.49, P < 0.001$). Those who snorted mephedrone were also significantly more likely to use the drug more frequently than those using orally ($\chi^2 (5, n = 880) = 27.96, P < 0.001$), with 59.2% (n = 368) of those snorting the drug having used it at least monthly over the last 12 months.

The average length of a typical session was 10.4 hours (SD = 11.5). The average amount used was 0.91 g (SD = 0.84). There was a significant positive correlation between dose and duration of a typical session ($r = 0.45, P < 0.001$). The findings are consistent with previous suggestions that some individuals administer repeated doses throughout a session, with 8.2% (n = 69) reporting a typical session lasting 2 or fewer hours, 38.4% (n = 323) reporting a typical session lasting from 3 to 6 hours, 37.2% (n = 313) 7 to 12 hours, 9.6% (n = 81) from 13 to 24 hours and 6.6% (n = 56) more than 24 hours.

The frequencies of a range of stimulant-related physiological effects, including excessive sweating, palpitations, nausea, headache, increased sex drive and cold blue fingers, are given in Table 2. There was a significant dose–response relationship for the incidence of increased sex drive ($F_{(8679)} = 7.40, P < 0.001$) and excessive sweating ($F_{(1880)} = 8.23, P < 0.001$). Route of administration was unrelated to the incidence of any effect except palpitations which were reported significantly more frequently by those taking the drug intranasally ($\chi^2 (4, n = 889) = 15.08, P < 0.01$).

Participants who reported ever having used cocaine and also used mephedrone (n = 857) were asked to compare the quality and duration of mephedrone’s ‘high’ to that obtained from cocaine and to compare addictiveness and relative risks of the two drugs. The most common route of use was also taken into account for this subsample. These results are presented in Table 3.

The majority of respondents who had previously used cocaine reported that mephedrone provided a longer-lasting (65.2%) and better high (54.6%) than cocaine, with the same level of risk (47.3%) as cocaine, albeit being less addictive (55.7%).

However, those who snorted the drug were significantly more likely to rate mephedrone as more addictive than cocaine ($\chi^2 (2, n = 792) = 8.04, P < 0.02$) and as carrying more risks ($\chi^2 (2, n = 787) = 7.97, P < 0.02$) than cocaine compared to those taking the drug orally. Those who reported taking the drug orally were significantly more likely to indicate that the duration of high was longer compared to that from cocaine ($\chi^2 (2, n = 791) = 14.80, P < 0.001$). There was no impact of route of use on the comparative perception of the quality of the high. There was a dose–response relationship between the comparative quality of the high ($F_{(2798)} = 6.81, P < 0.001$) and the addictiveness of the drug ($F_{(2791)} = 9.49, P < 0.001$).

**DISCUSSION**

This is the largest report on patterns of use and associated psychotropic/physiological effects of mephedrone in a
human population. The findings suggest that the drug has become popular at the very least among a group of experienced polydrug users associated with the dance music scene. The results indicate that mephedrone consumption results in typical stimulant-related physiological effects, which appear to be dose-related. The findings regarding how mephedrone is perceived compared to cocaine are consistent with the possibility that the drug presents with high levels of abuse liability. This is supported by the finding that the majority of users who have used cocaine previously perceive mephedrone to have a better high than cocaine, regardless of route of administration. The intranasal route of use appears to be associated strongly with increased abuse liability, with those using by this route using significantly larger amounts more often and rating the drug as more addictive than those using the drug by the oral route. This may be related to a more rapid rise in plasma levels of the drug when taken intranasally [21]. Although questions regarding tolerance were not asked about specifically, the finding that more frequent use was associated with significantly higher average levels of consumption is consistent with the development of tolerance. It seems likely that some people will become dependent.

More than two-thirds of respondents reported consuming half a gram or more over a session, a finding that is consistent with online reports that mephedrone has a shorter duration of action and is less potent compared to MDMA or amphetamine [1]. Online reports suggest that effects commence 1–20 minutes after oral use, peaking at 45–60 minutes, with a come-down occurring 60–120 minutes after use [1].

This study’s findings of common stimulant effects such as palpitations and excessive sweating are consistent with those seen with typical sympathomimetic substances such as amphetamine and cathinone (which is identified in the leaves of khat) [22]. Other effects, including headache, nausea and increased sex drive, have also been reported following use of amphetamine-type stimulants [23]. It is unclear why only sweating and sex drive showed a significant dose–response relationship. If mephedrone shares any of the potential cardiotoxic effects of cathinone/khat, then use in excess or in those with predisposing cardiac conditions may also represent a risk factor for cardiac events [24]. The 15.3% of respondents who reported ever having experiencing cold blue fingers or toes suggests that mephedrone may also share peripheral vasoconstrictive activity seen with other amphetamines and cathine/cathinone [25]. There are also several case reports that have linked the intravenous abuse of the related compound methcathinone (ephedrone) with a parkinsonian syndrome suggestive of dopaminergic neurotoxicity, albeit possibly related to manganese toxicity [26,27]. Although online forums describe mephedrone use via injecting, smoking and rectal use, the current study enquired only about oral, intranasal and intravenous (i.v.) use. However no i.v. use was mentioned by these users.

This study did not explore the prevalence of serious adverse effects or the incidence of psychological experiences such as panic, anxiety, paranoia or perceptual disturbance. However, given the drug’s apparent sympathomimetic effects it is possible that some individuals,
especially after taking higher doses, will be at risk of experiencing such symptoms.

Overall, the findings are consistent with reports that compare mephedrone variously to speed (amphetamine), MDMA, a combination of amphetamine–cocaine, amphetamine–MDMA, butylone and methylene [1,3,10]. According to online analysis and focus groups, mephedrone is desirable as it elicits euphoria, sociability, stimulation and auditory enhancement, with a smoother ‘come-up’ and ‘come-down’ than MDMA (similar to methylene) and with the absence of a hangover the following day [1,3,10]. This study did not explore the potential for the drug to induce pro-social, entactogenic and empathogenic effects that are seen with MDMA, but it may be these qualities that led users to rate the quality of the drugs high as being superior to that of cocaine.

The question remains as to why mephedrone has suddenly become so popular. While widespread web-based marketing and ease of online accessibility, combined with versatility in terms of route of administration, and its legal status no doubt play a role, it is likely that other factors are also important. During the last decade there has been a steady decline in the purity of cocaine in the United Kingdom, from 45% in 2004 to 26.4% in 2009 [28]. Similar trends have been observed for ecstasy in both the United Kingdom and Europe, with many pills having been found to contain BZP or methchlorophenylpiperazine (MCP) [2,28,29]. Conversely, mephedrone and related products are marketed by online retailers as being consistently high in purity, often 99.7% pure [1]. Thus, dissatisfaction with the illicit drug market, coupled with the perception of quality associated with mephedrone, may have led to ripe market conditions for an effective licit competitor to gain a foothold.

In addition, the appeal of mephedrone may not be limited to just the end user. At present, high yields from relatively straightforward manufacturing processes utilizing accessible precursors means that the attraction of synthetic stimulant compounds such as mephedrone to web-based companies and potentially organized crime is considerable. The mark-up on such products is likely to be enormous, and they may overall prove more profitable than illicit synthetic stimulants such as MDMA. What the impact of recent legislation will be upon cost, availability and purity is uncertain. There are already reports that mephedrone has simply been re-packaged and re-branded and marketed online as a currently legal alternative [30]. The possibility that mephedrone will migrate to the illicit market is high. The potential impact of the interplay between access and legality on the UK recreational drug market, together with the policy implications of this, are discussed by Measham and colleagues [31].

LIMITATIONS

Although of a good size, this study is limited by the self-nomining nature of the sample and the self-report methodology. These limitations and others are discussed fully in Winstock et al. and McCambridge et al. [16,17,19,20]. However, we have shown previously that self-report studies among dance drug-using populations may be a valid and effective tool for monitoring drug trends and detecting the appearance of new drugs [17,19]. Drug users who are associated with the dance music scene can be seen to represent a sentinel population of drug users likely to represent a harder end of users [16]. This paper suggests that there has been a sharp rise in popularity of mephedrone; however, as we did not ask when participants first used mephedrone, and in the absence of any baseline epidemiological use data, this can ultimately only be an informed supposition. Finally, as with all studies that rely upon self-reported consequences of illicit substances, there is no way of confirming that the substance upon which participants have based their responses was in fact mephedrone, or the actual amounts consumed, particularly given the confusion that exists between mephedrone and other similar-sounding compounds such as methedrine, methylene and methadone, and the lack of information on product packaging. In addition, given the high rate of polydrug use among this group, it is possible that user reports of mephedrone’s effects were modified and potentially confounded by the concurrent ingestion of other substances, including alcohol. However, in research investigating new and emerging drug trends reliance upon user reports in the first instance is a necessary approach, especially in the case of ‘legal highs’, for which data from seizures, and clinical and toxicological studies are often limited, if not unavailable. That the results of the current study have confirmed data gained from online analysis, focus groups and case reports serves to highlight the importance of this methodology in the early research of new recreational drugs.

CONCLUSION

The rapid emergence of mephedrone in this sentinel drug-using population is indicative of a phenomenon of web-based information sharing and the near-global availability of easy and relatively cheap access to a range of potent psychoactive drugs [32,33]. It is unclear to what degree changes in legislation will impact upon the availability of the drug. Although web sales will decline it is probable that the drug will make a rapid transition to the illicit street market.

Currently, harm reduction advice can only take the form of general common sense precautions that apply to
any psychoactive drug; in particular, avoiding using mephedrone at all, or at least avoiding use in combination with other stimulant drugs or alcohol, avoiding use by those already taking cardiac or psychiatric medications and avoiding the development of tolerance by restricting use to the smallest amounts separated by the greatest periods of time [34].

In the absence of any further information, those working within clinical settings should consider mephedrone and other legal high stimulant use in young people presenting with symptoms suggestive of a sympathomimetic over-stimulation.

This survey represents the first systematic attempt to describe the pattern of mephedrone use in the United Kingdom and to identify abuse potential and perceived harms in a sentinel drug-using population. Further basic science, epidemiological and clinical research is required to determine the nature and extent of risk associated with its use.

**Declarations of interest**

None.

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