European Monitoring Centre
for Drugs and Drug Addiction

Appendix 1 to Annex 1 (Technical report on mephedrone):

MEPHEDRONE: ASSESSMENT OF HEALTH RISKS AND HARMS

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Note: This study is unpublished.

MEPHEDRONE: ASSESSMENT OF HEALTH RISKS AND HARMS

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Preliminary report

PURPOSE

There has been a sharp rise in the availability and consumption of mephedrone and other synthesized cathinone class -keto analogues of amphetamines in the UK. The authors have an ongoing research programme on new synthetic substances and have been commissioned by the EMCDDA to report on the health risks and harms of mephedrone as part of the Centre's risk assessment process. This report summarises the work conducted to date (23rd June 2010) as part of the assessment of mephedrone health risks and harms undertaken by Drs Winstock's and Marsden's group for the EMCDDA.

BACKGROUND

Psychoactive substance use is a shifting phenomenon in which new and emerging substances take their place in communities across the EU as recreational drugs used by young people. While substances have been produced and marketed with the explicit aim of circumventing legislative restrictions for several decades, their current potency, profile and availability in combination with global web-based marketing and distribution networks poses a new challenge for policy makers (Winstock and Ramsey 2010). There is wide variability in the use of substances both within and between member states, but several substances have attracted widespread concern in Europe, none more so than mephedrone (Winstock et al 2010). Despite these concerns and recent legislation scheduling cathinones and a number of other synthetic stimulants in the UK and elsewhere, there has been no systematic assessment of the perceived effects of these drugs on users and the associated health and social risks and harms arising from their consumption. The aim of the current study is to shed light on these questions.

Mephedrone appears to be used by several population groups, including young adults involved in the dance and music scene, mainstream young adults, and also younger users in mid through to late adolescence and young adulthood (15-19 years). Young adult users of psychoactive substances (who are the main population using these substances) are unlikely to be in contact with treatment services. They tend to be a sentinel but somewhat difficult to access population. Traditional survey and screening methods are problematic and there are very few epidemiological surveys of drug use among the general adult population in Europe. Aside from the substantial cost of staging large-scale surveys using probability sampling methods, the target populations are relatively hidden and may not respond well to direct contact. Although considerable caution must be exercised when using purposive sampling methods, this approach compares well with probability methods. Moreover, cross-sectional surveys using the sample methodology enable some basic conclusions to be drawn about time trends where threats to the reliability and validity of data can be shown to be constant (McCambridge el al 2005 and 2007).

Since 1999, our research group has been staging an annual survey of nightclub drug users has been conducted in conjunction with *Mixmag*, a specialist dance music magazine. Mixmag had a history of extended drug-related copy in its pages. It was considered a credible vehicle to use for opportunistic research that provided inexpensive and rapid access to large numbers of the target population (Winstock et al 2001). With research ethical approvals secured, readers were invited to return by freepost a questionnaire printed in the magazine itself. This option was supplemented by online access to the questionnaire in 2003. In 2009 the annual survey was conducted for the first time in 5 years and

with the support of the editorial staff and research team we developed an innovative web-based survey platform as part of the website called *Don't Stay In* (DSI). This website is the first accessed by open text search using this phrase in Google (http://www.dontstayin.com/). It attracts young people with an interest in music, dance, and events. The annual survey was heavily published on both the 'dontstayin' website and the Mixmag homepage. Between November 2009 and May 2010 over 3500 people completed the on-line survey.

SAMPLE POPLULATION

Approximately 600 participants in the on line survey gave contact details and expressed a willingness to participate in further research. The current sample was drawn from members of this group who were identified as ever having used mephedrone and who had provided their mobile telephone numbers (>200 individuals).

DESIGN AND RESEARCH QUESTIONS

The study was a cross-sectional survey, administered as an abridged structured telephone interview, with biological screening for mephedrone and similar compounds. Naturally, the most desirable approach to assess the profile of a new drug of abuse would have been via a comprehensive data gathering exercise with a large sample from diverse using populations. We did not have this opportunity – so our work inevitably has limitations; but we expect that our approach may have valuable implications for the design, implementation, analysis and interpretation of substance use risk and harm research. It may also be the case that in studying relatively new users of a substance, there may be little harms experienced – but on the other hand early assessment of emerging negative effects and experiences is also valuable in its own right.

STUDY INTERVIEW INSTRUMENT

The team already had some early data on mephedrone from the initial on-line survey (Winstock et al under revision 2010) as to what the profile of use and associated harms may be. Based on a review of available on-line discussion-forum and a review of mephedrone conducted by the Psychonaut group, the research team developed an abridged structured interview for telephone administration. The questions were aimed at identifying the abuse liability and patterns of use of mephedrone, its risk and positive effect profile and motivation for use. The questionnaire also explored the drug in comparison to cocaine and MDMA in a broad attempt to 'footprint' the drugs in terms of abuse potential and overall effect profile. Through a pool of candidate items and cognitive testing, we have developed a 20 minute interview with 61 items (the questionnaire is provided in the appendix). The structure and variable set is summarised in Table 1:

Interview Structure

Section 1: **Demographics**	1.1 Age 1.2 Sex 1.3 Height 1.4 Weight 1.5 Employment status
Section 2: **Stimulant comparisons**	2.1 Frequency of cocaine and ecstasy use 2.2 Effects comparison between ecstasy, cocaine and mephedrone 2.3a Influence of mephedrone on ecstasy 2.3b Preference to use mephedrone over ecstasy and cocaine
Section 3: **First mephedrone session**	3.1 First dose amount and route taken 3.2 Number of doses 3.3 Session duration 3.4 Total amount used in session 3.5 All administration route(s) used 3.6 Other drugs taken during session
Section 4: **Summary of mephedrone**	4.1 Month/year first and last occasion 4.2 Days used each month from first to last 4.3 Max number of 2+ consecutive days used <u>Typical session</u> 4.4 Use alone or in company 4.5a Amount and admin route for first dose 4.5b Estimated number of lines/bombs from 1g 4.6 Number of doses 4.7 Time between first and second dose 4.8 Total amount respondent uses in typical session 4.9 Total amount used 4.10 All admin routes used in session 4.11 Alcohol and other substances consumed 4.12 Estimate of total amount of mephedrone used most recent month <u>Max session</u> 4.13 Total amount respondent used on max session 4.14 Duration of max session 4.15 Alcohol and other drugs used <u>Overall summary</u> 4.16 How ever obtained mephedrone 4.17 Internet sites bought from 4.17a Typical amount from single internet purchase 4.17b Max amount from single internet purchase 4.18 Appearance and odour

	4.19 All different situations/places used 4.20 Mephedrone use motivations 4.21 Frequency and intensity of effects 4.22 Most common routes 4.23 Routes wouldn't use again 4.24 Hangover/withdrawal effects 4.25 Mephedrone dependence 4.26 Had emergency medical treatment 4.27 ever fainted, collapsed, fitted (other drugs)
Section 5: **Other stimulant use**	5.1 Ever used methylone (times used) 5.2 Ever used butylone (times used) 5.3 Ever used MDPV (times used) 5.4 Ever used flephedrone (times used) 5.5 Mephedrone makes more like use other stimulant drugs 5.6 Will use mephedrone again? (if not, reason?)

BIOLOGICAL ANALYSIS

One of the often cited limitations of self report studies of emerging drugs of abuse is the uncertainty that the participants are actually taking the substance they think they are consuming. In order to address this concern and provide further information on the toxicological and metabolic profile of mephedrone we requested all participants who expressed an intention to use mephedrone again to send us a urine sample as soon after use as possible for laboratory analysis. Our colleagues at St George's have developed a protocol for cathinone derivative screening by GCMS and LCMSMS. For GC-MS screening, they have developed a procedure for ten methcathinone related compounds (Cath,MC, EC, 4-MMC, 2-FMC, 3-FMC, 4-FMC dimethylcathinone (DMC), 4-methoxymethylaminobutyrone (4-MAB) and 4-methoxymethcathinone (4-MoxyMC)). Cath and MC have been purchased from Sigma-Aldrich. 4MMC was purchased from LGC Promochem. All other derivatives of Cath and MC were synthesised 'in-house' by Kingston University. The contents of capsules or powders were dissolved in methanol and analysed by gas chromatography with mass spectrometric (GCMS) detection in scan mode. Chromatographic separation was achieved for all derivatives over a 12min run. All urine samples will be analysed on a Shimadzu QP2010 gas chromatograph mass spectrometer with an HP5MS column (30m x 0.25mm, 0.50µm).

For the LC-MS-MS screening, a quantitative method has been developed for two of the principle derivatives seen in biological samples (4-MMC and 3-FMC). Liquid chromatography with tandem mass spectrometric detection will be used to confirm and quantitative 4-MMC and 3-FMC in the urine samples. 4-Methylmethcathinone metabolites; 4-Methylephedrine and 4-methylcathinine, are currently being added to this method for screening and confirmation.

Background and risk covariates

Demographic	• Age • Gender • Body-Mass Index
Other substance use	• Other substances taken during mephedrone session
Mephedrone	• Uses alone • Route (oral vs. smoking/injecting) • Whether bought from internet (max purchased) • Use of other cathinones • Total number of mephedrone sessions (initiation to survey) • Number of doses on typical session (and max session) • Duration of session • Total amount used on session (possibly log transformed) • Using mephedrone for two or more days consecutively • Number of different forms of mephedrone used

Mephedrone 'response' measures

The core measures in the interview relate to mephedrone harms experienced acutely during a session as well as in the days following a session (withdrawal symptoms).

Mephedrone	• Negative effects:
	  ▪ Restless, agitated, aggressive, panicky
	  ▪ Paranoid-type delusions
	  ▪ Cardio-vascular
	  ▪ Circulatory/peripheral
	  ▪ Neurological
	• Withdrawal symptoms
	• DSM-IV dependence symptoms
	• Emergency medical treatment presentation
	• Collapsed while using

Results

Given that we have not completed coding for all questionnaires and have not completed the analysis on submitted urine samples the current draft report will only present a headline summary of the patterns of use (including dependence) and acute positive and negative effects and withdrawal symptoms associated with the use of mephedrone and then profile these according to sub-groups which we identify. The majority of the findings will be given in the form of graphs, with explicit numerical clarification only provided for sentinel findings.

Sample size (100)

A total of 109 participants have to date completed the questionnaire. This preliminary report is based on the 100 questionnaires that have been coded to date. To date 14 urine samples have been analysed 9 fully using GCMS. The remaining 5 have been analysed by GCMS only so far with LC-MS-MS analyses currently being conducted.

Status	n
Completed interview and data coded	100*
Respondents invited to send urine sample	28
Future users who agree to provide urine sample	14
Samples arrived at laboratory	14

Sample characteristics

The sample was 23 % female, with a mean age of 25.1yrs. The average height of the males was 1.80m, weight 74.5kgs (mean BMI 23), of the females 1.64m, weight 59.1kgs (mean BMI 21.8).55% of the sample were employed, 31% in education and 5% unemployed = 5.0%.In keeping with the sample that they had been drawn from their lifetime use of other stimulant was very high, with 96% ever having used Ecstasy and 92% cocaine.

First use

Detailed information was obtained regarding the time and pattern of their first ever use as a baseline measure. All used participants reported their first use between 2008-2010 (88% in 2009). 83% reported their first dose was administered as a “line” of the drug (as opposed to tipped out powder, a pill or an emptied capsule) that estimated as being 96.6mg. The route of administration of this first dose was most commonly (73.5%) intranasal (snorting), with 10.8% reporting bombing (swallowing often in a cigarette paper); 14.5% in drink and 1.2% IV. A mean of 5.6 doses (totalling an average of 605.5mg) was administered on this first occasion of use over a session that lasted a mean of 8.6 hours. On this first occasion of use 89% reported drinking alcohol, 17% used cocaine, 23% used ecstasy, 34% used cannabis, and 24% used ketamine.

Typical mephedrone session

Information was then obtained on a typical session of use focusing on dose, frequency and setting. On average participants reported having been using for 6.1 mo (s.d. = 3.1). All participants reported using with others (a mean of 10 (s.d 7.9) other users), with no reports of typical use being alone. 83% administer the first dose of a session as a line of the drug most commonly through the intranasal route (79.0%), with 9.9% reporting bombing; 11.1% in drink and 0% IV). The first administered doe was estimated to be 124.8 mg (28.2mg more than initiation), with the modal time between doses being 30 mins or 1 hr. Over the course of a mean typical session lasting 13.9 hrs (s.d. = 16.59) an average of 1.09 gm was consumed though the range was huge (100-9000 mg), During a typical session 82% reported drinking alcohol, 36% cannabis, 35% ketamine, 26% using cocaine, 23% ecstasy, 2% GBL and 1% amphetamine.

Summary of use over the last month of use

Participants were asked to estimate the total amount of mephedrone used over the last month of use. The range was 50mg – 15gms; median = 1.5gms; mode = 1gm.

Maximum session since initiation

Participants were asked to describe their heaviest session of use since they started taking mephedrone and what proportion had used the drug on more than 2 consecutive days. Participants estimated that the total amount used in their heaviest session ranged from 100mg – 16 gms; median = 1.5 gms; mode = 1 gm. The estimated duration of max session varied widely between 1-192 hrs with a median/mode of 12hrs. 47% reported that they had used for more than 2 days in row. For these participants a median of 3 days consecutive use was reported. Table 1 shows the correlates of larger maximum amounts used (50mg-1.4g / >1.5gm)

Table 1 Correlates of larger maximum quantity used

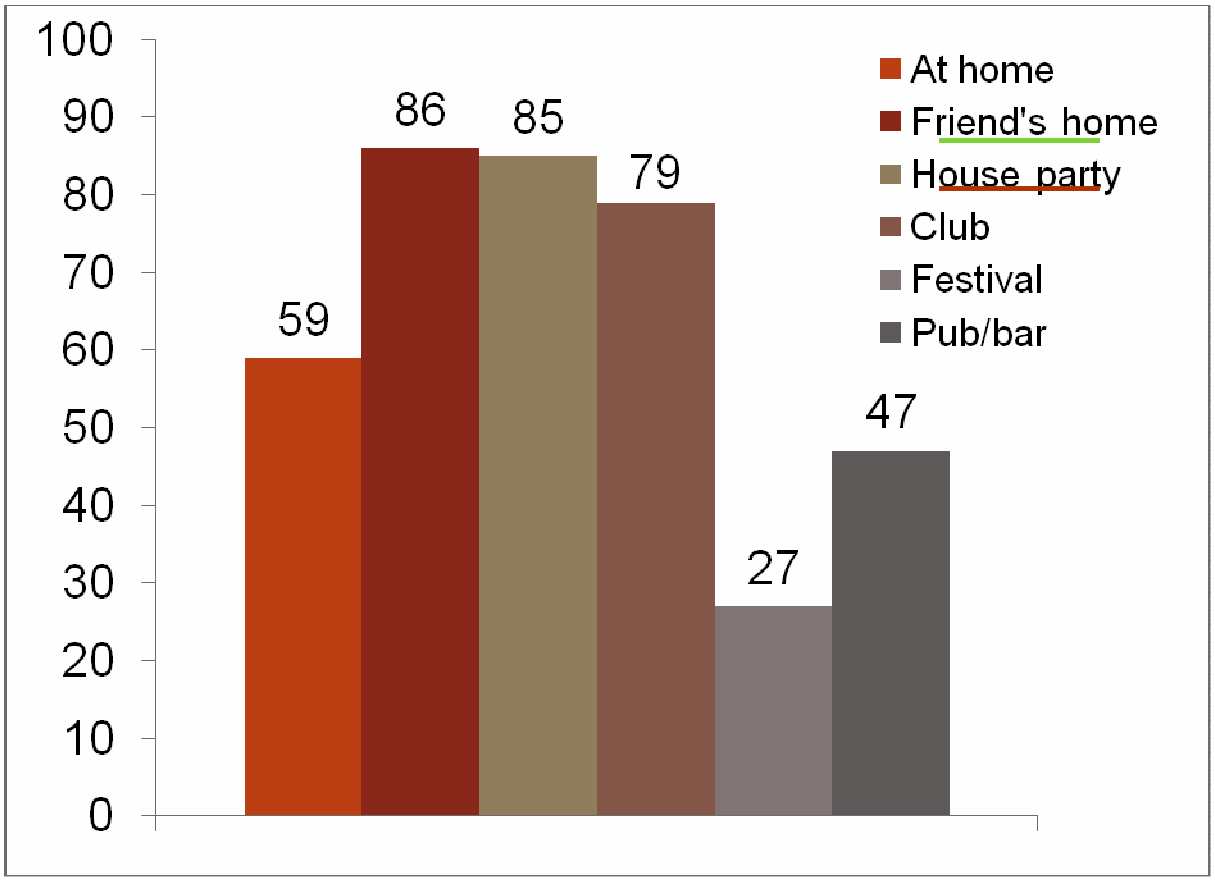
Variable	P-value	Adjusted OR
Age	0.04	0.89
Felt panic when using	0.03	0.33
Felt paranoid when using	*0.02*	*3.24*
Had headache when using	*0.02*	*2.55*
Had sweats when using	0.01	16.56
Developed tolerance	0.02	0.262

Had craving to use day after	0.02	0.48

Situations where mephedrone has been used

Participants reported ever having used mephedrone at a friend's home (86%), a house party (85%), a club (79%), at home (59%), pub/bar (47%), and a festival (27%). Most common were a friend's home or house party (see Figure 1)

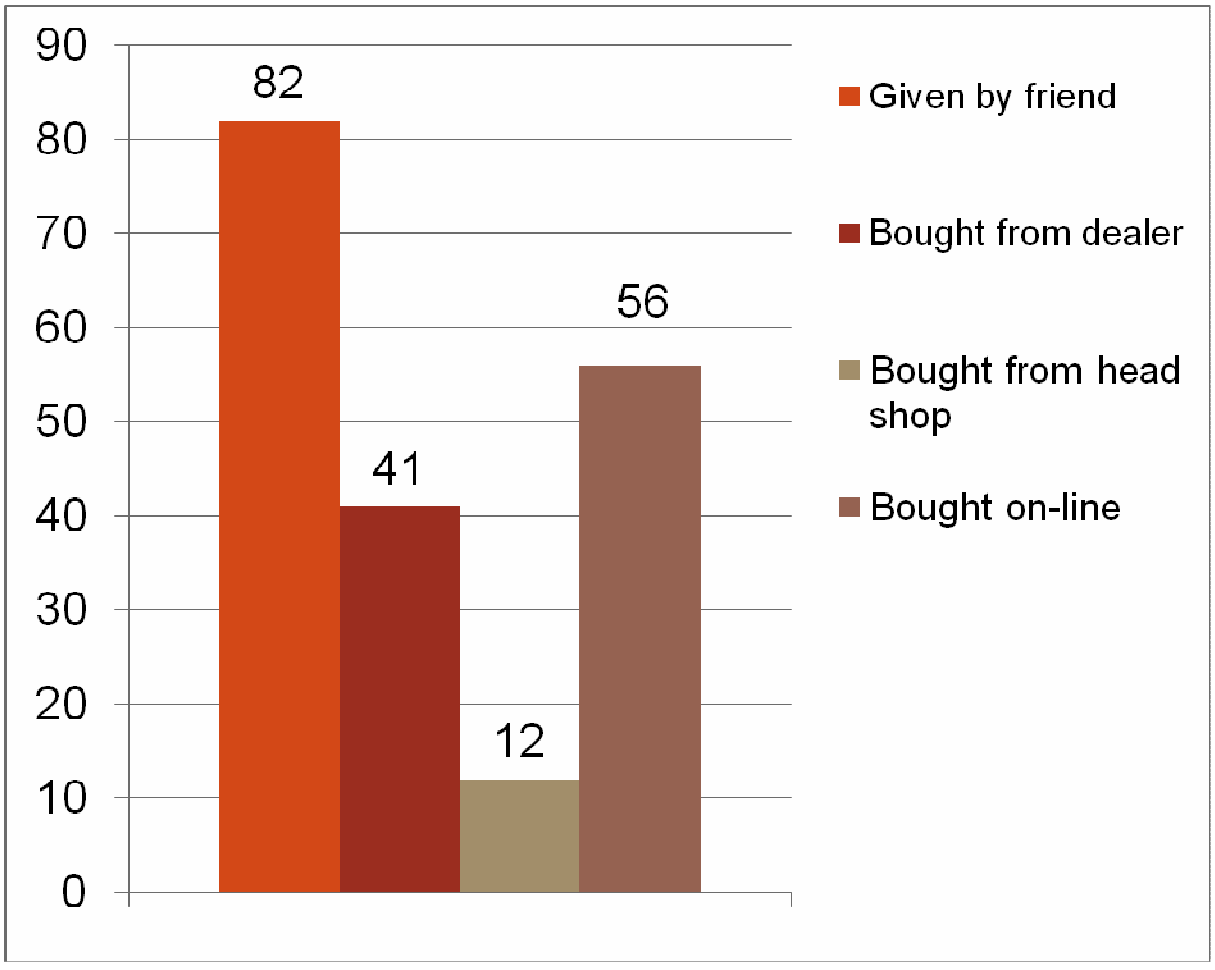
Figure 1 Where people use mephedrone



Ways of obtaining mephedrone

Participants were asked how they had ever obtained mephedrone, the most common place were on-line and from friends. The median amount purchased was 5gm with a mode of 2gm (range 1- 50 gms). Research Chemicals, UK Legals, Mephedrone2U, PlantFoodPalace and Mr Meph were the most commonly reported sites for purchase.

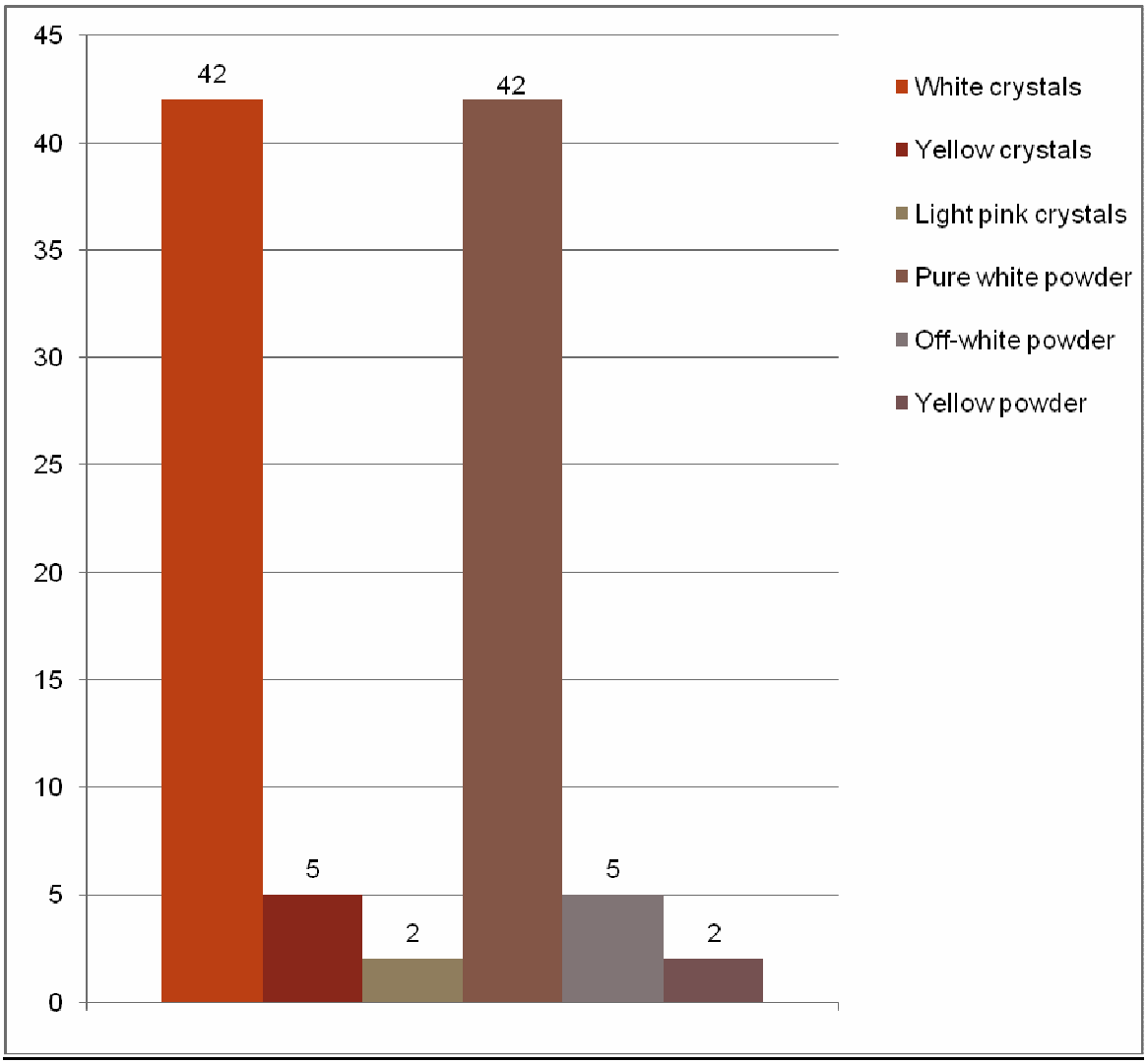
Figure 2 Ways of obtaining mephedrone



Usual appearance and smell of mephedrone

Participants were asked to describe physical characteristics (from a selection of provided options) of the purchased product (see figure 3)

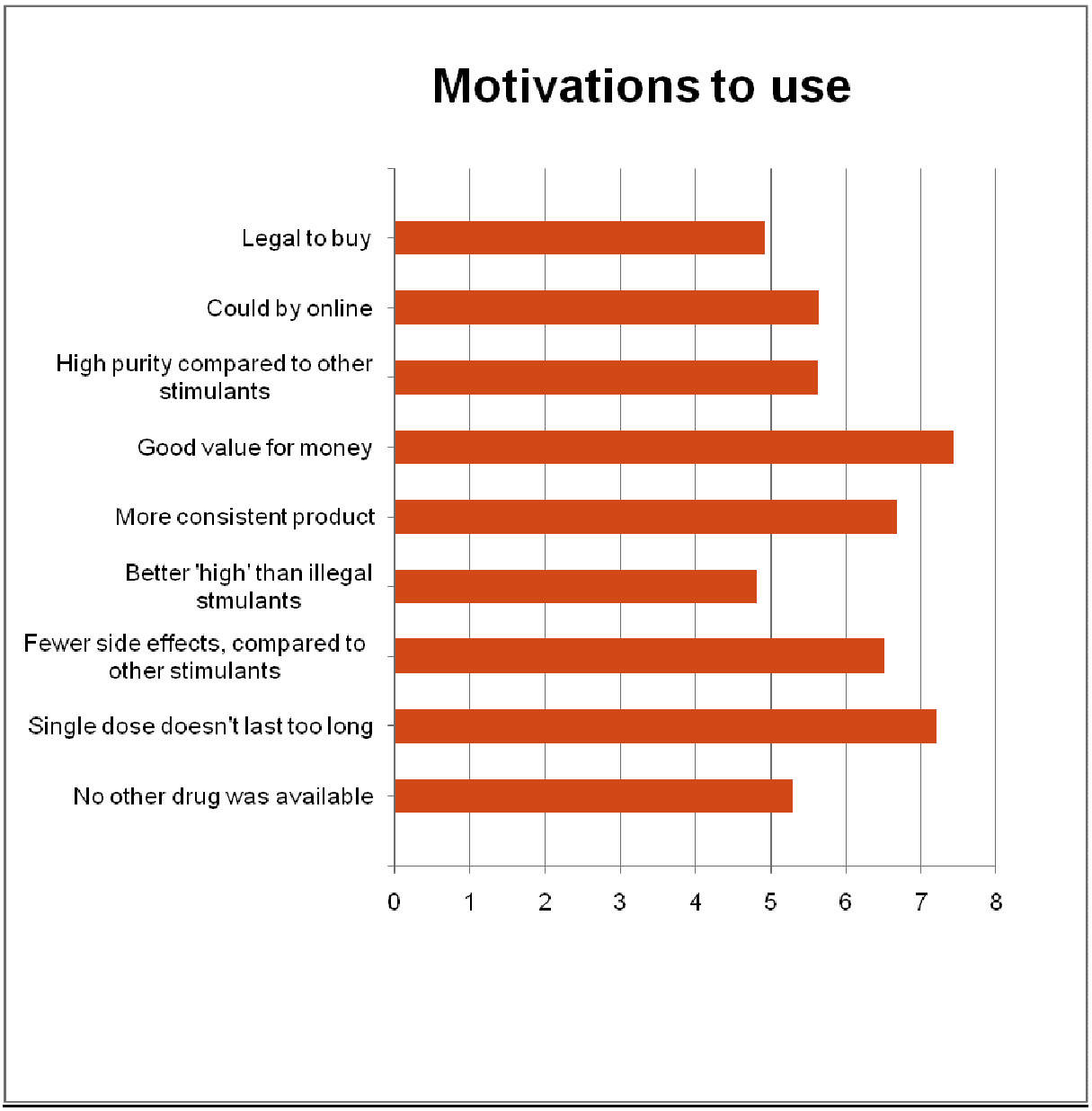
Figure 3 Physical characteristics of purchased mephedrone



Motivations for use (figure 4)

Participants were asked what motivated them to use mephedrone and were asked to rate on a scale from 0 to 10 where 0 is "no influence at all" and 10 would be "the maximum influence possible", how motivating a range factors have been when you've taken mephedrone. Value for money, consistency of product, side effect profile and short duration of effect were reported as being more important than its legal status or availability on-line.

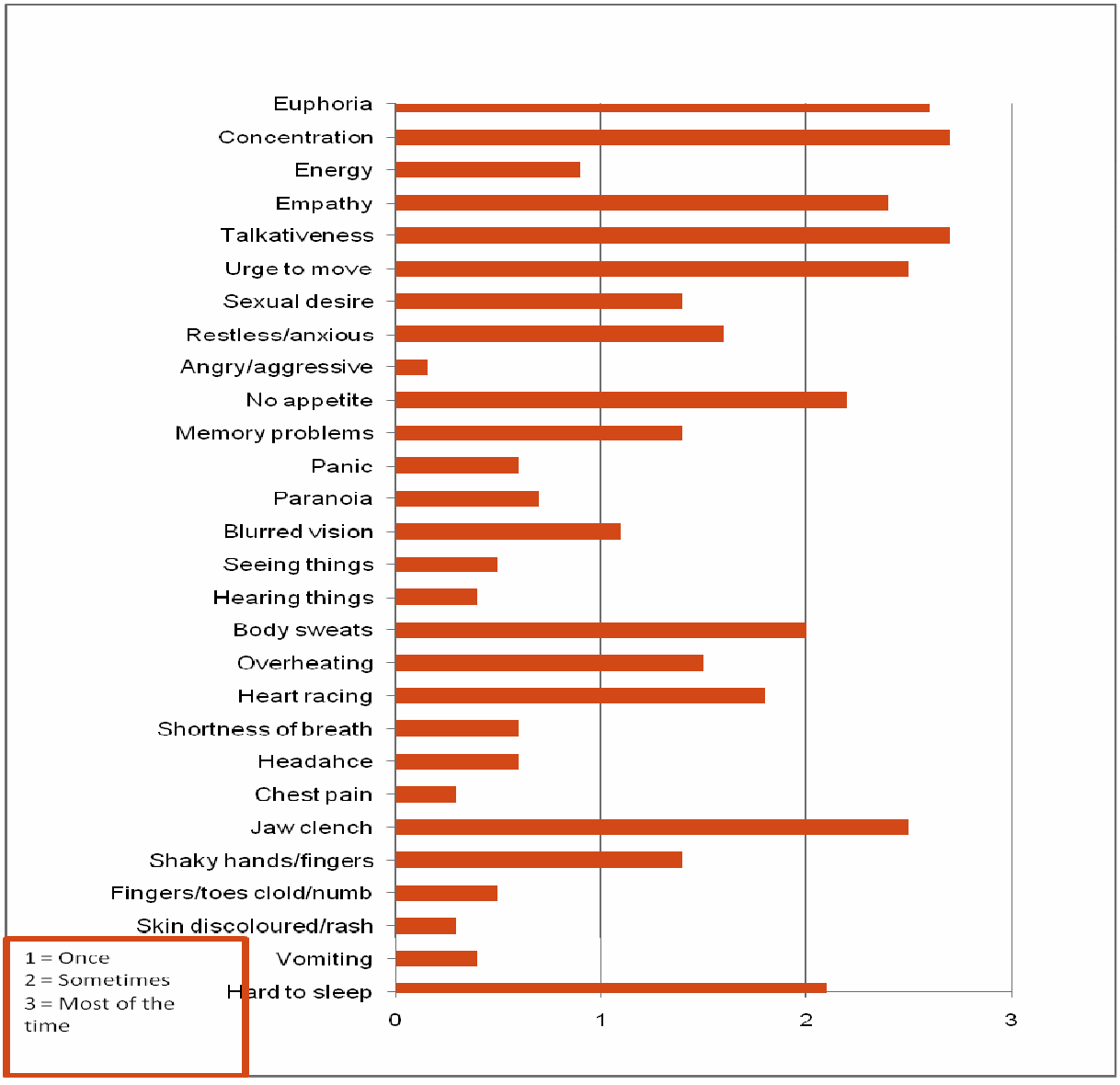
Figure 4 Motivation to use mephedrone



Effect profile (see figure 5)

Participants were asked about the frequency (how often 'never', 'once', 'sometimes', 'most of the time' *and* intensity (how intense 'mild', 'moderate' 'intense') of 28 typical stimulant and empathogen drug effects (both positive and negative and physical and psychological). The results are shown in figure 5. Mephedrone's predominant effect profile is that of a typical stimulant drug with evidence of frequent sympathomimmetic physical effects. The drug also appears to have a quite marked prosocial profile with relatively infrequent adverse psychological effects.

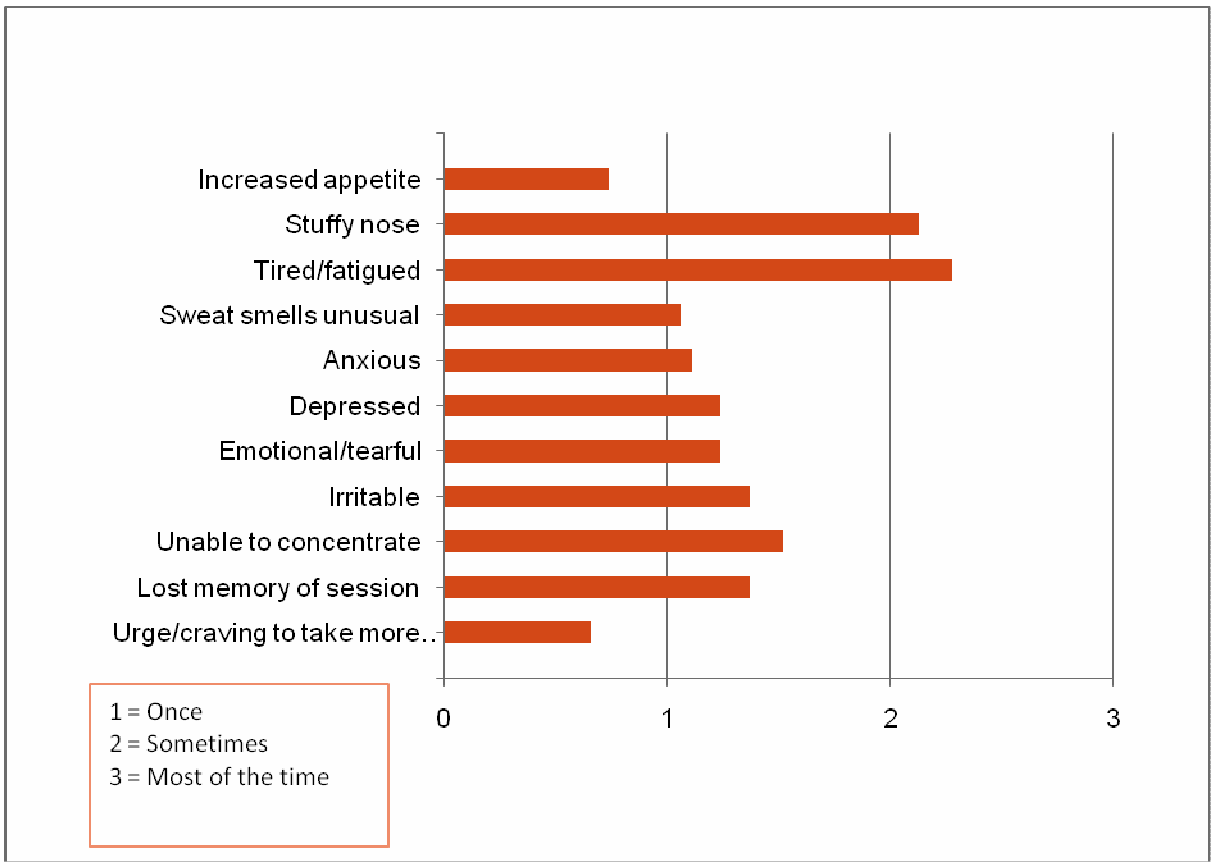
Figure 5 Frequency of intensity of mephedrone effects



Withdrawal (comedown) symptoms and severity

Participants were asked about how they felt during the next day or two after a session by indicating how frequently each of a number of typical stimulant withdrawal symptoms were experienced and their intensity. The frequency of withdrawal symptoms is shown in table 6.

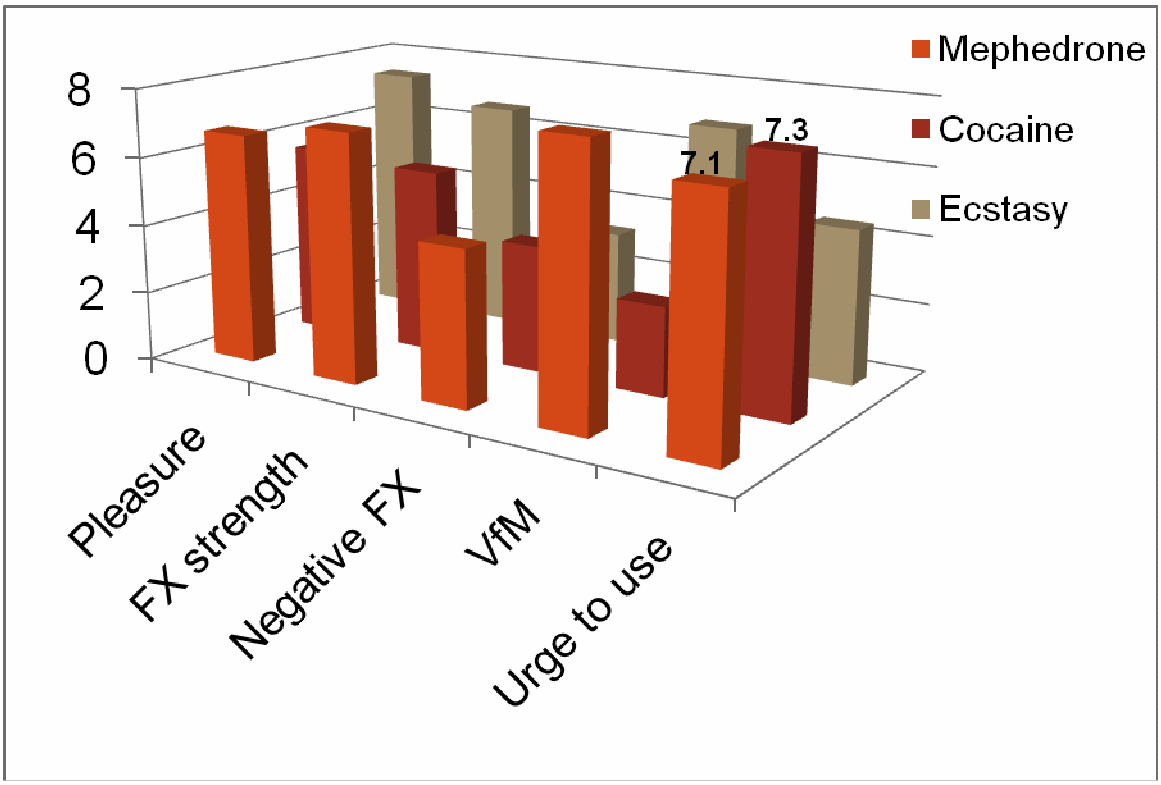
Table 6 Frequency of mephedrone withdrawal effects



Subjective effects compared to cocaine and ecstasy.

Participants were asked to rate each of the 3 drugs (as they are available currently) out of 10 (0= low 10= high) across a range of broad descriptors; the 'pleasurable high' of the drug, the 'negative effects of the drug when high', the 'strength of effect', the 'urge to want more of the drug when using' and value for money. As can be seen in figure 7 across all domains, mephedrone scored more highly than either cocaine or ecstasy including negative effects. The impression from these questions is that mephedrone is more similar to ecstasy except that its urge profile is comparable to cocaine.

Figure 7 Subjective comparisons of mephedrone, cocaine and ecstasy (rating 0-10 scale)



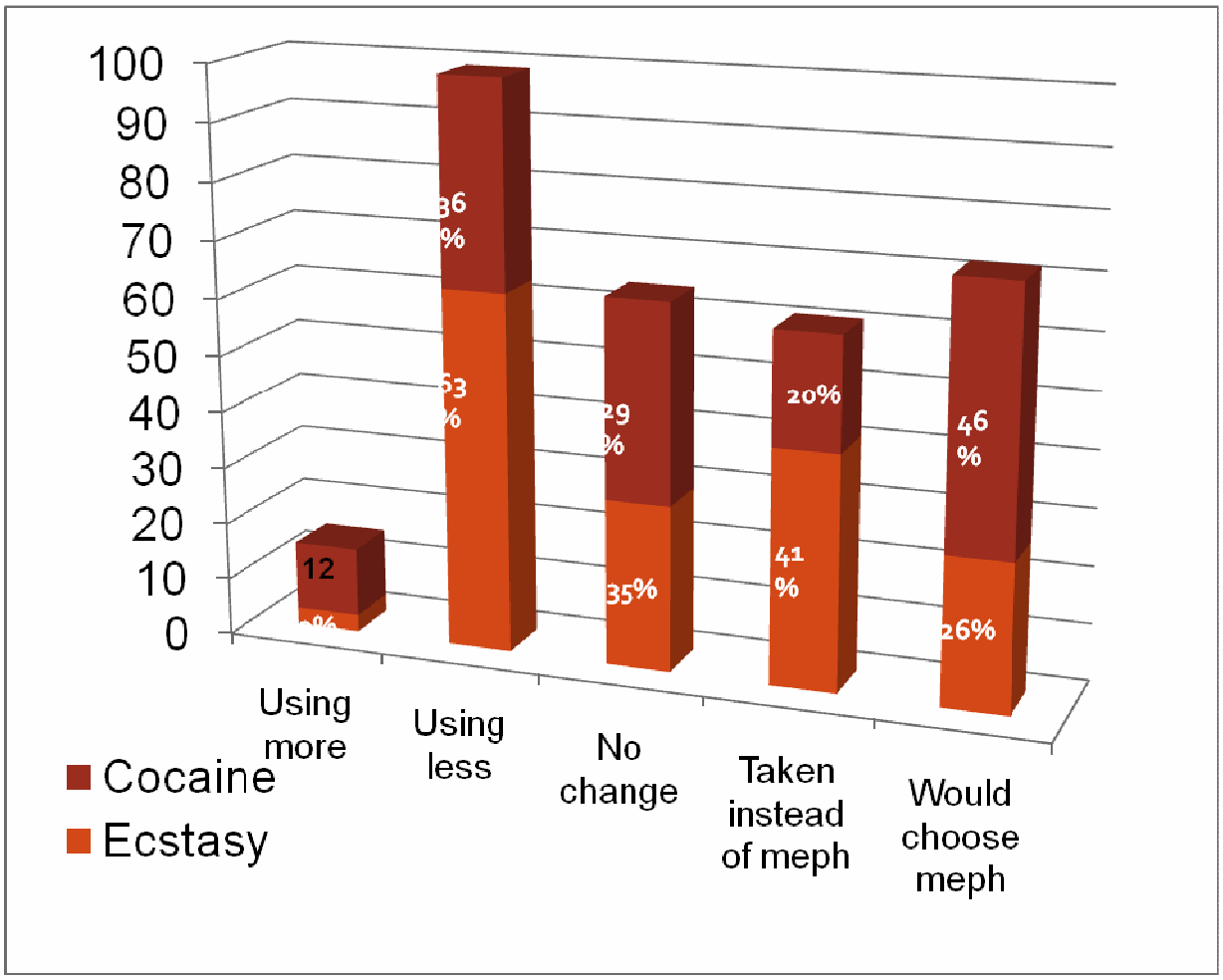
Effects of mephedrone on consumption of cocaine and ecstasy and preferred drug (see table 8)

Participants were asked about the impact of their mephedrone use on their consumption of cocaine and ecstasy.

63% reported that they now took less MDMA, 36% reported that they now took less cocaine. 41% said they had ever taken mephedrone instead of ecstasy with 20% saying they used it instead of cocaine.

Finally participants were asked that if there was a choice between mephedrone and ecstasy and mephedrone and cocaine which would they chose. 46% reported they would chose mephedrone over cocaine with only 26% saying they would take mephedrone over ecstasy (see figure 8).

Figure 8 The effect of mephedrone on cocaine and ecstasy use and preference



Assessing for DSM dependence

Participants were assessed against DSM-IV dependence criteria (see figure 9). One third met 3 or more criteria and may be considered as dependent (figure 10).

Figure 9 Incidence of mephedrone-related problems (%)

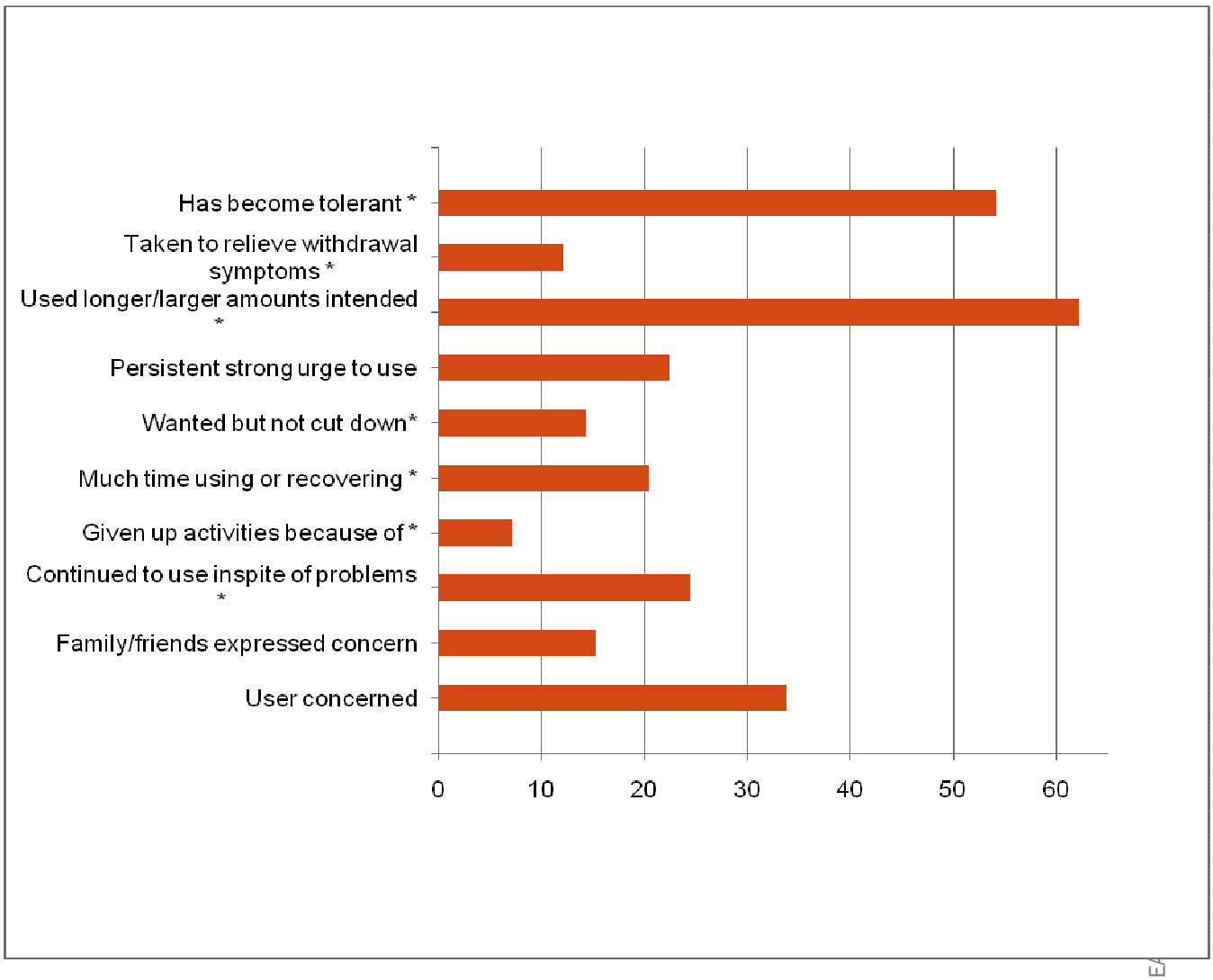
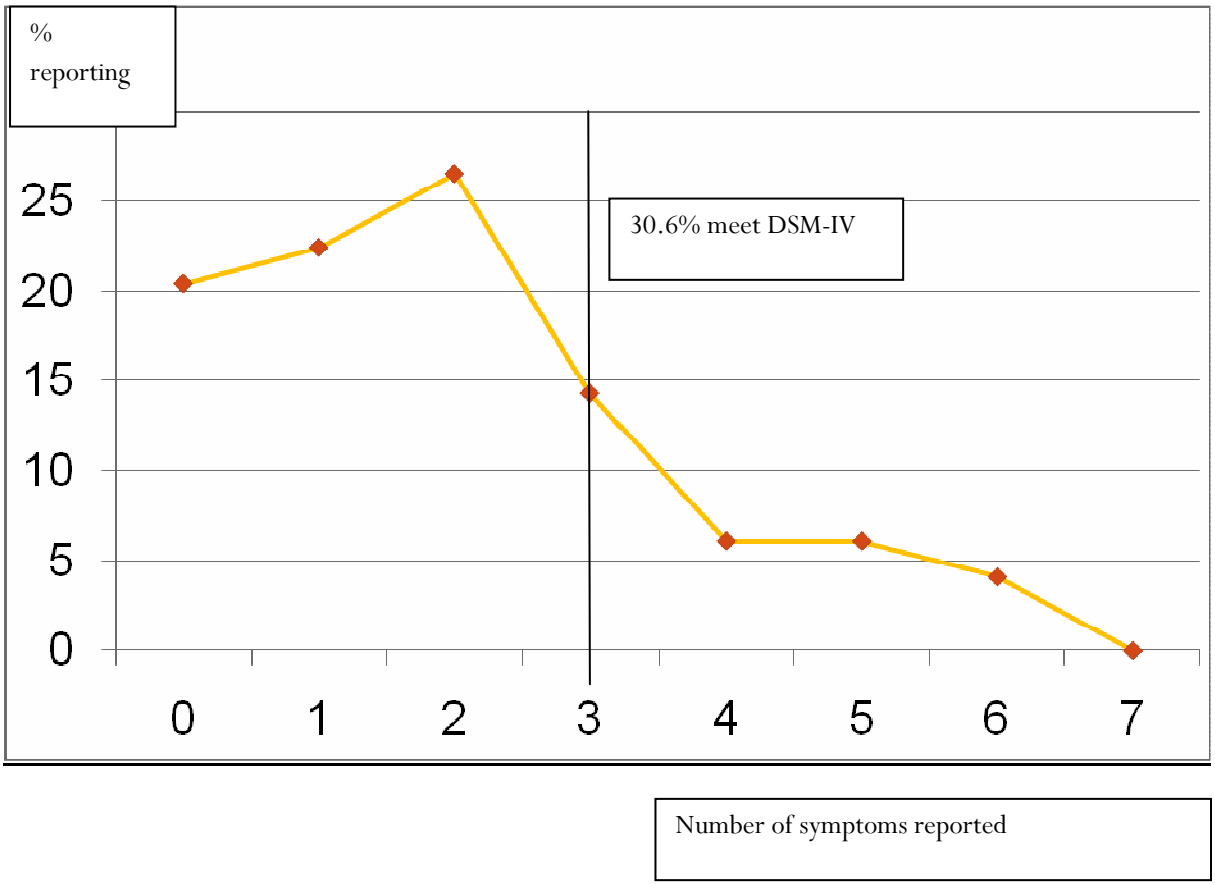


Figure 10 DSM –IV criteria symptoms



Intention to use next month

Participants were asked if they intended to use mephedrone again. 37% said 'no' or 'that is was very unlikely', 47%* said yes in the next month and 16% yes in the next 2 months. Of these 47 participants, 26 agreed to send in a urine sample. We have received 14 samples at laboratory to date (54%). Correlates of intention to use are shown in table 2. Correlates of intention never to use are shown in table 3.

Table 2 Correlates of intention to use next month

Variable	P-value	Adjusted OR
Heavier maximum use	***0.02***	***4.87***
Has developed tolerance	***0.02***	***3.37***
Felt strong urge to use	***0.03***	***4.12***
Using for longer periods	0.02	0.24

Table 3 correlates of intention never to use again

Variable	P-value	Adjusted OR
Age	0.04	0.89
Felt panic when using	0.03	0.33
Felt paranoid when using	0.02	3.24
Had headache when using	0.02	2.55
Had sweats when using	0.01	16.56
Developed tolerance	0.02	0.262
Had craving to use day after	0.02	0.48

Biological screening (see appendix for protocol)

Participants who expressed the intention to use mephedrone in the subsequent month were requested to provide a urine specimen for toxicological analysis. In addition to the sample participants were all asked to record how much mephedrone they had used and what other substances if any they had taken in the three days prior to providing the sample.

At the time of writing, a total of 14 samples have been received. Of these 14 urine sample 9 have been analysed fully using GCMS and LC-MS-MS. The remaining 5 have been analysed by GCMS only so far with LC-MS-MS analyses currently being conducted.

The planned stability and metabolite study is still pending. Provisional results show a limitation of the GCMS in detecting the metabolites. The recorded peaks appear to be of different strengths in different people, and not obviously dependant on the amount of mephedrone taken. For example, some people with a greater peak for mephedrone still do not show a clear metabolite peak, when compared to someone with an enormous metabolite peak and small mephedrone peak. The precise pattern appears to depend on the time the mephedrone was taken and individual variations in metabolism.

It is possible that the LCMSMS will give a clearer picture though and show some pattern. One interesting finding is the mismatch between declared rugs consumed and those identified at screening. This may represent adulteration at the point of sale, incomplete disclosure or failure to recall accurately all the substances taken over a period of use.

We would like to acknowledge the significant work carried out at St Georges Toxicology Unit by Susannah Davies and John Ramsey on behalf of the project.

The findings to date are provided on the next page in table 4 .

Table 4 Toxicology

Case No. (meph)	Index no.	Rec. date	Date of Form for 'today'	Mephedrone declared (yesterday, unless stated)	Other drugs declared (yesterday, unless stated)	Results
001	K14	07-Apr-10	28-Mar-10	<2g	Cigarettes, 6 pints alcohol, cannabis <1g,	4-MMC + Desalkyl met. (Nicotine)
002	K1	12-Apr-10	05-Apr-10	<0.5g	Cocaine <0.5g	4-MMC + Desalkyl met.
003	T32	14-Apr-10	12-Apr-10	<1g (yesterday) <1g (2 days)	Methylone <1g	4-MMC + Desalkyl met. + Methylone
004	T9	14-Apr-10	10-Apr-10	<1g	MDMA 0.1g	4-MMC + Desalkyl met. + MDMA
005	K27	13-Apr-10	10-Apr-10	<2g	Ecstasy 5 pills, cocaine <0.5g	4-MMC + Desalkyl met. + MDMA + Ketamine + BZP, TFMPP, MeOPP.
006	K34	15-Apr-10	11-Apr-10	<0.5g	None stated	4-MMC ? BZP + TFMPP (not reported)
007	K23	21-Apr-10	19-Apr-10	<3g	None stated	4-MMC + Desalkyl met. (Nicotine)
008	K38	29-Apr-10	26-Apr-10	<0.5g	None stated	4-MMC
009	K29	06-May-10	04-May-10	<0.5g	MDMA <0.5g	4-MMC + Desalkyl met. +MDMA
010	T81	02-Jun-10	Unstated	<0.5g	<2.0g cocaine	4-MMC, MDMA, cocaine and ketamine (Nicotine)
011	Z15	02-Jun-10	31-May-10	Yesterday: <1.0g 2days ago: <1g 3 days ago: <0.5g	Yesterday: <0.5g cocaine cup of coffee 2 days ago: <0.5g cocaine	4-MMC + Desalkyl met. (Nicotine)
012	T60	03-Jun-10	29-May-10	<2.0g	<0.5g cocaine	4-MMC (+ Procaine?*)
013	T62	09-Jun-10	07-Jun-10	Yesterday: <0.5g 2days ago: <0.5g	Yesterday: <0.5g ketamine, <0.5g cocaine. 2days ago: <0.5g cocaine	4-MMC + Desalkyl met. + Ketamine (+desmethyltramadol?**)
014	T58	09-Jun-10	07-Jun-10	<0.5g	None stated	4-MMC (low)

Where the metabolite of 4-MMC has not been detected, the GCMS often shows a 44 ion at the correct retention time, but is insufficient for library identification. LC-MS-MS is being set up to incorporate metabolites.

Examinations performed to date

Meph 001 - 009:

GC-MS: Piperazine derivatives, cathinone derivatives, general drugs screen.

LC-MS-MS: MDPV, 4-MMC, Methylone,

Meph 010 - 014:

GC-MS: Piperazine derivatives, cathinone derivatives, general drugs screen.

Procaine is an adulterant found in cocaine

desmethyltramadol is the metabolite of tramadol, which can be abused by opioid abusers

LC-MS-MS: Pending

Limitations

This is only a preliminary report with both additional data entry and manipulation planned to optimise the potential findings from this study. There is also further toxicological work to be conducted. As with any study that explores patterns of drug use and effects that relies upon self report measures there is the possibility of recall and response bias. There are inherent limitations of studies that use non random self selecting samples. However' such approaches are often required when conducting early research in a new drug. The sample although representing sentinel groups of harder users may not be typical of users, who are not associated with the dance drug scene. The sample' is small in size compared to the large numbers of users and there is no way of determining the representativeness of this sample to the wider population, particularly younger users, those with less drug using experience and those who regularly inject drugs. Users may be reluctant to disclose adverse experiences to a researcher and thus the findings may represent an overly positive view of the substance The fact that about one third said they did not intend to use again does suggest however that this is not the case. Finally, it is possible that the reported effects do not reflect the results of consuming mephedrone in isolation. The concurrent consumption of other psychoactive substances especially alcohol with mephedrone was common among this group and it is possible that the effect profile described represents a combined drug effect in some users.

Discussion

This is one of the first studies that provides a structured assessment of the patterns of use, effect profile and abuse liability associated with the use of mephedrone. It is the first to incorporate toxicological analysis and thus provides important information on the utility of existing screening methods and its metabolism.

The major findings of the study to date are that mephedrone has an effect profile that is more similar to ecstasy than cocaine except for its shorter duration of action and urge to use which are more similar to cocaine. Clinical presentations are likely to share features seen in association with other commonly used illicit substances such as MDMA and cocaine. The reported effect profile suggests a relatively low incidence (compared to cocaine) of adverse psychopathological experiences and aggressive behaviours ,perhaps offset by quite marked empathogenic effects and its short duration of action. Its physical effect profile is very typical of stimulants and does suggest that mephedrone may have the potential at higher doses to result in a sympathetic toxidrome with emergency presentations related to agitation, panic, dehydration, overheating and cardiovascular dysregulation and paranoid episodes. These findings are consistent with its chemical structure and a presumed mechanism of action that involves the release and or inhibition of reuptake of monoamine neurotransmitters. The effect profile reported in this study is consistent with previously reported dose-related subjective effects including euphoria, increased energy, increased libido, sweating, tachycardia, headache and teeth grinding (Psychonaut web mapping project, Measham et al 2010, Newcombe at el 2009, Winstock and Mitcheson 2009).

The withdrawal symptoms (perhaps more accurately described as a 'comedown') do not appear to be significant for most users, with the primary symptoms of nasal congestion and fatigue most probably related to route of use and lack of sleep, respectively. However the other reported findings , if clustering in a subgroup of heavier users would be consistent with a stimulant withdrawal syndrome.

Of particular interest is the data collected on mephedrone related problems and dependence. The findings suggest that the drug has a high abuse liability with over 30% of the sample reporting 3 or more DSM criteria of dependence and being classified as dependent. Tolerance, loss of control a strong urge to use and using despite problems predominate. The findings are consistent with the high abuse liability reported in the Mixmag survey (Winstock et al 2010 in press).

The study also adds to the limited literature on patterns of use, dosing schedules and typical amounts used. Intranasal use is by far the most consistent route of administration with doses being administered every 30-60 minutes over the course of a session (typically 8-12 hours in length) which may last several days in the case of some users. Although the average consumption over a session is about 1gm there are sub group of heavier users who report consuming far more (maximum reported session in this study was 16gm).

A finding that will warrant further study is the very high level of concurrent consumption of other illict drugs and alcohol. It is unknown how the consumption of these substances may modify the effect profile of mephedrone or the pattern of risk behaviours or metabolism of the drug. It is likely that

combined stimulant consumption will increase the risk of sympathomimmetic toxicity. The concurrent consumption of alcohol may increase both disinhibition and memory impairment, increasing the likelihood of a range of high risk behaviours. How combined use will impact upon the potential development of more toxic metabolites is not known. The very high level of combined use with ketamine may be reflective of the population from which the study population was drawn. However the combination of a dissociative substance with one that is more prosocial may be considered as unexpected. The acute risks of combining ketamine with mephedrone will most probably be related to unintended injury, excess dosing, adverse psychopathological experience or those related to cardiovascular overstimulation.

More important from a policy point of view are the findings on motivation for use and the impact of mephedrone upon the use of cocaine and ecstasy. The findings support the complex relationship between factors such as availability, cost, perceived quality and drug effect in determining the choice of which drug to use (Measham et al 2010). These factors seem more important than the legal status of a drug and it was interesting to note that over 40% of the sample reported ever having purchased mephedrone from a dealer. Whether recent legislation will lead to an increase in price and fall in purity remains to be seen. If this is the case then at least some of the motivating factors for use such as value for money and perceived high purity compared to other drugs may be given less weight.

Consideration of the result of the toxicological analysis will be deferred until the analytical processes are complete.

Finally, the authors consider the approach adopted in the current study to be appropriate to the rapid investigation and risk assessment of new substances of abuse. Benefiting from access to sentinel drug using participants who are often the first to experiment with novel substances, the research group believe that the approach taken could be used in subsequent risk assessment processes to allow 'foot-printing' of drug effect, risk and abuse liability.

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Statistical note

The Adjust ORs are output from a backwards elimination (using likelihood ratio criterion) logistic regression, blocked with the following personal demographic variables: age, sex, height and weight, followed by alcohol, cocaine, cannabis and ketamine use on a typical mephedrone session covariates and then the mephedrone effects, withdrawal symptoms (indicator coded 0,1 for now) and the problem (dependence) items. This was done in SPSS. All of the logistic regression results are very provisional at this stage, but give flavour of the interesting correlations at work in the data we feel. We are limited to the extent that we can push the regression as the sample size is small for the number of covariates being stuck in.

Appendices – survey instrument and biological screening protocol

Mephedrone Survey 2010

Institute of Psychiatry, King's College London

Study ethical approval number: 141/02 Field version: 3.2

PRN ☐ **Date of contact** ☐ **Date of interview** ☐ **rviewer ID** ☐

Read out

Hi [*contact name:*], My name is _____. I am a researcher at **King's College London**.

Can I just check that you completed the **MixMag/ Don't Stay In** survey and may are interested in taking part in further research we do on drug issues? ☐ If No – thank and terminate

We're doing some research focusing on **MEPHEDRONE** (pronounced: *mef-e-drone*). This is sometimes called "**Meow Meow**", **M-Cat** or **4-MMC**). [if asked, chemical name is 4-methylmethcathinone]

We trying to find out what people think of this drug, what effects they are getting, both good things and also the less good things. There's been almost no research on this drug and we don't know what effects people are getting. Our aim is to develop health information for mephedrone users.

Have you ever taken mephedrone? Yes ☐ If "No, never" ☐ – thank, and terminate.

Would you be interested in taking part in our survey? It will take about 15 minutes to complete.

If "No, not convenient right now" ☐ When can I call back? Day _____ Month _____ Time __: __ [24 hr.]

[check the date and time and the number to use].

If convenient to complete interview:

Read out

I just need to record your consent to take part.

I'm going to ask about your experiences of using mephedrone and any other stimulants you may have tried.

I'm not going to ask for you full name and the data will only be seen by myself, Adam and our team.

Let me stress that we are asking everyone the same questions, so some of them may not apply to you. If you prefer not to answer a question just let me know and we'll move on.

Of course, you can decide to stop the interview at any time and withdraw from the study without giving a reason. And if you wish we will remove your contact details from our database.

So, are you happy to take part in the survey? Yes ☐ No ☐

If No – would you like us to delete your details from our database and not contact you again about our future research?

Yes, withdraw completely ☐ No, happy to be contacted about other research ☐

Time interview started: ___ : ___ [24 hour format]

SECTION 1 – DEMOGRAPHICS

Let's start by recording some background information about you.

1.1 How old are you? ☐ (age last birthday) **1.2** Record Male ☐ Female ☐

1.3 What is your height? **("about" if uncertain)** ☐ Feet **or** ☐ Metres

1.4 What is your weight? **("about" if uncertain)** ☐ Kilos **or** ☐ Stones **or** ☐ Pounds

1.5 Are you: Working (FT) ☐ Working (PT) ☐ College (FT) ☐ College (PT) ☐ Unemployed ☐

SECTION 2 – STIMULANT COMPARISONS

2.1 Ok, let's set the scene for the interview in the context of other stimulants and your views on how mephedrone compares with these. Have you:

Ever taken?	No	Yes	*If Yes*	Age first used?	*How often taken in most recent month used?* Number sessions or tick>	Once a week (4)	Twice a week (8)	Three times a week (12)	Four times a week (16)	Five sessions a week (20)
Ecstasy	☐	☐	⇒	☐	⇒ ☐	☐	☐	☐	☐	☐
Cocaine	☐	☐	⇒	☐	⇒ ☐	☐	☐	☐	☐	☐

2.2 ***Interviewer – complete for ecstasy and cocaine (if ever used either or both) and for mephedrone***

Thinking about the ecstasy and cocaine that is generally around now, using a scale from 0 to 10, how would you rate: rate

	Ecstasy	*Cocaine*	*Mephedrone*
The pleasurable high: ***(where 10 = best ever had)***	☐	☐	☐
Strength of effect: ***(where 10 = extremely strong)***	☐	☐	☐
Negative effects when high: ***(where 10 = best ever had)***	☐	☐	☐
Value-for-money of: ***(where 10 = best experienced)***	☐	☐	☐
The urge to want more of the drug when taking: ***(where 10 = extremely)***	☐	☐	☐

2.3 Since the time you started taking mephedrone, have you: (tick one only)

	Ecstasy	**Cocaine**
Been using more:	☐	☐
Been using less:	☐	☐
Or, has using mephedrone not changed how often you take:	☐	☐
Has there ever been a time when you took mephedrone instead of:	☐	☐

If there was a choice to make between …

…. mephedrone or ecstasy, would choose to take mephedrone?	Yes	☐	☐
… mephedrone or cocaine, would choose to take mephedrone?	Yes	☐	☐

SECTION 3 – FIRST MEPHEDRONE SESSION

3.1 Can you now think back to the ***first time*** *you ever took* ***MEPHEDRONE***:

First time you took:	***What amount was this dose?***					***How did you take it?***			
	50mg	100mg	125mg	250mg		Snort	Bomb	In drink	Inject
Line	☐	☐	☐	☐	⇨	☐	☐	☐	☐
Tipped out powder	☐	☐	☐	☐	⇨	☐	☐	☐	☐
Capsule	☐	☐	☐	☐	⇨	☐	☐	☐	☐
Pill	☐	☐	☐	☐	⇨	☐	☐	☐	☐

Other ☐ ***record verbatim and*** **amount** and **how taken**: ☐

3.2 On that first session, how **many more doses** did you take? ☐ Dose(s)

3.3 How **long** would you say that first session **lasted for in total**? ☐ Hour(s)

(the time between **first dose** on that session and when you had come down form the **last dose** but were still awake)

3.4

	How much would you estimate you took **in total** on that **first session**? 50mg ☐ 100mg (1/10g) ☐ 125mg (1/8g) ☐ 0mg (¼ g) 5☐mg (½ g) ☐ 1gram ☐ 1.5 grams ☐ 2 grams ☐ More than 2 grams ☐ ***Or verbatim***: ☐
3.5	Did you take it any other way, apart from _____ (route for first dose)? ***Probe***: ***"any other way?"*** Snort ☐ Bomb ☐ In drink ☐ Rubbed on gums ☐ Smoked ☐ Injected ☐ Other ☐ ***describe***: ☐
3.6	Did you drink **alcohol** during that first session? Yes ☐ ☐ Did you take **any other drugs** during the session (before you slept)? ***Probe "anything else?"*** No ☐ Cocaine ☐ Ecstasy ☐annabis ☐Ketamine A☐hetamine ☐ Other(s) *describe:* ☐

SECTION 4 – SUMMARY OF MEPHEDRONE USE

ESTIMATE OF TOTAL SESSIONS

4.1	So, when was that **first** session you used?	Year		Month	
	And when was the **last** time you used?	Year		Month	

So you've been using mephedrone for ____ (months) **[time between first and last month]**

Interviewer – complete session record – starting with FIRST month and ending with LAST month

4.2	**Start FIRST**	**No. SESSIONS** *or tick* ⇨	Once a week (4)	Twice a week (8)	Three times a week (12)	Four times a week (16)	5 sessions a week (20)
	M___ Yr ___		☐	☐	☐	☐	☐
			☐	☐	☐	☐	☐

M___ Yr ___

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

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M___ Yr ___ ☐ ☐ ☐ ☐ ☐

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

M___ Yr ___ ☐ ☐ ☐ ☐ ☐

	M___ Yr ___	☐	☐	☐	☐	☐
	M___ Yr ___	☐	☐	☐	☐	☐

4.3 Have you used mephedrone for **2 or more days in a row**? Yes ☐ No ☐

If Yes: what's the **total number of consecutive days** you have used? ☐

TYPICAL SESSION

I want to ask you about a ***typical*** *session in the* ***most recent month*** *you have used* **(clarify month)**.

4.4 Generally, do you use: **alone** ☐ ***or*** are **other people** using with you ☐

☐

4.5 In a **typical session**, think about your ***first dose***:

	What amount?						***How takes?***			
First dose is:	50mg	100mg	125mg	250mg	500mg		Snort	Bomb	In drink	Inject
Line	☐	☐	☐	☐	☐	⇨	☐	☐	☐	☐
Tipped out powder	☐	☐	☐	☐	☐	⇨	☐	☐	☐	☐

Capsule ☐ ☐ ☐ ☐ ☐ ⇨ ☐ ☐ ☐ ☐

Pill ☐ ☐ ☐ ☐ ☐ ⇨ ☐ ☐ ☐ ☐

Other ☐ ***record verbatim*** **amount** and **how taken**: _____

If taken as "line" – ask: **How many lines would you say you would get out of a 1g?** ☐

☐

On average, how **many more doses** do you take? ☐ Dose(s) **(if 1 only skip to Q3.8)**

4.7 ***If more than one dose***, about **how much time** is there on average between doses?

30 minutes ☐ 1 hour ☐ 1.5 hrs ☐ 2 hrs ☐ 2.5 hrs ☐ 3 hrs ☐ Longer ☐

☐

4.8 How **long** would you say a typical session **lasts for in total**? ☐ Hour(s)

(the time between **first dose** on that session and when you had come down form the **last dose** but are still awake)

4.9 How much would you estimate you take **in total** during a **typical session**?

50mg ☐ 100mg (1/10g) ☐ 125mg (1/8g) ☐ 50mg (¼ g) ☐ 5☐mg (½ g) 1gram ☐

☐ ☐ ☐ ☐ ☐ ☐ ☐

4.10 Do you take it **another way**, apart from _____ (route first dose in Q3.5)? ***Probe*: *any other way?***

Snort ☐ Bomb ☐ In drink ☐ Rubbed on gums ☐ Smoked ☐ Injected ☐

Other ☐ ***describe***:

4.11 Do you drink **alcohol** during a typical session? Yes ☐ ☐

Do you take **any other drugs**? ***Probe "anything else?"***

No ☐ Cocaine ☐ Ecstasy ☐ annabis ☐ Ketamine A☐hetamine ☐

Other(s) *describe:*

4.12 Could you estimate how **much mephedrone in total** you use in the most recent month?

50mg or less ☐ 100mg (1/10g) ☐ 125mg (1/8g) ☐ 0mg (¼ g) ☐ mg (½ g) ☐

1gram ☐ 1.5 grams ☐ 2 grams ☐ 3 grams ☐ grams ☐ grams 6☐ ms ☐

4.13 What the most **mephedrone** you have **ever taken** in one session?

50mg or less ☐ 100mg (1/10g) ☐ 125mg (1/8g) ☐ 0mg (¼ g) ☐ mg (½ g) ☐

1gram ☐ 1.5 grams ☐ 2 grams ☐ 3 grams ☐ grams ☐ grams 6☐ ms ☐

Hour(s)

(the time between **first dose** on that session and when you had come down form the **last dose** but are still awake)

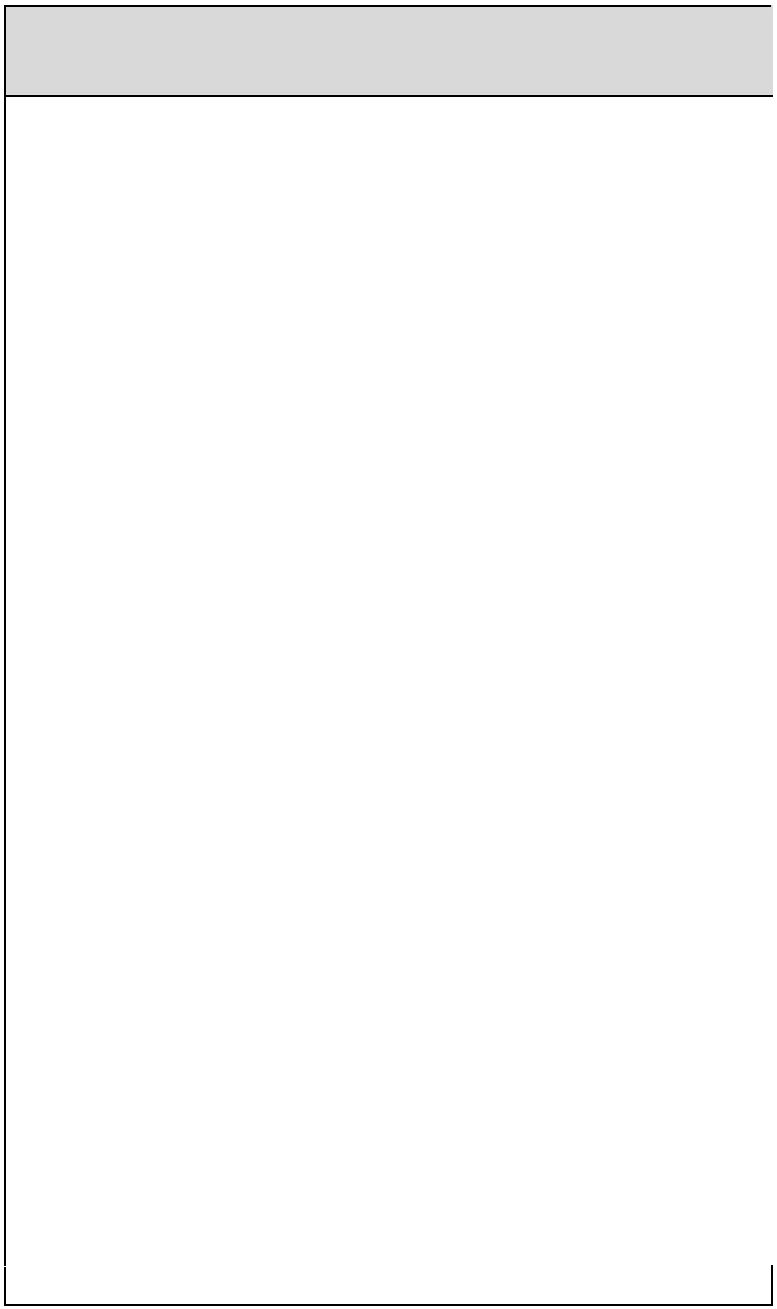
4.15	Do you drink **alcohol** during that big session? Yes ☐ ☐ Do you take **any other drugs?** ***Probe "anything else?"*** No ☐ Cocaine ☐ Ecstasy ☐ annabis ☐ Ketamine A☐ hetamine ☐

OVERALL SUMMARY

I'm going to ask you some overall questions about mephedrone.

4.16	Thinking about how you have obtained mephedrone, have you **ever**: **(ask each)** Been given mephedrone by a friend? ☐ Bought from a dealer? ☐ Bought from a head shop? ☐ Bought from an internet site? ☐ **Which most commonly obtained from?: underline** **(if No internet, skip to Q4.18)**

4.17	*If bought on the internet*: can you recall the name of the website, or websites, you have most commonly bought mephedrone from: ***(don't prompt, just record all mentioned)*** AmazingPlantFood ☐ BrandCrazy ☐ Broadening-Horizons ☐ MephedroneOnline ☐ BuyMephedrone ☐ Charlie-Boy ☐ DiscoFood ☐ FlowerPowderFeeder ☐ Mephedrone2U Mephindustries ☐ MrMeph ☐ oughtPlantFood ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐



4.18	What has the mephedrone you have most commonly taken **looked like when first taken out of the wrap or packet**? Tick most common <u>type</u> then ask about any smell. ***Before using, did you notice that this had a particular <u>smell</u>?*** No Slight Strong Slight Strong Other - *describe*

			sweet	sweet	chemical	Chemical	
White crystals	☐	⇨ ☐	☐	☐	☐	☐	☐ _____
Yellow crystals	☐	⇨ ☐	☐	☐	☐	☐	☐ _____
Light pink crystals	☐	⇨ ☐	☐	☐	☐	☐	☐ _____
Pure white power	☐	⇨ ☐	☐	☐	☐	☐	☐ _____
Off-white power	☐	⇨ ☐	☐	☐	☐	☐	☐ _____
Yellow powder	☐	⇨ ☐	☐	☐	☐	☐	☐ _____
Pill	☐	⇨ ☐	☐	☐	☐	☐	☐ _____
Capsule	☐	⇨ ☐	☐	☐	☐	☐	☐ _____
Other _____	☐	⇨ ☐	☐	☐	☐	☐	☐ _____

4.19 Can you list the different **situations** (places) you've **ever** taken mephedrone? ***Prompt:***

At your home ☐ At a friend's home ☐ t a house party ☐ club A☐stival ☐

At a pub/bar ☐ Other ☐ *escribe:* _____

3.19a Where have you taken mephedrone most often? ***Interviewer: underline one of the above***

4.20 Here's a list of some things that can **motivate** someone to use mephedrone. On a scale from "0" to "10" where "0" is "no influence at all" and 10 would be "the maximum influence possible", how motivating have the following been when you've taken mephedrone*:* *(**one** number only)*

It was legal to buy it	☐ 0-10
It was easy to buy on the internet and delivered to my home	☐ 0-10
Mephedrone has a high level of of purity, compared to illegal stimulants	☐ 0-10
It was good value for money	☐ 0-10
It is a more consistent product	☐ 0-10
You get a better high from mephedrone, compared to illegal stimulants	☐ 0-10
It has fewer side effects, compared to illegal stimulants	☐ 0-10
A single dose of mephedrone doesn't last too long	0-10
No other drug was available to me at the time, so I bought mephedrone	0-10

4.21 I'll read out a list of some effects that mephedrone can have. When taking mephedrone, please tell me **how often** you have experienced each of these effects by replying "**never**", "**once only**", or "**sometimes**", or "**most of the time**".

	How often				***How intense***		
	Never	Once	Sometimes	Most of	Mild	Moder-	Intense

How often did you feel:	(0)	(1)	(2)	the time (3)	***If experienced >***	(1)	ate (2)	(3)
Euphoric	☐	☐	☐	☐	⇨	☐	☐	☐
Increased energy	☐	☐	☐	☐	⇨	☐	☐	☐
Improved concentration	☐	☐	☐	☐	⇨	☐	☐	☐
Empathy with others	☐	☐	☐	☐	⇨	☐	☐	☐
Urge to talk	☐	☐	☐	☐	⇨	☐	☐	☐
Urge to move, do things	☐	☐	☐	☐	⇨	☐	☐	☐
Increased sexual desire	☐	☐	☐	☐	⇨	☐	☐	☐
Restless or anxious	☐	☐	☐	☐	⇨	☐	☐	☐
Angry or aggressive	☐	☐	☐	☐	⇨	☐	☐	☐
Agitated	☐	☐	☐	☐	⇨	☐	☐	☐
No appetite for food	☐	☐	☐	☐	⇨	☐	☐	☐
You were forgetting things	☐	☐	☐	☐	⇨	☐	☐	☐
Panicky	☐	☐	☐	☐	⇨	☐	☐	☐
Paranoid	☐	☐	☐	☐	⇨	☐	☐	☐
	☐	☐	☐	☐	⇨	☐	☐	☐

Blurred vision									
Seeing things not there	☐	☐	☐	☐	⟹	☐	☐	☐	
Hearing things not there	☐	☐	☐	☐	⟹	☐	☐	☐	
Body sweating	☐	☐	☐	☐	⟹	☐	☐	☐	
Overheating	☐	☐	☐	☐	⟹	☐	☐	☐	
Heart racing or erratic	☐	☐	☐	☐	⟹	☐	☐	☐	
Shortness of breath	☐	☐	☐	☐	⟹	☐	☐	☐	
Headache	☐	☐	☐	☐	⟹	☐	☐	☐	
Chest pain	☐	☐	☐	☐	⟹	☐	☐	☐	
Clenching jaw, grinding teeth	☐	☐	☐	☐	⟹	☐	☐	☐	
Shaky hands, fingers	☐	☐	☐	☐	⟹	☐	☐	☐	
Fingers/toes cold or numb	☐	☐	☐	☐	⟹	☐	☐	☐	
Skin discoloured (blue/red)	☐	☐	☐	☐	⟹	☐	☐	☐	
Skin rash	☐	☐	☐	☐	⟹	☐	☐	☐	
Vomiting	☐	☐	☐	☐	⟹	☐	☐	☐	
Hard to sleep, end of session	☐	☐	☐	☐	⟹	☐	☐	☐	

4.22	Across all the sessions you've had, what's the way you've **most commonly** taken mephedrone? Snort/sniff ☐ Bomb ☐ Rub on gums ☐ Smoke ☐ Inject ☐ Other ☐ describe: _____

4.23	Are there any **ways** of taking mephedrone you probably you **wouldn't** do again? ***Prompt and probe*** Snort/sniff ☐ Swallow in paper ☐ Rub on gums ☐ Smoke ☐ Inject ☐ Other ☐ describe: _____

4.24 Can you think now about how you felt during the **next day or two** after a session. I'll read out some feelings that people can experience. Please summarise for me **how often** you have experienced each one and how **intense the effect** has been.

	How often					***How intense***		
How often did you feel:	Never (0)	Once (1)	Sometimes (2)	Most of the time (3)	***If experienced***	Mild(1)	Moder-ate (2)	Intense(3)
Increased appetite	☐	☐	☐	☐	⇨	☐	☐	☐
You had a stuffy nose	☐	☐	☐	☐	⇨	☐	☐	☐

	Tired or fatigued	☐	☐	☐	☐	⟶	☐	☐	☐
	Your sweat smelled unusual	☐	☐	☐	☐	⟶	☐	☐	☐
	Anxious	☐	☐	☐	☐	⟶	☐	☐	☐
	Depressed	☐	☐	☐	☐	⟶	☐	☐	☐
	Emotional or tearful	☐	☐	☐	☐	⟶	☐	☐	☐
	Irritable	☐	☐	☐	☐	⟶	☐	☐	☐
	Unable to concentrate	☐	☐	☐	☐	⟶	☐	☐	☐
	You lost memory of session	☐	☐	☐	☐	⟶	☐	☐	☐
	An urge or craving to take more mephedrone	☐	☐	☐	☐	⟶	☐	☐	☐

4.25 ***Thinking overall across the time since you have been taking mephedrone:***

	Yes	No
1. Have you found that your usual dose hasn't had the same effect as when you first starting taking it?		
2. Have you taken mephedrone for longer or in larger amounts that you had intended?		
3. Have you had a persistent desire or strong urge to take it?		
4. Have you wanted to cut down or take it less often but not been successful ?		
5. Would you say you have spent a great deal of time either getting mephedrone, taking it or recovering?		

	6. Have you given up important social, occupational, or recreational activities because of it?		
	7. Have you continued to take it even though you've had physical/psychological problems?		
	8. Have friends or family expressed concern to you about your use of mephedrone?		
	9. Have *you* been concerned about your use of mephedrone?		
	10. Have you taken mephedrone or another stimulant drug to help relieve mephedrone withdrawals?		

4.26 After taking mephedrone, have you ever had **emergency medical treatment** or gone to **hospital**?

No ☐ **If no, skip to Q4.27** Yes ☐ ***If Yes***:

a. How much mephedrone had you taken? _____ **record**

b. How long had the session been that time? _____ **hours**

c. Had you been drinking alcohol? Yes ☐ No ☐

d. Had you taken any other drugs in that session? ***Record and probe:***

Cocaine ☐ Amphetamine ☐ Cannabis ☐ Ketamine ☐

Other (specify): _____

4.27	After taking mephedrone, have you ever fainted or collapsed? No ☐ **If no, go to Section 5** Yes ☐ ***If Yes***: **a.** How much mephedrone had you taken? _____ **record** **b.** How long had the session been that time? _____ **hours** **c.** Had you been drinking alcohol? Yes ☐ No ☐ **d.** Had you taken any other drugs in that session? ***Record and probe:*** Cocaine ☐ Amphetamine ☐ Cannabis ☐ Ketamine ☐

SECTION 5 – OTHER CATHINONES

There are some other stimulants with similar effects to mephedrone.

5.1 Have you ever heard of **methylone**? (*meth-e-lone*)

[aka M1 or Bk-MDMA or MDMC; chemical name: 4-methylenedioxy-N-methylcathinone]

No ☐ Yes ☐ *If "Yes", have you used it?* No ☐ s *If "Yes", how many times?* ☐

Or record verbatim: _____

5.2 Have you ever heard of **butylone** (*bew-til-one*)

[aka B1, or Bk-MDBD or Mitzseezs; chemical name: 3,4-benzodioxolylbutanamine)]

☐ ☐ ☐ ☐ ☐

5.3 Have you ever heard of **M.D.P.V.**?

[aka SuperCoke; chemical name: **M**ethylene**D**ioxy**P**yro**V**alerone]

☐ ☐ ☐ ☐ ☐

5.4 Have you ever heard of **flephedrone**?

[aka4FMC; chemical name: 4-fluoromethcathinone; 4-FMC]

☐ ☐ ☐ ☐ ☐

5.5	Do you think that using **mephedrone** has made it more likely that you will try other stimulant drugs? No ☐ Yes ☐ *Record any verbatim*: _____

TURN OVER

5.6	Do you think you will take **mephedrone** again: Yes, in the next month ☐ Yes, in the next 2 months ☐, very unlikely ☐ ***Or record verbatim***: _____

Time interview ended: ___ : ___ [24 hour format]

If answer to Q5.6 is "No, very unlikely" –

What is the main reason for this?

Thanks very much for taking part in our survey!

If answer to Q5.6 is "Yes, in the next month or two months"

Interviewer - Read Out:

Thanks very much for taking part in our survey. **We have one more request**.

Mephedrone is such a new substance that we don't really know anything about how it is metabolised by the body. Also, there are several different types of cathinone stimulants and we don't know which ones are being used.

So, we'd like to send you a kit in the post and ask you to take a small sample of your urine the day

after your next mephedrone session and send it back to our lab.

Our laboratory will screen the sample for mephedrone and other cathinones and the sample is then destroyed. This information is only seen by us and the results will then be made anonymous.

If you like, we can send you a personal feedback report on the results and also a £20 HMV voucher as a thank you. This can also be used at Waterstones Book store.

It would really enhance our understanding of how mephedrone works if you could help us out like this. Would you be able to help?

Yes __ No __ If yes – interviewer describe the process

Biological Assessment of Cathinone Use Protocol

Details of Chief Investigator:	Details of Co-Investigator:
Dr Adam R Winstock Addiction Science Building Windsor Walk, SE5 8AF	Dr John Marsden Addiction Science Building Windsor Walk, SE5 8AF
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Research Protocol

Overview

This protocol describes the biological assessment of cathinone use among recreational drug users who have completed brief telephone interview about their cathinone and other use and related health risks and harms (REC 141/03). Only those indicating they may use mephedrone in the future will be approached to participate in the next phase of the study. There will be no obligation to participate. These informed, consenting participants will be send a urine test collection kit and asked to mail a sample back for analysis the following day after taking a cathinone substance. Their postal address will be kept separate from their survey data. The sample will be analysed at the St George's Hospital Toxicology Unit using LC/MS procedures to determine metabolites of the exact compound(s) consumed. If requested by the participant a brief feedback of these results will be provided in addition a gift voucher in recognition of their time.

Scientific justification

Cathinone stimulants are increasingly available on the internet and sold as 'research chemicals' or as plant food or bath salts to hide their identity and intended purpose. The cathinones are β-keto analogues of d-amphetamine, but there are several compounds (including Methedrone, 3-fluoromethcathinone, and MDPV (Methylenedioxypyrovalerone) – some of which are already controlled by the Misuse of Drugs Act, some not. For example, methcathinone is a Class B drug and pyrovalerone (an obsolete anorectic) a Class C drug. Furthermore, some cathinones are in fact β-keto analogue of ecstasy (MDMA), not amphetamine (e.g. methylone and β-keto MDEA). One the key issues in the present study is to distinguish mephedrone, methylone and methedrone from each other as well as confirm that cathinones had in fact been used by participating

individuals. This is important because of a potential asymmetrical health risk gradient. For example, methedrone is the β-keto analogue of PMMA. This and PMA are much more toxic than other phenethylamines. Methedrone has been associated with one fatal case in Sweden. But there has been almost no research on this in the UK and little is known about the metabolism of these compounds in man.

Ethical issues and confidentiality

Only those participants who have completed our telephone interview on mephedrone use and have indicated at the end of the telephone study that may use mephedrone again will be offered the opportunity participant in the biological screening study. Unlike the telephone study, we need some means of contacting participants for this study by email and by post. We will use a mixture of participant identification (name or alias), research number and postal address marked for the attention only of the participant nominated name. Feedback results sent my email or by post will also be identified by the participant's choice of name. Urine samples will be destroyed after testing.

Procedure

The will be 7 steps:

1) At the end of the telephone interview, all cathinone users will be asked if they think it possible that they will use this drug again in the next 30 days. If they answer "No", the process will be terminated.

2) The interviewer will then describe our additional study to examine precise nature of cathinone compounds being used by people taking part in our research and invited to take part. The process of contact, identity protection and feedback of results will be described. If the individual is not interested in taking part, they will again be thanked for their participation in the telephone research and the process will be terminated at this point.

(3) The interviewer will assign the individual a Participant Information Number (PIN) and an alias name. The interviewer will then give this information to the participant and ask them to send a confirmation email to the IoP email address of Dr. Winstock. This information will also be send by text. The participant will be asked to contact Dr Winstock him by email indicating their interest in taking part, and giving their address to receive materials. We will ask the subject line on the email to read: "for the attention of Dr Winstock only".

(4) Dr. Winstock will then mail out a test kit to the specified address (see below for description of included material in the test kit).

(5) The participant will provide a sample of their urine the following day on which they have used mephedrone and mail the container back to the St George's Hospital Toxicology Unit, indicating if they would like a feedback report and a gift store voucher.

(6) After analysis, pro-forma feedback report will then send to Dr Winstock by email. This feedback form will only have the PIN identification (and will indicate if the participant would like a copy and has requested a gift-store voucher). Feedback information will specify the cathinone detected (if any), a well as any amphetamine and phenethylamine metabolites with semi-quantitative information for each compound detected.

(7) Dr Winstock will send out the feedback report to the participant's email address and their voucher to the specified mail address. The feedback report information will then be compiled into the main data file for the telephone survey for research analysis and aggregated reporting of results.

Test kit

The test kit sent to each participant will contain the following materials:

Study information sheet

Study consent form and material transfer agreement

Urine collection cup and mail-safe container

Freepost return envelope