New Psychoactive Substance Use among Regular Psychostimulant Users in Australia, 2010-2015

Rachel Sutherland[*1], Amy Peacock[2], Elizabeth Whittaker[1], Amanda Roxburgh[1], Simon Lenton[3], Allison Matthews[2], Kerryn Butler[1], Marina Nelson[3], Lucinda Burns[1], Raimondo Bruno[2]

[1]National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW, 2052, Australia

[2] School of Medicine (Psychology), Faculty of Health, University of Tasmania, Hobart, TAS, 7001, Australia

[3]National Drug Research Institute, Curtin University, Shenton Park, WA, 6845, Australia

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Corresponding Author*: Rachel Sutherland

National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW, 2052, AUSTRALIA; Phone: +61 2 9385 0256; Facsimile: +61 (0)2 9385 0222; E-mail: rachels@unsw.edu.au

Abstract

Objective: To examine the rates and patterns of new psychoactive substance (NPS) use amongst regular psychostimulant users (RPU) in Australia.

Method: Data were obtained from the 2010-2015 Ecstasy and related Drugs Reporting System (EDRS), which comprised a total cross-sectional sample of 4,122 RPU.

Results: Recent use of 'any' NPS increased from 33% in 2010 to 40% in 2015, although trends of use differed significantly across NPS classes. The correlates associated with NPS use also varied across NPS classes: frequent (i.e. weekly or more) ecstasy users were more likely to report recent phenethylamine use; LSD users were more likely to report recent phenethylamine and tryptamine use; and daily cannabis users were more likely to report recent synthetic cannabinoid use than RPU who had not used NPS. 'Poly' NPS consumers were found to be a particularly high risk group and were significantly more likely to be younger, male, report daily cannabis use, report weekly or more ecstasy use, report recent LSD use, have higher levels of poly drug use, have overdosed on any drug in the past year, and to have engaged in past month criminal activity.

Conclusion: NPS use has been established as a significant and ongoing practice amongst our sample of RPU. It appears that RPU seek out NPS with similar properties to the illicit drugs that they are already consuming, with poly NPS consumers found to be a particularly high risk group.

Keywords: New psychoactive substances; NPS; synthetic cannabinoids; synthetic cathinones; tryptamines; phenethylamines; psychostimulants

1. Introduction

Over the past decade, countries worldwide have witnessed the rapid emergence of substances collectively referred to as 'new psychoactive substances' (NPS). NPS are substances which often do not fall under international drug controls but which may pose a public health threat (United Nations Office on Drugs and Crime (UNODC), 2013). The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has identified 13 categories of NPS: aminoindanes, arylalkylamines, arylcyclohexylamines, benzodiazepines, synthetic cannabinoids, synthetic cathinones, indolalkylamines (i.e. tryptamines), opioids, phenethylamines, piperazine derivates, piperidines and pyrrolidines, plants and extracts, and others (EMCDDA, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015). In 2014, over 450 NPS were being monitored by EMCDDA, the majority of which fell into the synthetic cathinone and synthetic cannabinoid categories (EMCDDA, 2015).

The extent to which NPS are used globally remains unclear, with prevalence rates varying considerably across countries. Data from the European Union indicated that, in 2014, 3% of people aged 15-24 had used an NPS in the past year, with use highest in Ireland, Spain and France (5% respectively) (European Commission, 2014). The Crime Survey for England and Wales found that 0.6% and 0.5% of 16-59 year olds reported past year use of mephedrone and salvia respectively (Home Office, 2014); in the United States, 4.8% of adolescents (grade 8-12) reported past year use of synthetic cannabinoids in 2014 and 0.8% reported use of synthetic stimulants (Miech et al., 2014). In Australia, the 2013 National Drug Strategy Household Survey showed that 1.2% of the general population had used synthetic cannabinoids in the last 12 months, and 0.4% had used another NPS (Australian Institute of Health & Welfare (AIHW), 2014).

Whilst general population estimates appear to be relatively low, rates of NPS use are elevated amongst high risk groups, such as illicit drug users and those engaged in the night time economy (Bretteville-Jensen et al., 2013; Bonar et al., 2014; Burns et al., 2014; Kelly et al., 2013; Moore et al.,

2013; Stafford & Burns, 2015; Vento et al., 2014; Winstock, 2015). For example, a study of gay dance club patrons in London found that amongst those who had used ecstasy pills in the past month, 75% had also used mephedrone (Moore et al., 2013); whilst a survey of 1,740 nightlife venue patrons in the US found that 8.2% had used synthetic cannabinoids and 1.1% had used mephedrone in the past year (Kelly et al., 2013).

Presently, there is limited literature on the socio-demographic profile of NPS consumers. Studies examining the correlates of NPS use have found that those who are younger, male, had used other drugs and had higher levels of poly drug use were more likely to have used an NPS (Bonar et al., 2014; Bruno et al., 2012; Burns et al., 2014; Emmanuel & Attarad, 2006; Lawn et al., 2014; Palamar, 2015; Palamar & Acosta, 2015). More detailed studies have also identified younger age of drug initiation, more problematic drug use (e.g. bingeing) and online purchasing behaviours as being correlated with NPS use (Burns et al., 2014). Given the vast array of NPS that are available, it is likely that NPS consumers are a heterogeneous group. For example, in a recent study, stimulant NPS users were found to be similar to regular ecstasy users, while psychedelic NPS users were a distinct group of users who had initiated ecstasy use at a younger age, had higher levels of poly drug use and were more likely to experience legal, psychological and social drug-related problems (Bruno et al., 2012). Given these differences, it was argued that harm reduction messages need to be tailored according to the NPS being used.

The public health risks associated with NPS are many and varied. Synthetic cannabinoids, for example, have been associated with acute and persistent psychosis, tachycardia, agitation, hallucinations, hypertension, vomiting, chest pain, seizures and myoclonia (Every-Palmer, 2010; Hermanns-Clausen, 2012); whilst mephedrone has been shown to impair working memory (Freeman et al., 2012), and has been associated with jaw clenching, reduced appetite, insomnia, agitation, tachycardia and dependence (Dargan et al., 2010; Dargan et al., 2011; Winstock et al., 2011). In addition, data from the Global Drug Survey showed that the risk of seeking emergency medical

treatment was 30 times higher amongst synthetic cannabinoid users than herbal cannabis users, whilst 'other' NPS users were about three times more likely to seek emergency medical treatment compared to traditional illicit drug users (Winstock, 2015).

Given the different risk profiles associated with NPS use, it is essential to obtain a more nuanced understanding of who are most at risk for using these substances. This will improve our ability to tailor harm reduction messages to the appropriate target groups. Subsequently, the aims of this paper are twofold:

1) To examine the prevalence of NPS use amongst a sample of regular psychostimulant users (RPU) in Australia, from 2010-2015.

2) To determine whether correlates of use vary across the following five NPS classes; phenethylamines, tryptamines, synthetic cannabinoids, synthetic cathinones, and 'poly' NPS (i.e. use of more than one NPS class).

2. Method

2.1 Study design

This paper uses six years of data (2010-2015) from the Ecstasy and related Drugs Reporting System (EDRS) (for full protocol details, see Sindicich & Burns, 2015). The EDRS is a national monitoring study aimed at detecting emerging trends in illicit drug markets and has been conducted annually in all Australian jurisdictions since 2003. The EDRS has received ethical approval from the University of New South Wales Human Research Ethics Committee (HC10071, HC15015), as well as from the relevant ethics committees in each jurisdiction.

2.2 Participants and procedure

EDRS participants (hereafter referred to as 'regular psychostimulant users' (RPU)) comprised a non-random self-selected sample recruited annually through street-press advertisements, online forums and peer referral. Eligibility criteria were; at least monthly use of ecstasy or psychostimulants in the preceding six months, 16 years of age or older, and residence in the city of interview for at least 12 months prior to the interview. Face-to-face one-hour structured interviews were conducted by trained interviewers at a negotiated time and location. All information was confidential and anonymous.

2.2 Measures relevant to the current study

2.2.1 Outcome variables

From 2010-2015, participants were asked about their past six month use of 26 specific NPS (see Table 1 for a full list, with street names provided in brackets); an open text 'other' option was provided to capture any additional NPS not listed in the survey. These NPS have been categorised into eight of the thirteen categories identified by the EMCDDA; namely synthetic cannabinoids, synthetic cathinones (i.e. stimulant and entactogen phenethylamines), phenethylamines (i.e. psychedelic phenethylamines), tryptamines, piperazines, plant and extracts, aminoindanes and arylcyclohexylamines.

2.2.2 Correlates

In addition to demographic questions (i.e. age, sex, sexual orientation, employment and educational status), participants were asked about their past six-month use of licit and illicit substances; the total number of illicit drug classes used in the past six months (excluding NPS) was used to measure levels of poly drug use (maximum of 17 drug classes). Participants completed the 5-item Severity of Dependence Scale (SDS; Gossop et al., 1995) in relation to ecstasy use, whereby a cut-off score of ≥3 was considered indicative of ecstasy dependence (Bruno et al., 2011). Participants were also asked if

they had binged on stimulants in the past six months (defined as the use of stimulants for 48 hours or more without sleep).

The Alcohol Use Disorders Identification Test (AUDIT) was administered to identify participants with potential alcohol-related problems (Saunders et al., 1993). A cut-off score of ≥16 was used to measure hazardous and harmful alcohol use (Babor & Higgins-Biddle, 2000). From its inception, the EDRS has measured crime using the Criminality Scale of the Opiate Treatment Index (OTI; Darke et al., 1991). This scale gathers self-report data on four types of crime: property crime; dealing; fraud; and violent crime (in the month preceding interview).

Across all years, participants were administered the Kessler 10 (K10) Psychological Distress Scale to assess psychological distress (Kessler et al., 2003). The K10 is a 10-item screening tool utilizing a five-point response scale (1 'none of the time' to 5 'all of the time'); a cut-off score of ≥22 (score range 10-50) was used to measure high to very high psychological distress (Andrews & Slade, 2001). Participants also answered self-report questions about their mental health over the previous six-month period.

Participants were asked if they had participated in the EDRS previously; this question was used to exclude repeat participants.

2.3 Statistical analysis

2.3.1 Rates of NPS use

Rates of use were generated by collapsing the various NPS to determine if participants had consumed 'any' NPS in the six months preceding interview. Using the groupings identified by the EMCDDA, rates of use were then broken down into the following classes; synthetic cannabinoids, synthetic cathinones, phenethylamines, tryptamines, piperazines, plants and extracts, aminoindanes

and arylcyclohexylamines. Paired comparisons of percentages reporting use were made across adjacent years (e.g. 2010-2011; 2011-2012) with 95% confidence intervals (95% CI) reported.

2.3.2 Correlates of NPS use

Socio-demographic profiles were compared across the four most commonly used NPS classes (i.e. synthetic cathinones, synthetic cannabinoids, phenethylamines and tryptamines). The sample was divided into groups based on use of these substances in the six months preceding interview and compared to non NPS using participants (e.g. recent cathinone use only vs. no recent NPS use). In order to maintain distinct groups of NPS users (see Supplementary Material, Table 8 for overlap between NPS classes), participants who had used more than one NPS class were excluded from this analysis and included in the 'poly' NPS use group. As synthetic cannabinoids were first specifically asked about in 2011, this analysis was limited to 2011-2015 data (with all repeat participants excluded from 2012-2015 data).

Between-group comparisons of categorical variables were analysed using odds ratios (OR) with 95% confidence intervals reported. For normally distributed continuous variables, *t*-tests were employed with means and standard deviations (SDs) reported. The Benjamini-Hochberg procedure was applied to control the false discovery rate and was used because it yields much greater power than the widely applied Bonferroni technique (Thissen et al., 2002).

Variables found to be significant based on bivariate comparisons were entered into a multivariable logistic regression model, which estimated adjusted odds ratios (AOR) after controlling for potential confounders. To allow comparability across the five NPS categories, the same variables were entered into each of the regression models (this allows us to determine if the same variables are associated with different NPS classes and if they differ in magnitude). Associations were set for statistical significance at $p < 0.05$. All analyses were conducted using IBM SPSS Statistics for Windows release 22.0 (IBM Corporation, 2013).

3. Results

3.1 Demographics

Across 2010-2015, 4,122 participants were recruited and interviewed for the EDRS, of which 529 were repeat participants (see Supplementary Material, Table 7). Sixty-four percent of the entire RPU cohort were male with a mean age of 23.6 years (SD 6.2; range 16-64), 97% were of English speaking background, 47% were tertiary qualified, 69% were employed in some capacity, 32% were students, 16% were unemployed and 3% were currently in drug treatment. Twelve percent of the 2010-2015 cohort identified as gay, lesbian, bisexual or transgendered (GLBT). More detailed demographics of each year's sample have been reported elsewhere (Sindicich & Burns, 2011, 2012, 2013, 2014, 2015).

3.2 Rates of recent NPS use

From 2010-2015, 41.9% of the entire sample (n=1,655) reported use of 'any' NPS in the six months preceding interview. Specifically, one-third (32.9%) of RPU reported recent use of any NPS in 2010; this increased to 41.7% in 2011 (p=0.002), before reaching a peak of 51.6% in 2012 (p=0.002). Recent NPS use remained stable in 2013 (46.6%), before declining significantly in 2014 (40.6%; p=0.023) and then stabilising in 2015 (40.2%) (Table 1).

Insert Table 1

Looking at the different classes of NPS (see Table 1), cathinones were originally the most prevalent NPS being used by participants, with almost one-fifth (18.5%) of RPU reporting recent (i.e. past six month) use in 2010. However, by 2015 this had declined significantly, with 7.7% reporting use of cathinones in the six months preceding interview (p<0.001). Conversely, in 2010 both phenethylamines and tryptamines had been used by 8% of RPU in the six months preceding

interview; however, by 2015 rates of use had increased to 18.6% (p<0.001) and 10.9% (p=0.037) respectively, making them the two most commonly used groups of NPS in these years.

The use of synthetic cannabinoids was specifically asked about for the first time in 2011, with 6.6% of RPU reporting use within the six months preceding interview. This increased significantly in 2012 to 16.1% of the sample (p<0.001) and remained stable in 2013 (16.1%). However, in 2014 use of recent synthetic cannabinoids declined to rates observed in 2011 (6.9%; p<0.001), before stabilising in 2015 (6.4%).

The use of piperazines, plant-based NPS and aminoindanes remained uncommon across all years. Specifically, from 2010-2015, the use of piperazines declined from 4.9% to 0% (p<0.001); plant-based NPS increased from 2.0% to 5.0% (p=0.005); and there was no change in the use of aminoindanes or arylcyclohexylamines.

These trends remained consistent even when repeat participants were excluded (see Supplementary Material, Table 8).

3.2 Correlates of NPS use

3.2.1 Phenethylamines

At the bivariate level, RPU who reported recent phenethylamine use were more likely to be under the age of 25 (OR 3.41, p<0.001), male (OR 1.67, p=0.001), report weekly or more ecstasy use (OR 1.86, p<0.001), report recent (i.e., past six month) LSD use (OR 3.06, p<0.001), and report recent use of a greater number of drug classes (p<0.001), when compared to RPU who had not used any NPS in the preceding six months.

When significant bivariate correlates were entered into a multivariable logistic regression model (controlling for year), age, sex, weekly or more ecstasy use, recent LSD use and greater levels of poly drug use remained significant.

Insert Table 2

3.2.2 Tryptamines

At the bivariate level, RPU who reported recent tryptamine use were more likely to report being male (OR 1.72, p=0.008), weekly or more ecstasy use (OR 1.89, p<0.001), recent LSD use (OR 4.14, p<0.001), daily cannabis use (OR 2.89, p<0.001), having binged on a stimulant drug (OR 1.71, p=0.004), use of a greater number of drug classes (5.9 vs. 4.3, p<0.001), and past month criminal activity (OR 2.11, p<0.001), when compared to RPU who had not used any NPS in the preceding six months.

When the variables significant at the bivariate level were entered into a multivariable logistic regression model, controlling for year, the following variables remained significant; daily cannabis use, recent LSD use and greater levels of poly drug use.

Insert Table 3

3.2.3 Synthetic cannabinoids

At the bivariate level, RPU who reported recent use of synthetic cannabinoids were more likely to report daily tobacco use (OR 1.76, p=0.001), daily cannabis use (OR 2.74, p<0.001), and past month criminal activity (OR 2.10, p<0.001), when compared to RPU who had not used any NPS in the preceding six months. Conversely, recent cocaine users were less likely to report recent use of synthetic cannabinoids (OR 0.46, p=0.001).

When the variables significant at the bivariate level were entered into a multivariable logistic regression model, controlling for year, the following variables were significant; daily cannabis use, recent cocaine use, past month criminal activity and greater levels of poly drug use.

Insert Table 4

3.2.4 Synthetic cathinones

No variables were significantly correlated with recent synthetic cathinone use at the bivariate level. When a multivariable logistic regression was conducted (controlling for year), daily tobacco use and greater levels of poly drug use were found to be significantly associated with recent synthetic cathinone use. Cocaine use was also associated with recent synthetic cathinone use, although this did not reach statistical significance.

Insert Table 5

3.2.5 Poly NPS use

At the bivariate level, RPU who reported poly-NPS use in the past six months were more likely to be under the age of 25 (OR 1.77, $p<0.001$), male (OR 2.23, $p<0.001$), have initiated ecstasy use before 18 years of age (OR 2.08, $p<0.001$), be unemployed (OR 1.48, $p=0.005$), report daily tobacco (OR 1.84, $p<0.001$) and cannabis (OR 2.89, $p<0.001$) use, report weekly or more ecstasy use (OR 2.34, $p<0.001$), report recent methamphetamine (OR 2.20, $p<0.001$) and LSD (OR 6.36, $p<0.001$) use, have binged on a stimulant drug (OR 2.56, $p<0.001$), have used a greater number of drug classes ($p<0.001$), have overdosed on a drug in the past year (OR 1.85, $p<0.001$), have engaged in past month criminal activity (OR 2.68, $p<0.001$), have high levels of psychological distress (OR 1.45, $p=0.002$), and to self-report a mental health problem (OR 1.36, $p=0.008$), when compared to RPU who had not used any NPS in the preceding six months.

When the variables significant at the bivariate level were entered into a multivariable logistic regression model, controlling for year, the following variables remained significant; age, sex, daily cannabis use, weekly or more ecstasy use, recent LSD use, recent cocaine use, greater levels of poly drug use, past year drug overdose and past month criminal activity.

Insert Table 6

4. Discussion

Despite fluctuations in use of specific forms over the past six years, the use of NPS has been established as a significant and ongoing practice amongst cross-sectional samples of RPU in Australia. Whilst it is difficult to make any direct comparisons to other studies (particularly given differences in time frames, samples and categorisations of NPS), it does appear that the changes noted in our sample mirror a number of international trends (European Commission, 2014; Home Office, 2014; Miech et al., 2014). Indeed, the globalisation of drug marketplaces has increased the accessibility and volatility of drugs such as NPS (Griffiths et al., 2010), and it is essential that projects such as the EDRS continue to monitor these substances so that changing trends can be detected in a timely manner.

It is unknown what might be driving the specific trends observed in this paper; however, consumer acceptability and legislative changes are factors to consider. In 2013, EDRS participants were asked to rate the positive, negative and hangover effects of NPS, and how likely they would be to consume the substance again. DMT and 2CB received the highest ratings for pleasurability and likelihood to take again, whilst mephedrone and synthetic cannabinoids were viewed less favourably and reportedly had worse side effects (Matthews et al., 2013; Sindicich & Burns, 2014). Similarly, a self-selecting online sample of DMT and NBOMe users found that when compared to other hallucinogens (i.e. LSD, magic mushrooms and ketamine) both DMT and NBOMe were rated favourably in terms of strength of effect and pleasurability (Lawn et al., 2014; Winstock et al., 2013).

In contrast, a global study of dual 'natural' and synthetic cannabis users found that 93% of participants preferred natural cannabis over synthetic cannabis (Winstock & Barratt, 2013). It seems likely that our sample of RPU experimented with a range of NPS, continuing to use those deemed 'acceptable' in terms of their psychopharmacological and side effects, and ceasing use of those that were not. This theory is supported by findings that DMT, 2C-x and NBOMe remain the most commonly sold NPS on dark net marketplaces (Van Buskirk et al., 2015), however, it would be of benefit for future research to explicitly test this hypothesis through a close examination of the motivations for consuming specific NPS.

Another factor to consider is the impact of legislative changes. Given the varying legislative frameworks across jurisdictions and the different dates of implementation, it is beyond the scope of this paper to determine whether the scheduling of NPS may have contributed to the trends observed in this paper. For example, in 2012, the Australian Therapeutic Goods Administration introduced a blanket ban on any type of synthetic cannabinoid that produced the same pharmacological effect as cannabis (Bright et al., 2013). In 2014 there was a significant decline in the use of synthetic cannabinoids amongst our sample of RPU; however, it is unclear if this was a lagged effect of the legislation (due to practices such as stockpiling) or if it was due to other, unrelated factors such as consumer acceptability. Given that this is a sample of illicit drug users, it seems unlikely that the criminalisation of NPS use would have dissuaded use of these substances, although it would have reduced their availability. Furthermore, legislative changes fail to explain the increase in phenethylamines and tryptamines observed in this paper. Nevertheless, it is important that further research evaluate the impact of Australian legislation on the NPS marketplace to provide an evidence-base for the efficacy of these regulatory approaches.

This paper also illustrates the heterogeneity of NPS consumers, with the correlates of use varying across NPS classes. Perhaps not surprisingly, our findings suggest that RPU seek out NPS that have

similar properties to the 'traditional' illicit drugs that they are already using. More specifically, frequent ecstasy users were more likely to report recent use of phenethylamine-type NPS, LSD users were more likely to report recent use of phenethylamines (many of which have psychedelic properties) and tryptamines, and daily cannabis users were more likely to report recent use of synthetic cannabinoids. Cocaine users were more likely to report recent use of synthetic cathinones, although this did not reach statistical significance.

Use of a larger number of 'established' illicit drugs emerged as the only consistent predictor of NPS use. This suggests that NPS users may represent a more innovative group of 'psychonaut' drug users, a term used to describe people who actively seek out new substances for the purposes of achieving altered states of consciousness (EMCCDA, 2004). It is important to note that for participants using a single NPS class this did not equate to a greater likelihood of drug-related harms. This was somewhat surprising, particularly given that clinical studies have shown that drugs such as NBOMe have been linked to a number of deaths and hospitalisations, despite its short history of human consumption (Wood et al., 2015).

Rather, poly-NPS users were found to be the riskiest group of NPS consumers; in addition to having high levels of poly-drug use, this group were also more likely to have engaged in past month criminal activity and to have overdosed on any drug in the past year. These behaviours carry serious public health implications, particularly given the ever increasing number of NPS being identified, the limited knowledge of the short- and long-term effects of these drugs, and a lack of information on how they interact with other drugs. It is recommended that credible harm reduction messages be disseminated amongst these populations, with a particular focus on the potential risks of combining NPS and 'traditional' illicit drugs (for example, see Winstock et al., 2010).

4.1 Limitations

This study has certain limitations. Firstly, the EDRS sample is not representative, which means that our findings are not generalizable to all RPU in Australia. Rather, it is a sentinel sample which allows for the early identification of trends in illicit drug markets, which is particularly important when monitoring marketplaces which are rapidly changing (as is the case of NPS). Secondly, our analysis is reliant upon self-report data from participants which may be subject to bias. Although evidence points to sufficient validity and reliability of self-report in studies assessing illicit drug use (Darke, 1998), it is possible that participants may have incorrectly identified the NPS being consumed (i.e. it may have been sold to them as one thing, but have been something else) and it would be of benefit for future studies to corroborate their findings through chemical analysis. Finally, the EDRS only specifically asked about 26 different NPS and as such rates of use may be underestimated.

4.2 Conclusions

Whilst NPS use has been established as a significant and ongoing practice amongst our sample of RPU, it remains a highly dynamic marketplace with the popularity of NPS classes changing significantly across 2010-2015. It appears that RPU seek out NPS with similar properties to the traditional illicit drugs that they are already consuming. Poly NPS consumers were found to be a particularly high risk group and as such it is essential that credible harm reductions messages be distributed amongst these populations.

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Contributors

This work was undertaken by the National Drug and Alcohol Research Centre in Australia. All authors contributed to the writing and review of the manuscript.

Conflict of interest

No conflicts declared.

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Table 1: Rates[#] of NPS amongst RPU, 2010-2015

	2010 %	2011 % (95% CI; *p*)	2012 % (95% CI; *p*)	2013 % (95% CI; *p*)	2014 % (95% CI; *p*)	2015 % (95% CI; *p*)	2010-2015* % 95% CI; *p* value
SYNTHETIC CATHINONES Mephedrone (miaow, 4MMC); Methylone (bk-MDMA); MDPV (Ivory Wave); Other substituted cathinone	**18.5**	**17.7** (-0.04, 0.05; *p*=0.796)	**11.4 (0.02, 0.11; *p*=0.004)**	**9.2** (-0.01, 0.06; *p*=0.229)	**8.0** (-0.02, 0.04; *p*=0.466)	**7.7** (-0.02, 0.03; *p*=0.919)	**11.6** ↓ **0.07, 0.14; *p*<0.001**
PHENETHYLAMINES 2C-I; 2C-B (Bromo, TWOs, trystacy); 2C-E (hummingbird, europa); 2C-Other; Benzo Fury (6-APB); PMA; DOI (death on impact); NBOMe (25I, 25B, 25C)	**8.0**	**15.6 (-0.11, -0.04; *p*<0.001)**	**14.6** (-0.03, 0.05; *p*=0.706)	**20.7 (-0.10, -0.02; *p*=0.008)**	**21.3** (-0.05, 0.04; *p*=0.846)	**18.6** (-0.01, 0.07; *p*=0.210)	**16.9** ↑ **-0.14, -0.07; *p*<0.001**
TRYPTAMINES DMT; 5-Meo-DMT	**7.5**	**14.1 (-0.10, -0.03; *p*<0.001)**	**14.2** (-0.04, 0.04; *p*=0.960)	**14.6** (-0.04, 0.04; *p*=0.911)	**14.4** (-0.03, 0.04; *p*=0.962)	**10.9 (0.002, 0.07; *p*=0.045)**	**12.6** ↑ **-0.07, -0.003; *p*=0.037**
SYNTHETIC CANNABINOIDS K2/Spice; Kronic; Other synthetic cannainoid	-	**6.6**	**16.1 (-0.13, -0.06; *p*<0.001)**	**16.1** (-0.04, 0.04; *p*=0.960)	**6.9 (0.06, 0.13; *p*<0.001)**	**6.4** (-0.02, 0.03; *p*=0.797)	**10.1** – -0.03, 0.03; *p*=0.994
PIPERAZINES BZP	**4.9**	**1.7 (0.01, 0.05; *p*=0.005)**	**1.2** (-0.01, 0.02; *p*=0.690)	**0.3** (0.001, 0.02; *p*=0.106)	**0.3** (-0.01, 0.01; *p*=0.729)	**0** (-0.003, 0.01; *p*=0.500)	**1.3** ↓ **0.03, 0.07; *p*<0.001**
PLANTS & EXTRACTS LSA (Hawaiian Baby); Mescaline; Salvia Divinorum; Datura (Angel's trumpet); Ayahuasca	**2.0**	**7.2 (-0.08, -0.03; *p*<0.001)**	**7.7** (-0.04, 0.03; *p*=0.840)	**6.4** (-0.02, 0.04; *p*=0.455)	**4.4** (-0.003, 0.05; *p*=0.102)	**5.0** (-0.03, 0.02; *p*=0.655)	**5.3** ↑ **-0.05, -0.01; *p*=0.005**
AMINOINDANES MDAI; 5-IAI	-	-	**0.9**	**0.7** (-0.01, 0.01; *p*=0.977)	**0.5** (-0.01, 0.01; *p*=0.815)	**0.4** (-0.01, 0.01; *p*=0.950)	**0.6** – -0.004, 0.02; *p*=0.441
ARYLCYCLOHEXYLAMINES Methoxetamine (MXE)	-	-	**1.4**	**2.2** (-0.02, 0.01; *p*=0.408)	**1.6** (-0.01, 0.02; *p*=0.544)	**2.2** (-0.02, 0.01; *p*=0.494)	**1.9** – -0.02, 0.01; *p*=0.369
ANY NPS %	**32.9**	**41.7 (-0.14, -0.03; *p*=0.002)**	**51.6 (-0.16, -0.04; *p*=0.002)**	**46.6** (-0.01, 0.11; *p*=0.092)	**40.6 (0.01, 0.11; *p*=0.023)**	**40.2** (-0.04, 0.05; *p*=0.915)	**41.9** ↑ **-0.12, -0.02; *p*=0.006**

[#]in the past six months; *for synthetic cannabinoids this refers to 2011-2015 figures; for aminoindanes and arylcyclohexylamines this refers to 2012-2015 figures; Pairwise comparisons were made across adjacent years; i.e. 2010 vs 2011; 2011 vs 2012; 2012 vs 2013; 2013 vs 2014; 2014 vs 2015; 95% CI refers to the differences across adjacent years, except for the final column where they refer to differences in 2010 vs 2015 percentages; ↑ = a significant increase in 2010 vs 2015 figures; ↓ = a significant decrease in 2010 vs 2015 figures. – no change in 2010 vs 2015 figures. Significant findings have been bolded.

Table 2: Correlates of recent phenethylamine use amongst RPU, 2011-2015

		Phenethylamine use past six months				Multivariable		
		No NPS use (n=1,693)	Yes (n=251)	OR (95% CI) /test statistic[a]	*p* value	AOR[b]	95% CI	*p*-value
Demographics	Age (<25) %	69.2	88.4	3.41 (2.28, 5.08)	<0.001*	2.66	1.71, 4.14	<0.001
	Sex (male) %	60.3	71.7	1.67 (1.25, 2.23)	0.001*	1.59	1.15, 2.21	0.005
	Age first tried ecstasy (<18)	46.4	54.4	1.38 (1.06, 1.80)	0.018	1.03	0.75, 1.40	0.874
	Tertiary qualifications %	47.9	39.9	0.72 (0.55, 0.95)	0.019			
	GLBT %	11.0	9.6	0.85 (0.54, 1.33)	0.481			
	Unemployed %	15.3	13.1	0.84 (0.57, 1.24)	0.373	0.86	0.54, 1.36	0.513
Drug Use	Daily tobacco use[#] %	38.6	40.0	1.06 (0.81, 1.39)	0.673	1.02	0.73, 1.42	0.910
	Daily cannabis use[#] %	13.5	16.5	1.27 (0.88, 1.82)	0.202	1.16	0.72, 1.72	0.623
	Ecstasy use[#] (≥weekly) %	23.0	35.7	1.86 (1.39, 2.47)	<0.001*	1.69	1.21, 2.36	0.002
	Methamphetamine use[#] %	44.8	41.0	0.86 (0.65, 1.12)	0.259	0.78	0.55, 1.09	0.146
	LSD use[#] %	29.5	56.2	3.06 (2.34, 4.01)	<0.001*	1.58	1.12, 2.23	0.009
	Cocaine use[#] %	41.3	44.2	1.13 (0.86, 1.47)	0.379	0.71	0.51, 0.99	0.045
	AUDIT score ≥16 %	38.4	32.1	0.76 (0.57, 1.01)	0.055			
	Binged on stimulant drug[#] %	32.9	34.8	1.09 (0.83, 1.44)	0.543	0.98	0.70, 1.37	0.901
	Ecstasy SDS score (≥3)[#] %	20.0	22.8	1.18 (0.83, 1.68)	0.347			
	Number of drug classes[#^] (mean; SD)	4.3 (1.97)	5.5 (2.11)	t_{318}=-8.67	<0.001*	1.29	1.18, 1.42	<0.001
	Overdose (past year) %	35.2	40.8	1.27 (0.97, 1.67)	0.084	1.18	0.87, 1.60	0.293
Other	Any crime (past month) %	30.4	42.5	1.69 (1.29, 2.22)	<0.001*	1.24	0.90, 1.69	0.191
	K10 score ≥22 %	27.4	24.9	0.88 (0.65, 1.19)	0.401	0.70	0.47, 1.02	0.065
	Self-reported mental health problem[#] %	28.7	31.9	1.16 (0.87, 1.55)	0.302	1.38	0.96, 1.96	0.079

Note: OR = odds ratio; CI=confidence interval; AOR=adjusted odds ratio; SDS=severity of dependence scale; GLBT=gay, lesbian, bisexual or transgendered.

[*]denotes significance using the Benjamini-Hochberg procedure; [#]in the six months preceding interview; ^Maximum of 17 drug classes (includes ecstasy, methamphetamine, illicit pharmaceutical stimulants, cocaine, LSD, MDA, ketamine, GHB, amyl nitrite, nitrous oxide, cannabis, heroin, other opioids, illicit antidepressants, illicit benzodiazepines, magic mushrooms, steroids).

[a] Bivariate analysis were conducted, with odds ratios (OR) presented here for categorical outcomes; independent samples t-tests were conducted for parametric continuous data.

[b] Multivariable analyses were conducted using significant variables from all five bivariate models: i.e. significant variables from the phenethylamine bivariate comparisons (age, sex, weekly or more ecstasy use, LSD use, poly drug use and past month criminal activity), and significant variables from the tryptamine, synthetic cannabinoid and poly NPS bivariate comparisons (age of ecstasy initiation, methamphetamine use, daily tobacco use, daily cannabis use, cocaine use, binged on a stimulant drug, employment status, overdose, K10 score and mental health problem). Year was also included in the model to control for changes over time.

Table 3: Correlates of recent tryptamine use amongst RPU, 2011-2015

		Tryptamine use past six months				Multivariable		
		No NPS use (n=1,693)	Yes (n=123)	OR (95%CI) /test statistic[a]	*p* value	AOR[b]	95% CI	*p*-value
Demographics	Age (<25) %	69.2	65.0	0.83 (0.56, 1.22)	0.335	0.80	0.51, 1.26	0.338
	Sex (male) %	60.3	72.4	1.72 (1.15, 2.59)	0.008*	1.53	0.97, 2.39	0.065
	Age first tried ecstasy (<18)	46.4	56.9	1.53 (1.06, 2.21)	0.024	1.10	0.73, 1.67	0.646
	Tertiary qualifications %	47.9	50.4	1.11 (0.77, 1.60)	0.591			
	GLBT %	11.0	8.1	0.71 (0.37, 1.39)	0.315			
	Unemployed %	15.3	19.5	1.34 (0.84, 2.14)	0.213	0.99	0.57, 1.72	0.976
Drug Use	Daily tobacco use[#] %	38.6	45.5	1.33 (0.92, 1.92)	0.129	0.94	0.60, 1.47	0.790
	Daily cannabis use[#] %	13.5	31.1	2.89 (1.92, 4.35)	<0.001*	2.25	1.38, 3.67	0.001
	Ecstasy use[#] (≥weekly) %	23.0	36.1	1.89 (1.28, 2.78)	0.001*	1.24	0.79, 1.95	0.352
	Methamphetamine use[#] %	44.8	50.4	1.25 (0.87, 1.80)	0.230	0.77	0.49, 1.21	0.255
	LSD use[#] %	29.5	63.4	4.14 (2.83, 6.06)	<0.001*	2.18	1.37, 3.46	0.001
	Cocaine use[#] %	41.3	47.2	1.27 (0.88, 1.83)	0.203	0.82	0.53, 1.29	0.398
	AUDIT score ≥16 %	38.4	30.3	0.70 (0.47, 1.04)	0.074			
	Binged on stimulant drug[#] %	32.9	45.5	1.71 (1.18, 2.47)	0.004*	1.23	0.80, 1.91	0.348
	Ecstasy SDS score (≥3)[#] %	20.0	11.5	0.52 (0.27, 0.98)	0.041			
	Number of drug classes[#^] (mean; SD)	4.3 (1.97)	5.9 (1.85)	t_{1800}=-8.74	<0.001*	1.31	1.16, 1.48	<0.001
	Overdose (past year) %	35.2	44.7	1.49 (1.03, 2.16)	0.033	1.34	0.89, 2.01	0.160
Other	Any crime (past month) %	30.4	48.0	2.11 (1.46, 3.05)	<0.001*	1.51	0.99, 2.30	0.059
	K10 score ≥22 %	27.4	30.0	1.13 (0.76, 1.70)	0.544	0.73	0.44, 1.20	0.212
	Self-reported mental health problem[#] %	28.7	35.2	1.35 (0.92, 1.99)	0.124	1.38	0.86, 2.20	0.183

Note: OR = odds ratio; CI=confidence interval; AOR=adjusted odds ratio; SDS=severity of dependence scale; GLBT=gay, lesbian, bisexual or transgendered.

[*]denotes significance using the Benjamini-Hochberg procedure; [#]in the six months preceding interview; ^Maximum of 17 drug classes (includes ecstasy, methamphetamine, illicit pharmaceutical stimulants, cocaine, LSD, MDA, ketamine, GHB, amyl nitrite, nitrous oxide, cannabis, heroin, other opioids, illicit antidepressants, illicit benzodiazepines, magic mushrooms, steroids).

[a] Bivariate analysis were conducted, with odds ratios (OR) presented here for categorical outcomes; independent samples t-tests were conducted for parametric continuous data.

[b] Multivariable analyses were conducted using the significant variables from all five bivariate models; i.e. significant variables from the tryptamine bivariate comparisons (sex, daily cannabis use, weekly or more ecstasy use, LSD use, binged on a stimulant drug, poly drug use and past month criminal activity), and significant variables from the phenethylamine, synthetic cannabinoid and poly NPS bivariate comparisons (age, age of ecstasy initiation, methamphetamine use, daily tobacco use, cocaine use, employment status, overdose, K10 score and mental health problem). Year was also included in the model to control for changes over time.

Table 4: Correlates of recent synthetic cannabinoid use amongst RPU, 2011-2015

		Synthetic cannabinoid use past six months				Multivariable		
		No NPS use (n=1,693)	Yes (n=141)	OR (95%CI) /test statistic[a]	*p* value	AOR[b]	95% CI	*p*-value
Demographics	Age (<25) %	69.2	75.2	1.35 (0.91, 2.00)	0.138	1.45	0.92, 2.27	0.108
	Sex (male) %	60.3	67.4	1.36 (0.94, 1.96)	0.098	1.37	0.93, 2.03	0.115
	Age first tried ecstasy (<18)	46.4	56.7	1.52 (1.07, 2.14)	0.018	1.19	0.81, 1.74	0.382
	Tertiary qualifications %	47.9	44.0	0.85 (0.60, 1.21)	0.371			
	GLBT %	11.0	12.8	1.18 (0.70, 1.98)	0.533			
	Unemployed %	15.3	17.7	1.19 (0.76, 1.88)	0.443	0.90	0.55, 1.49	0.682
Drug Use	Daily tobacco use[#] %	38.6	52.5	1.76 (1.24, 2.48)	0.001*	1.30	0.87, 1.93	0.199
	Daily cannabis use[#] %	13.5	30.0	2.74 (1.86, 4.04)	<0.001*	2.13	1.37, 3.32	0.001
	Ecstasy use[#] (≥weekly) %	23.0	23.6	1.03 (0.69, 1.55)	0.878	0.76	0.49, 1.18	0.216
	Methamphetamine use[#] %	44.8	53.2	1.40 (0.99, 1.97)	0.055	0.95	0.63, 1.43	0.813
	LSD use[#] %	29.5	33.3	1.19 (0.83, 1.72)	0.340	0.80	0.52, 1.25	0.330
	Cocaine use[#] %	41.3	28.4	0.56 (0.39, 0.82)	0.003*	0.46	0.30, 0.72	0.001
	AUDIT score ≥16 %	38.4	45.7	1.35 (0.95, 1.91)	0.090			
	Binged on stimulant drug[#] %	32.9	42.6	1.51 (1.07, 2.15)	0.019	1.19	0.80, 1.77	0.395
	Ecstasy SDS score (≥3)[#] %	20.0	20.5	1.03 (0.66, 1.61)	0.898			
	Number of drug classes[#^] (mean; SD)	4.3 (1.97)	4.70 (1.93)	t_{1820}=-2.47	0.014	1.16	1.03, 1.30	0.015
	Overdose (past year) %	35.2	38.3	1.14 (0.80, 1.63)	0.456	1.16	0.76, 1.63	0.575
Other	Any crime (past month) %	30.4	47.9	2.10 (1.48, 2.98)	<0.001*	1.50	1.02, 2.22	0.040
	K10 score ≥22 %	27.4	32.9	1.29 (0.90, 1.87)	0.169	0.88	0.56, 1.36	0.554
	Self-reported mental health problem[#] %	28.7	36.9	1.45 (1.02, 2.08)	0.040	1.37	0.90, 2.09	0.139

Note: OR = odds ratio; CI=confidence interval; AOR=adjusted odds ratio; SDS=severity of dependence scale; GLBT=gay, lesbian, bisexual or transgendered.

[*]denotes significance using the Benjamini-Hochberg procedure; [#]in the six months preceding interview; ^Maximum of 17 drug classes (includes ecstasy, methamphetamine, illicit pharmaceutical stimulants, cocaine, LSD, MDA, ketamine, GHB, amyl nitrite, nitrous oxide, cannabis, heroin, other opioids, illicit antidepressants, illicit benzodiazepines, magic mushrooms, steroids).

[a] Bivariate analysis were conducted, with odds ratios (OR) presented here for categorical outcomes; independent samples t-tests were conducted for parametric continuous data.

[b] Multivariable analyses were conducted using significant variables from all five bivariate models: i.e. significant variables from the synthetic cannabinoid bivariate comparisons (daily tobacco use, daily cannabis use, cocaine use and past month criminal activity), and significant variables from the phenethylamine and tryptamine bivariate comparisons (age, sex, age of ecstasy initiation, weekly or more ecstasy use, LSD use, methamphetamine use, employment status, binged on a stimulant drug, overdose, poly drug use, K10 score and mental health problem). Year was also included in the model to control for changes over time.

Table 5: Correlates of recent synthetic cathinone use amongst RPU, 2011-2015

		Synthetic cathinone use past six months				Multivariable		
		No NPS use (n=1,693)	Yes (n=94)	OR (95%CI) /test statistic[a]	*p* value	AOR[b]	95% CI	*p*-value
Demographics	Age (<25) %	69.2	64.9	0.82 (0.53, 1.27)	0.379	0.79	0.48, 1.30	0.352
	Sex (male) %	60.3	60.6	1.01 (0.66, 1.55)	0.949	1.10	0.69, 1.76	0.680
	Age first tried ecstasy (<18)	46.4	50.0	1.16 (0.76, 1.75)	0.495	1.00	0.63, 1.59	0.998
	Tertiary qualifications %	47.9	58.1	1.51 (0.99, 2.30)	0.056			
	GLBT %	11.0	9.6	0.85 (0.42, 1.72)	0.657			
	Unemployed %	15.3	9.6	0.59 (0.29, 1.18)	0.130	0.58	0.28, 1.22	0.152
Drug Use	Daily tobacco use[#] %	38.6	46.7	1.40 (0.92, 2.13)	0.120	1.65	1.03, 2.66	0.038
	Daily cannabis use[#] %	13.5	16.0	1.21 (0.69, 2.14)	0.505	0.91	0.46, 1.78	0.782
	Ecstasy use[#] (≥weekly) %	23.0	18.7	0.77 (0.45, 1.32)	0.338	0.71	0.40, 1.26	0.246
	Methamphetamine use[#] %	44.8	51.1	1.28 (0.85, 1.95)	0.237	0.96	0.58, 1.58	0.858
	LSD use[#] %	29.5	30.1	1.03 (0.65, 1.62)	0.902	0.78	0.44, 1.36	0.376
	Cocaine use[#] %	41.3	53.2	1.62 (1.07, 2.45)	0.023	1.36	0.82, 2.24	0.230
	AUDIT score ≥16 %	38.4	42.6	1.19 (0.78, 1.81)	0.426			
	Binged on a stimulant drug[#] %	32.9	36.2	1.16 (0.75, 1.79)	0.441	1.02	0.62, 1.68	0.933
	Ecstasy SDS score (≥3)[#] %	20.0	26.6	1.45 (0.87, 2.42)	0.157			
	Number of drug classes[#^] (mean; SD)	4.3 (1.97)	4.88 (1.78)	t_{1771}=-2.87	0.004	1.16	1.01, 1.34	0.037
	Overdose (past year) %	35.2	33.0	0.91 (0.58, 1.41)	0.664	0.82	0.51, 1.31	0.397
Other	Any crime (past month) %	30.4	38.3	1.42 (0.93, 2.18)	0.107	1.30	0.80, 2.12	0.287
	K10 score ≥22 %	27.4	29.0	1.08 (0.68, 1.72)	0.737	1.03	0.60, 1.76	0.927
	Self-reported mental health problem[#] %	28.7	34.0	1.28 (0.83, 1.99)	0.266	1.23	0.74, 2.06	0.423

Note: OR = odds ratio; CI=confidence interval; AOR=adjusted odds ratio; SDS=severity of dependence scale; GLBT=gay, lesbian, bisexual or transgendered.

[*]denotes significance using the Benjamini-Hochberg procedure; [#]in the six months preceding interview; ^Maximum of 17 drug classes (includes ecstasy, methamphetamine, illicit pharmaceutical stimulants, cocaine, LSD, MDA, ketamine, GHB, amyl nitrite, nitrous oxide, cannabis, heroin, other opioids, illicit antidepressants, illicit benzodiazepines, magic mushrooms, steroids).

[a] Bivariate analysis were conducted, with odds ratios (OR) presented here for categorical outcomes; independent samples t-tests were conducted for parametric continuous data.

[b] Multivariable analyses were conducted using significant variables from all five bivariate models: i.e. significant variables from the phenethylamine, tryptamine, synthetic cannabinoid and poly NPS bivariate comparisons (age, sex, age of ecstasy initiation, weekly or more ecstasy use, LSD use, daily tobacco use, daily cannabis use, cocaine use, methamphetamine use, employment status, binged on a stimulant drug, overdose, poly drug use, past month criminal activity, K10 score and mental health problem). Year was also included in the model to control for changes over time.

Table 6: Correlates of poly NPS use amongst RPU, 2011-2015

		Poly NPS use past six months				Multivariable		
		No NPS use (n=1,693)	Yes (n=399)	OR (95%CI)/test statistic[a]	*p* value	AOR[b]	95% CI	*p*-value
Demographics	Age (<25) %	69.2	79.9	1.77 (1.36, 2.32)	<0.001*	1.54	1.10, 2.16	0.011
	Sex (male) %	60.3	77.2	2.23 (1.73, 2.87)	<0.001*	1.85	1.36, 2.52	<0.001
	Age first tried ecstasy (<18)	46.4	64.3	2.08 (1.66, 2.61)	<0.001*	1.28	0.96, 1.71	0.095
	Tertiary qualifications %	47.9	43.1	0.83 (0.66, 1.03)	0.090			
	GLBT %	11.0	11.1	1.00 (0.71, 1.42)	0.996			
	Unemployed %	15.3	21.1	1.48 (1.12, 1.94)	0.005*	0.97	0.67, 1.39	0.858
Drug Use	Daily tobacco use[#] %	38.6	53.7	1.84 (1.48, 2.30)	<0.001*	1.15	0.86, 1.56	0.345
	Daily cannabis use[#] %	13.5	31.2	2.89 (2.24, 3.73)	<0.001*	1.67	1.19, 2.36	0.003
	Ecstasy use[#] (≥weekly) %	23.0	41.2	2.34 (1.86, 2.95)	<0.001*	1.44	1.07, 1.95	0.017
	Methamphetamine use[#] %	44.8	64.2	2.20 (1.76, 2.76)	<0.001*	0.81	0.59, 1.10	0.180
	LSD use[#] %	29.5	72.7	6.36 (4.98, 8.11)	<0.001*	2.18	1.60, 2.97	<0.001
	Cocaine use[#] %	41.3	44.6	1.15 (0.92, 1.43)	0.226	0.47	0.34, 0.65	<0.001
	AUDIT score ≥16 %	38.4	34.8	0.85 (0.68, 1.07)	0.173			
	Binged on a stimulant drug[#] %	32.9	55.6	2.56 (2.05, 3.20)	<0.001*	1.28	0.95, 1.72	0.108
	Ecstasy SDS score (≥3)[#] %	20.0	23.4	1.22 (0.93, 1.62)	0.158			
	Number of drug classes[#^] (mean; SD)	4.3 (1.97)	6.88 (2.40)	t_{526}=-19.99	<0.001*	1.56	1.44, 1.69	<0.001
	Overdose (past year) %	35.2	50.1	1.85 (1.49, 2.31)	<0.001*	1.56	1.19, 2.06	0.001
Other	Any crime (past month) %	30.4	53.9	2.68 (2.14, 3.36)	<0.001*	1.43	1.08, 1.90	0.013
	K10 score ≥22 %	27.4	35.5	1.45 (1.15, 1.84)	0.002*	0.83	0.60, 1.16	0.270
	Self-reported mental health problem[#] %	28.7	35.4	1.36 (1.08, 1.71)	0.008*	1.20	0.87, 1.66	0.261

Note: OR = odds ratio; CI=confidence interval; AOR=adjusted odds ratio; SDS=severity of dependence scale; GLBT=gay, lesbian, bisexual or transgendered.

[*]denotes significance using the Benjamini-Hochberg procedure; [#]in the six months preceding interview; ^Maximum of 17 drug classes (includes ecstasy, methamphetamine, illicit pharmaceutical stimulants, cocaine, LSD, MDA, ketamine, GHB, amyl nitrite, nitrous oxide, cannabis, heroin, other opioids, illicit antidepressants, illicit benzodiazepines, magic mushrooms, steroids).

[a] Bivariate analysis were conducted, with odds ratios (OR) presented here for categorical outcomes; independent samples t-tests were conducted for parametric continuous data.

[b] Multivariable analyses were conducted using significant variables from all five bivariate models: i.e. significant variables from the poly NPS bivariate comparisons (age, sex, age of ecstasy initiation, weekly or more ecstasy use, LSD use, daily tobacco use, daily cannabis use, methamphetamine use, employment status, binged on a stimulant drug, overdose, poly drug use, past month criminal activity, K10 score and mental health problem), and significant variables from the phenethylamine, tryptamine and synthetic cannabinoids bivariate comparisons (cocaine use). Year was also included in the model to control for changes over time.

SUPPLEMENTARY MATERIAL

Table 7: Number of participants, 2010-2015

	Total number of participants n	Number of repeat participants n (%)
2010	693	115 (16.6)
2011	574	104 (18.1)
2012	607	81 (13.3)
2013	685	65 (9.5)
2014	800	81 (10.1)
2015	763	83 (10.9)

Table 8: Recent NPS use: overlap between NPS classes, 2011-2015

	Phenethylamines	Tryptamines	Synthetic Cannabinoids	Synthetic Cathinones	Piperazines	Plants & extracts	Aminoindanes
Tryptamines (n)	140						
Synthetic cannabinoids (n)	86	69					
Synthetic cathinones (n)	89	77	33				
Piperazines (n)	5	5	5	10			
Plants & extracts (n)	56	69	44	29	3		
Aminoindanes (n)	7	5	4	3	1	4	
Arylcyclohexylamines (n)	18	23	7	16	0	1	2

For example: 140 participants had used phenethylamines and tryptamines; 86 had used phenethylamines and synthetic cannabinoids; 89 had used phenethylamines and synthetic cathinones.

Table 9: Rates[#] of NPS use amongst RPU, 2010-2015 (excludes repeat participants)

	2010 %	2011 % (95% CI; *p*)	2012 % (95% CI; *p*)	2013 % (95% CI; *p*)	2014 % (95% CI; *p*)	2015 % (95% CI; *p*)	2010-2015* % 95% CI; *p* value
SYNTHETIC CATHINONES Mephedrone (miaow, 4MMC); Methylone (bk-MDMA); MDPV (Ivory Wave); Other substituted cathinone	**18.5**	**17.5** (-0.04, 0.06; *p*=0.734)	**10.6** **(0.02, 0.11;** ***p*=0.003)**	**8.5** (-0.01, 0.06; *p*=0.273)	**7.4** (-0.02, 0.04; *p*=0.547)	**7.4** (-0.03, 0.03; *p*=0.933)	**11.3** ↓ **0.08, 0.15;** ***p*<0.001**
PHENETHYLAMINES 2C-I; 2C-B (Bromo, TWOs, trystacy); 2C-E (hummingbird, europa); 2C-Other; Benzo Fury (6-APB); PMA; DOI (death on impact); NBOMe (25I, 25B, 25C)	**8.0**	**16.3** **(-0.13, -0.04;** ***p*<0.001)**	**13.7** (-0.02, 0.07; *p*=0.318)	**20.7** **(-0.11, -0.02;** ***p*=0.004)**	**22.0** (-0.06, 0.03; *p*=0.609)	**18.5** (-0.01, 0.08; *p*=0.120)	**16.8** ↑ **-0.14, -0.07;** ***p*<0.001**
TRYPTAMINES DMT; 5-Meo-DMT	**7.5**	**14.2** **(-0.11, -0.03;** ***p*<0.001)**	**13.8** (-0.04, 0.05; *p*=0.961)	**14.0** (-0.04, 0.04; *p*=0.988)	**14.3** (-0.04, 0.04; *p*=0.947)	**10.8** (-0.000, 0.07; *p*=0.060)	**12.3** ↑ **-0.06, -0.002;** ***p*=0.047**
SYNTHETIC CANNABINOIDS K2/Spice; Kronic; Other synthetic cannainoid	-	**6.6**	**16.6** **(-0.14, -0.06;** ***p*<0.001)**	**16.0** (-0.04, 0.05; *p*=0.843)	**6.7** **(0.06, 0.13;** ***p*<0.001)**	**6.5** (-0.02, 0.03; *p*=0.958)	**10.1** – -0.03, 0.03; *p*=0.952
PIPERAZINES BZP	**4.9**	**1.6** **(0.01, 0.05;** ***p*=0.008)**	**1.2** (-0.01, 0.02; *p*=0.804)	**<0.1** (0.001, 0.02; *p*=0.069)	**<0.1** (-0.01, 0.01; *p*=0.896)	**0** (-0.003, 0.01; *p*=0.503)	**1.3** ↓ **0.03, 0.07;** ***p*<0.001**
PLANTS & EXTRACTS LSA (Hawaiian Baby); Mescaline; Salvia Divinorum; Datura (Angel's trumpet); Ayahuasca	**2.0**	**7.9** **(-0.09, -0.03;** ***p*<0.001)**	**7.7** (-0.03, 0.04; *p*=0.981)	**6.0** (-0.01, 0.05; *p*=0.347)	**4.5** (-0.01, 0.04; *p*=0.254)	**4.4** (-0.02, 0.03; *p*=0.928)	**5.1** ↑ **-0.04, -0.004;** ***p*=0.030**
AMINOINDANES MDAI; 5-IAI	-	-	**0.9**	**0.7** (-0.01, 0.01; *p*=0.913)	**<0.1** (-0.01, 0.01; *p*=0.841)	**<0.1** (-0.01, 0.01; *p*=0.951)	**0.5** – -0.003, 0.02; *p*=0.325
ARYLCYCLOHEXYLAMINES Methoxetamine (MXE)			**1.4**	**2.4** (-0.03, 0.01; *p*=0.276)	**1.0** (0.001, 0.03; *p*=0.062)	**1.5** (-0.02, 0.01; *p*=0.547)	**1.6** – -0.01, 0.01; *p*=0.902
ANY NPS %	**32.9**	**42.7** **(-0.16, -0.04;** ***p*=0.001)**	**50.8** **(-0.15, -0.02;** ***p*=0.019)**	**46.6** (-0.02, 0.10; *p*=0.196)	**40.5** **(0.01, 0.11;** ***p*=0.029)**	**39.6** (-0.04, 0.06; *p*=0.768)	**41.5** ↑ **-0.12, -0.02;** ***p*=0.013**

Note: For synthetic cathinones, phenethylamines, tryptamines, piperazines, and plants & extracts, 2011-2015 figures exclude repeat participants. For synthetic cannabinoids, 2012-2015 figures exclude repeat participants. For aminoindanes and arylcyclohexylamines, 2013-2015 figures exclude repeat participants; [#]in the past six months; *for synthetic cannabinoids this refers to 2011-2015 figures; for aminoindanes and arylcyclohexylamines this refers to 2012-2015 figures. Pairwise comparisons made across adjacent years; i.e. 2010 vs 2011; 2011 vs 2012; 2012 vs 2013; 2013 vs 2014; 2014 vs 2015; 95% CI refers to the differences across adjacent years, except for the final column where they refer to differences in 2010 vs 2015 percentages. ↑ = a significant increase in 2010 vs 2015 figures. ↓ = a significant decrease in 2010 vs 2015 figures. – no change in 2010 vs 2015 figures. Significant findings have been bolded.

Contributors

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***Conflict of interest statement**

Conflict of interest

No conflicts declared.

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