

Corkery John (Orcid ID: 0000-0002-3849-817X)

Lione Lisa (Orcid ID: 0000-0001-6694-6956)

Title: Impact of the UK Psychoactive Substances Act on awareness, use, experiences and knowledge of potential associated health risks of Novel Psychoactive Substances

Short Title: Impact of UK PSA 2016 on awareness, use, experiences and risk awareness of NPS

Authors: Elena Deligianni, Omari J. Daniel , John M. Corkery , Fabrizio Schifano and Lisa A. Lione

School of Life and Medical Sciences, Department of Clinical and Pharmaceutical Sciences,
University of Hertfordshire, Hatfield, UK

Correspondence email: l.lione@herts.ac.uk

Authors' emails: elena.deligianni@gmail.com , omarijordan@hotmail.co.uk ,
j.corkery@herts.ac.uk , f.schifano@herts.ac.uk

Target journal: British Journal of Clinical Pharmacology.

Research Themed Issue: Novel Psychoactive Substances

Dr Lisa A Lione is the Principal Investigator. No interventions were performed with human subjects / patients and or substances administered.

Word count: 4758 (2500-4000)

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/bcp.14123

Keywords: novel psychoactive substances (NPS), online survey, recreational use, policy, Psychoactive Substances Act 2016, psychoactive effects

Abstract (250 words)

Aims: The risk of potential harms prompted the UK government to introduce the Psychoactive Substances Act (PSA) in 2016. The aim of the present study was to evaluate the impact and effectiveness of this new legislation on patterns of NPS awareness, use, experiences and risk awareness in a self-selected sample of UK consumers to inform education and policy.

Methods: The Bristol Online Survey was advertised on the Bluelight drug forum and social media Facebook pages and University email between 7 January and 7 February 2015 (168 responses) and 9 March to 18 September 2017 (726 responses). UK country of residence responses were extracted for analysis (SPSS).

Results: In a predominantly university-educated, young (< 25 years) self-selecting sample, one year after introduction of the legislation, NPS use (in males, under 18s, those educated to school/college level, $p < 0.001$) has increased, whilst health risk awareness has not changed and remains poor. Users are switching to sourcing NPS via street dealers (49%) and the darknet (31%) and showing an increase in preference for the herbal NPS *Salvia divinorum* ($p < 0.05$). The main reasons for NPS use remain the influence of friends (69%) in a social setting and to 'get high' (76%) usually in combination with alcohol, cannabis or ecstasy.

Conclusions: Regulation alone, so far, has not impacted on health risk awareness, NPS drug demand and culture in our UK survey sample. Alongside regulation, NPS health promotion education (particularly in schools, colleges) is needed that addresses resilience and both the risks and beneficial effects of NPS.

What is already known about this subject:

- Government evaluation review of its 2016 PSA shows indications of reduced UK NPS use in the general population.
- No systematic evaluation of the impact and effectiveness of the UK 2016 PSA on patterns of NPS use, experiences and health risk perception has been undertaken in vulnerable user groups.

What this study adds:

- UK NPS use in under 18, school/college educated males has increased, whilst reasons, motivations and health risk perceptions of NPS have not changed.
- There is a shift to sourcing NPS from street dealers and the darknet and an increase in the harder to regulate herb *Salvia Divinorium*.
- Statutory drug education programmes in schools providing resilience and risk management skills on drug use are needed alongside policy.

Introduction (718 words)

The emergence of Novel Psychoactive Substances (NPSs) has created a challenge for drug policy-makers worldwide and a substantial global threat for public health. NPSs vary widely with inconsistent composition and potency often being significant factors in the health risks they pose. Up to 2017, over 60 countries have implemented legal responses to control NPS [1]. The European Union (EU) Early Warning System currently monitors over 670 NPS [2]. Various laws and controls have been created to tackle NPS diffusion across Europe [3] and even though there is no uniform consensus, two trends are identifiable. First, in line with public opinion, there appears to be a general move towards the use of the threat of prison to deter suppliers [4] and, second, it seems that countries are choosing not to use criminal sanctions for those possessing a new psychoactive substance for personal use [5].

The UK is one of the biggest consumers of NPSs in Europe with frequent reports of serious clinical and public health issues, particularly for vulnerable groups (prisoners, teenagers, homeless) [6]. Although NPSs account for a small share of drug-related harms in the UK, compared with traditional drugs, [7-9] the management [10] and severity of harms e.g. long-term health issues prompted the UK government to bring in the Psychoactive Substances Act (PSA) 2016 banning the production, supply, importation and exportation of NPS, but permitting possession (with some exemptions) [11].

The PSA 2016 does appear to have reduced UK-based online NPS stores and offline retail headshops [7,12]. Furthermore during 2017, 51 new NPSs were detected in Europe [2], fewer than the previous 3 years, which may, in part, be due to measures taken by some national governments in Europe, such as the UK, to target producers and retailers of NPSs by prohibiting their open sale as 'legal highs'. Despite this encouraging decline the overall number of NPSs available on the market continues to grow and there is evidence that high potency substances are increasing [7,13] and that legal markets are being displaced by

alternative routes, such as street-level drug dealing or crypto-markets [7,14]. Prohibition will not address supply of NPSs via the largely untraceable area of the internet, especially the darknet, nor will it address drug demand – the basic human desire for seeking pleasure and altered states of consciousness. Worryingly, since 2014, the number of UK drug-users who have bought their drugs from crypto-markets has risen from 12% to 25% [15].

Despite legislation being one of the primary means used to tackle NPS availability, no systematic evaluation of the impact and effectiveness of this UK ban on patterns of NPS use has been undertaken. Evidence of the impact and effectiveness of drugs policy enactment is captured by the number of drug-related deaths and offences, drug seizures, forensics, clinical case reports, and emergency department presentations. Alongside these sources, surveying users helps build an in-depth picture on the patterns of NPS use. However, few surveys capture NPSs users' perceptions of safety [16,17], their motivations [18-20], preferences and settings for NPS use and importantly their educational background. The search for pleasure is what drives consumer markets for psychoactive drugs, both legal and illegal, but, at present, public policy gives no weight to preferences. For example, preferences for NPSs differ across European (prefer stimulants) and US (prefer cannabimimetics) markets [21]. Understanding consumer reasons and motivations for NPS use would enhance government-targeted prevention interventions to the appropriate target groups [18].

It is, therefore, important that reliable and up-to-date survey data are available to inform education and policy in this area. We recently reported that public awareness of NPS and, importantly, perceptions of the potential health risks associated with NPS use was lacking in a small sample of predominantly university-educated young people, mainly from the UK and Greece [22] highlighting a need for governments to take responsibility for educating their own

consumer markets, as well as protecting them with legislation. Our online survey presented in this paper was designed and ran in 2015 and then again in 2017 with two aims – first to provide data on the impact of the PSA 2016 Act on UK consumer awareness and use of NPSs and - second to provide data on UK consumer NPSs preferences, motivations, experiences and health perceptions. Some of these survey findings were presented at the VIth International Novel Psychoactive Substances conference [23].

Methods (581 words)

Following our previous study available online between 7 January and 7 February 2015 (168 responses obtained) [22] our survey was updated to capture sourcing and setting for NPS use and relaunched online between 9 March and 18 September 2017 (726 responses). UK country of residence responses were extracted for analysis and comparison of NPS awareness and use in 2015 and 2017, one year before and one year after the introduction of the UK PSA 2016.

To elicit the views of individuals and to get a wide range of views in a short time, an online survey was considered the most appropriate method, having been previously used by the authors in order to obtain information on NPS [22]. The survey was developed using Bristol Online Survey (www.survey.bris.ac.uk), a Web survey development service with wide readership. This product was used as it is freely available to the University of Hertfordshire, provides analytical tools, and is easy to use. The survey instrument was designed to capture patterns of NPS awareness (had they heard of NPS or ‘legal highs’), use, preference, motivations, experiences and health risk perceptions.

In the updated 2017 survey there were 38 structured questions split into four sections. The first two sections were mandatory (11 questions on demographics and NPS awareness, use, and

perceived harms). Respondents were informed that they should only complete the third section if they had taken an NPS on at least one occasion in the past. Finally, the fourth section was specific to those that had taken ketamine on at least one occasion in the past. A copy of the survey will be provided upon request.

The survey was in English and advertised on DS Daily News, the Bluelight drug forum (www.bluelight.org) and promoted using University email, social media Facebook pages (including UKC Psychedelics Society, University of Hertfordshire Bioscience society, Life and Medical Sciences international students, Psychedelic Experience). The survey was anonymous, took 15 minutes to complete and comprised questions requiring both restricted/categorical and/or open responses. Social media enabled easy and fast distribution of the survey through personal accounts and university groups. The drug forum was an important source for targeting drug users, but also individuals with an interest in drug-related issues.

The inclusion criteria were the following: (a) no restriction in terms of age, gender, sexual orientation, or region of participants; (b) non-users and users of NPS could take part in the research; and (c) a good understanding of English was required for participants.

Descriptive statistics were performed to describe the basic features of data using the Bristol Online Survey tool. Chi-square tests were used to assess whether changes in demographics (age, gender, sexual orientation, educational background and employment status) affected NPS awareness and use in 2015 and 2017. The significance level was set to $*p < 0.05$ after a Bonferroni correction. IBM® SPSS Statistics (version 24) for MacOS Sierra 10.12.3 was used. A t-test for independent proportions (z-test) was used to compare the population proportional differences between the 2015 and 2017 independent samples and assess whether NPS awareness and use changed between 2015 and 2017. The significance level was set to $\#p < 0.05$.

The study was approved by the University of Hertfordshire's Health and Human Sciences Research Institute Ethics Committee (PHAEC/1042 (02)). Informed consent was assumed by individuals agreeing to proceed with the survey.

Nomenclature of Targets and Ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in <http://www.guidetopharmacology.org>, the common portal for data from the IUPHAR/BPS Guide to PHARMACOLOGY.

Results (1383 words)

The 2015 survey was completed by 168 respondents from 17 countries internationally over the one-month period it was online. The 2017 survey was completed by 726 respondents from 44 countries internationally during the six-month period that it was online. The responses from UK residents were extracted for our analysis.

Demographics of UK respondents

In the 2017 survey there were 500 UK (69%) respondents mainly from England (95%), a few from Scotland (2.8%) and Wales (2.2%); whilst in 2015 there were 58% UK respondents with no definition of specific regions. Despite the lower numbers of respondents in the one-month 2015 survey the demographics of both survey samples are largely the same ($p > 0.05$, Table 1), with the exception of significantly less respondents in the 18-25 aged group (54%) in 2017 sample compared with the 2015 sample (89%, $p < 0.05$), enabling comparison across the survey samples. The UK respondents in both samples (Table 1) are typically female, young (under 25), heterosexual and educated to higher education level. Further, the self-selected subset of UK respondents is similar for each survey sample identified from University of Hertfordshire sources (2015, 51%; 2017, 63%) and social media sources (2015, 49%; 2017 31%), with few

identified from specialised social media (e.g. DS Daily, 2015, 0%; 2017, 2%) and drug fora (2015, 0%; 2017, 4%).

Awareness of NPS

Gender, age and sexual orientation did not alter NPS awareness in both surveys (Table 2). The level of education influenced NPS awareness in 2015, where high school (75%) and undergraduates (80%) were more aware than college level (44%) and postgraduates (46%, $p < 0.05$). This was not the case in 2017 ($p > 0.05$), which reflects a significant increase in NPS awareness in postgraduate (83%) and college level (92%) respondents in 2017, compared with 2015 ($p < 0.05$, z-test), although differences may reflect the lower numbers of respondents in the 2015 groups. Similarly, employment impacted NPS awareness in 2015 which wasn't the case in the larger 2017 groups, where the unemployed and employed were equally aware, although there was a trend to less NPS awareness in the unemployed group seeking work (77%, $p = 0.07$).

Overall NPS awareness was not significantly higher following the legislation (2015, 72% vs 2017, 87%, $p > 0.05$, z-test), although the under 18 (2015, 0% vs 2017, 100%, $p < 0.001$) and 26-35 (2015, 40% vs 2017, 90%, $p = 0.01$) age groups and those educated to postgraduate (2015, 46% vs 2017, 83%, $p < 0.05$) and high school/ college level (2015, 54% vs 2017, 94%, $p = 0.01$) educated were significantly more aware of NPS following the ban.

Use of NPS

In both surveys NPS use was higher in males (Table 3) despite males and females being equally NPS aware (Table 2). Forty-eight percent of males versus only 13% females used NPSs in 2017 ($p < 0.001$) compared with 24% males versus 14% females in 2015 ($p > 0.05$). Sexual orientation did not alter NPS use ($p > 0.05$) whereas employment status significantly impacted NPS use in

both surveys ($p < 0.01$). High school and college educated respondents reported significantly higher use of NPS in 2017 (58% and 52% respectively) compared with the higher educated groups of undergraduates (23%) and Postgraduates (15%) ($p < 0.001$). Despite a similar higher education demographic in both surveys, NPS use was not altered across different educational groups in 2015, which is likely to reflect the low number of high school and college educated respondents in the 2015 survey. Similarly, the significant effect of age on NPS use in 2017 (not seen in 2015) likely reflects the low number of respondents in the under 18 age group. In both surveys this age group had the smallest number of respondents (2015, 1%; 2017, 2.6%) which will skew the % of NPS use and awareness. In 2017 NPS use correlated with age, i.e. the highest proportion of NPS users was the 100% NPS aware under 18s (62%), followed by 26-35 age group (39%), 18-25 (25%), 36-50 (25%) and over 50 (13%) ($p < 0.001$). Given the low numbers of respondents in the under 18 groups when combined with the 18-25 age group NPS use of the under 25s was comparable with the overall NPS use trend (2015, 18% versus 2017, 26%, $p > 0.05$). Although there was no significant change in overall NPS use since the legislation (2015, 17% 2017, 27%, $p = 0.2$, z-test) there was an increased trend in overall NPS use in males ($p = 0.12$, 24% to 48%), under 18s ($p = 0.11$, 0% to 62%) and those educated to high school/college level ($p = 0.12$, 23% to 54%).

Reasons and motivations for NPS use

The main reasons for using NPSs in the 2015 and 2017 respondents was their friends had taken them (2015, 82.4%; 2017, 68.7% Table 4) and being able to buy them online (2015, 47%; 2017, 43%). Cost remained a significant reason with just over one-third of 2015 and 2017 respondents citing the fact they are cheaper than other drugs. As expected, fewer 2017 NPS users stated the reason for using NPS was because they were not against the law (2017, 26.9%) compared with before the ban (2015, 41.2%, $p > 0.05$) reflecting some awareness of the PSA 2016 by users.

The main motivation for UK NPS use was to 'get high' (2015, 58.8%; 2017, 76.1%).

Source and setting of NPS use

Following the legislation, 2017 users most commonly purchased NPS by illegal routes (friends, street dealers and surface internet (23%, 24% and 22% frequency response) (Figure 1a).

Worryingly 31% of our NPS UK users (15% frequency response) purchased NPSs via the untraceable darknet indicating legal markets (headshops, 13% frequency response) are being displaced by alternative routes, such as street-level drug dealing or crypto-markets.

The UK 2017 NPS users (typically in their 20s and 30s) preferred to take NPS in a social setting at parties and clubs or at home with friends (27%, 24% and 27% frequency response) rather than alone (15%, Figure 1b) which fits with their demographic and main reasons for taking NPSs, which is with friends (Table 4). The 2017 NPS users most commonly sourced their information on NPSs from drug fora (42%) followed by social network sites (21%) and other (22%) (Figure 1c).

Types of NPS used

The total number of responses to types of NPS was higher in 2017 users (3-4 NPS per user) compared with 2015 users (1-2 NPS per user) reflected by an increased range of 'other' NPS used in 2017 (Figure 2). There was a significant increase in *salvia divinorum* use (2017, 45%; 2015, 6%, $p < 0.05$) and an increased trend in all types of NPS used by 2017 users (% response) since the legislation, except aerosols, methoxphenidine and diphenidine. Ketamine use was high in both surveys (2015, 77%; 2017, 94%), which will have reflected a preference for the ketamine derivative e.g. methoxetamine in both surveys.

Preference for other drugs used in combination with NPS

There were similar patterns in use and preference of other drugs (legal and illegal) in combination with NPS, before and after the legislation, with highest preference being for alcohol (2017, 73%; 2015, 88%), cannabis (2017, 63%; 2015, 65%) followed by ecstasy (2017, 53%; 2015, 47%) (Figure 3). Polydrug use was also similar in both survey samples where approximately 3 to 4 drugs were used per user even though 2017 users used a wider range of NPS (Figure 2). There was a significantly lower use for mephedrone since the legislation (2017, 11%; 2015, 41% $p < 0.05$).

Subjective effects of NPS used

There were similar patterns in the subjective effects of the NPS used by 2015 and 2017 respondents (Figure 4). The main positive effects noted by NPS users (2015 and 2017 survey respectively) was feeling relaxed (65% and 90%) and experiencing hallucinations (41% and 69%). Many users also reported anxiety (29% and 53%), lower inhibitions (24% and 50%) or a faster heart rate (29% and 58%) after use of NPSs.

User perception of health risks associated with NPS use

Only 17% of 2017 users considered NPS use as high risk compared with 35% of 2015 users ($p = 0.18$, Figure 5a). Further, nearly half of 2017 users (47%) considered NPS use carried a low risk, no risk or did not know if they carry a risk, compared with 35% of 2015 NPS users. Furthermore, the age of the 2017 users did not alter their perception of the health risks associated with NPS use, as the lack of risk awareness ($> 40\%$) was seen across all age groups ($p > 0.05$ age effect, Figure 5b).

Discussion (2076 words)

To the best of our knowledge this is the first report to assess UK NPS awareness, use, experiences and knowledge of potential associated health risks before and after implementation of the PSA 2016.

Increase in NPS awareness in UK residents educated to postgraduate and high school/college level

Although UK NPS awareness is not significantly higher following the PSA 2016 ($p=0.07$) only 13% remain unaware in 2017, compared with 28% in 2015. This is also higher than a UK student sample where 18% of the 446 students were unaware of NPS in 2014 [17] demonstrating the new UK legislation has increased awareness. A significant increase in NPS awareness was seen in those UK residents educated to postgraduate and high school/college level and corresponding age groups indicating more young UK residents are informed about NPS.

Increase in NPS use in male UK residents educated to school/college level and under 18s

Since the introduction of the PSA 2016 there is an increased trend in UK NPS use from 17% to 27% (Table 3, $p>0.05$) which is higher than 11.5% NPS use reported in England by GDS [15] and 0.4% NPS use reported by UK 2017/18 Crime Survey [24], although the Crime Survey covers residential households, and not drug-using subcultures such as students, in contrast to our survey. NPS use varies considerably depending on the demographic of respondents. A Eurobarometer survey [4] revealed that the lifetime experience of NPS use was 8% among European youth compared with 65.8% among a targeted population of nightclub visitors [25]. As our surveys were largely promoted through University email many respondents were under 35 years old and in higher education. The high 27% 2017 NPS use is in line with 31.4% NPS

use sampled from 446 UK students aged between 17-34 years [17]. A drug culture survey of 1401 students has also reported that nearly 1 in 5 (17%) students at British universities admitted to having taken NPS [26].

The significantly higher use by males in 2017 ($p < 0.001$) is supported by a previous survey carried out among young people in UK, where male respondents were significantly more likely than female users to have taken NPS [17] and the 2018 GDS [15] indicates that males (6.7%) were more than twice as likely to have used NPS in the last year than females (2.6%). Worryingly the presence of NPS in drug-related deaths is becoming more common in the UK and males made up almost three-quarters of drug-related deaths cases in 2015 and 2017 [27]. Many studies have shown that the use of NPS occurs in nearly all age groups, although the majority of users are believed to be young males [19, 28]. Our 2017 survey shows a highly significant effect of age on NPS use ($p < 0.001$) where use was highest in the 100% aware under 18 group. Although this group had the smallest number of respondents the high NPS use correlates with the most represented age of 140 UK NPS users being 17 years old [17]. Further, high school and college educated respondents had significantly higher NPS use compared with those educated at university in 2017, but not in 2015, which is likely to reflect sampling differences as the response level in college and school educated groups in 2015 was low. The fact that those educated to college or school level are more likely to use NPS in 2017 ($p < 0.001$, Table 3) (and not 2015), despite an increase in NPS awareness, indicates a need for improved drugs education in schools and colleges. A small study in North London recently demonstrated that 17% of 12 to 18 years olds admitted using NPS and none had received teaching specifically about NPS [29].

Reasons, motivations, experiences, preferences and health risk perception of UK NPS use remain unchanged

NPS-specific studies that take reason into account often emphasise external circumstances such as price, legal status and availability as crucial reasons for NPS use [18]. The main reasons cited by our users, before and after the legislation, were their friends taking NPS and being able to buy them online, followed by price, in line with other studies [17,30]. The influence of friends fits with preference to take NPSs in a social setting and sourcing NPSs from a friend. The European Commission Eurobarometer (2014) survey of over 13,000 young people noted that in the UK (before the ban) the most popular route for sourcing NPS was from a friend [4]. Worryingly, our survey demonstrates that, since the ban, NPSs are commonly purchased by illegal routes (friends 45%, street dealers, 49% and internet, 49%) in line with the 2017/2018 Crime Survey [7]. Other surveys also show a shift towards a greater reliance on real world interactions (friends, dealers) occurs when an NPS is banned [16,19,31], which indicates an overlapping between the traditional and novel markets is taking place. Predictably, our data indicate purchasing NPS from the previously legal headshops (26%) is being displaced by alternative illegal routes such as the darknet (31%), in line with recent GDS surveys [15,32] that show the UK is leading the world in the rise of purchasing drugs on the darknet where 1 in 4 (25%) of those who had used drugs in the past year had bought their drugs in this way. It is concerning that one-third of our knowledgeable UK NPS users have purchased NPS by this covert route.

The majority of our UK NPS users, before and after the legislation, were intrinsically motivated to 'get high' with their friends and make a night out much better, revealing a culture and desire to experience social and reciprocal sharing fitting with the demographic profile of our users being predominantly young students. Other studies surveying NPS users with similar

demographic profiles also suggest that NPS users are driven by enhancement of social situations, the enjoyable effects, and a desire to 'get high' [17, 20, 33]. Importantly, the majority of our NPS users indicated they were in control and would likely stop using NPSs if they had changes to extrinsic factors e.g. social demands and responsibilities. Further, our users didn't cite using NPSs to cope with life problems or addiction and dependency, which more likely leads to abuse and harm potential, also supported by that fact that only 6% (2015) and 18% (2017) of users took NPS more than once a week. It is also important to note that the distribution of this survey via University and drug fora makes for a selection of knowledgeable education seeking NPS users and not NPS users that are living under poor conditions, where they are unlikely to have access to discussion fora and the internet. Eighty percent of our 2017 NPS users sourced drugs information from drug fora and 43% cited 'other' peer reviewed sources indicating many users gain some scientific knowledge that might inform their NPS drug taking.

Previous studies have revealed that reasons and motivations for different types of NPS use can vary considerably [18,19,34,35]. These studies indicate that use of novel stimulants and hallucinogens is mainly motivated by self-exploration, facilitation of social situations, euphoria ('get high') and insignificantly associated with dependency. In line with the motivation to 'get high' and 'feel relaxed' our UK users (before and after the ban) preferred hallucinogenic dissociatives (e.g. methoxetamine) and psychedelics (e.g. *salvia divinorum*). Many NPS users also took ketamine (2015, 77%; 2017, 94%), which will have reflected their preference for the ketamine derivative methoxetamine reported to produce more intense and longer lasting dissociative effects than ketamine [36]. The increased use of the natural NPS, *salvia divinorum* ($p < 0.05$) may, in part, be because it is harder to control under the PSA 2016. Preference for *salvia divinorum* (20% and 39%) has been previously reported by UK students [17,26] and can lead to de-realisation and medical and psychopathological risks [37,38]. There was an increase

in the use of the synthetic cannabinoid 'spice' following the legislation (32.8% versus 5.8%, $p > 0.05$) which can produce a state of relaxation and of feeling "stoned" [39], even though use of cannabis remained the same. This increase between 2015 and 2017 in our UK users may reflect the significant global rise in synthetic cannabinoid use that has occurred in the world of NPS over this time [6,15,32], demonstrating that regularly monitoring of NPS use is important in such a fast-paced scene.

Polydrug use was similar (before and after the legislation) even though 2017 users took a wider range of NPS. The consumption of NPS was combined with alcohol, cannabis and ecstasy for the majority of users, in line with European drug use in young adults [40]. Under 18 NPS users in our survey reported taking cannabis and stimulants, including amphetamine, cocaine, lysergide and ecstasy. Cannabis remains the most commonly used illicit drug in the UK and the second most prevalent drug overall after alcohol, whilst ecstasy is the next most commonly reported illicit drug used in the UK [24]. Since the legislation, preference for mephedrone significantly reduced to 11.1% ($p < 0.05$) in line with a recent report of the decline in mephedrone use in the UK among 16 to 34-year-olds [24] and the recent global decline in synthetic cathinone use [6,15,32]. The increased range of NPS hallucinogen dissociatives and psychedelics taken by 2017 UK users, many of which have stimulant properties, will account for the increased report of acute positive (relaxed, hallucinations) and negative (anxious, faster heart beating, aggression, nausea) subjective effects. As well as a subjective effect of feeling stoned, 'spice' can be both stimulating and sedating, anxiogenic and anxiolytic [41] and unlike cannabis, can produce a 'hangover' state which may correspond with reports of headaches. Polydrug use of alcohol, cannabis, ecstasy and cocaine may well contribute to the reported subjective effects.

Despite the increase in NPS awareness we see a decreased trend in the perception of health risks associated with NPS use where 1 in 5 users considered NPS use as high risk compared with 1 in 3 before the ban. Moreover, nearly half of 2017 users considered NPS use carried a low risk, no risk or did not know if they carry a risk, compared with one-third in 2015. The fact that over 80% of our NPS users are typically well educated and well informed is surprising given that there is a significant knowledge gap on the health risks of NPS use across all age groups. Given that the main motivation for NPS use in our surveys is to 'get high' the unknown high-risk aspect of NPS may be an attractive feature for many users [42] particularly younger adolescents happy to take risks to attain novel psychoactive experiences from NPS (age group with the highest NPS use). This may explain why our younger NPS users continue to use NPS even though they don't know the risks or believe they are high risk. Notably, significantly more of the 2015 NPS users were under 25 and twice as many considered NPS as high risk, compared with the 2017 NPS users. A recent qualitative study [20] emphasised that the development of appropriate harm reduction policies should incorporate an understanding of the relationship between the risks and the beneficial effects of NPS to better resonate with young drug users [43].

The high rate of NPS use in our surveys will, in part, reflect the demographic of the self-selecting samples being young (typically 20s and 30s), risk takers with a greater interest in drugs and more likely to go clubbing and to parties, than the general population. Moreover, these self-selecting sub-populations may be more resistant to change, hence extrapolation to the wider UK population needs to be carefully considered. However, high UK NPS use in males, in the under 18s and those educated to a school and college level in our 2017 sample, highlights the current need for statutory universal drugs education in UK schools and colleges as part of the national curriculum. This education needs to address the risks and benefits of

drug taking and importantly resilience to risk factors (e.g. peer pressure), social and emotional skills [44-46]. This will not only educate but build resilience and empower young people to help them make positive choices for their health, including drugs choices when in peer pressure situations.

In conclusion our surveys demonstrate that regulation alone, so far, has not impacted on risk awareness and reasons and motivations for UK NPS use (drug demand and culture) and that determining the type of motivation in our NPS consumer groups (in this case mainly UK students) is essential for effective prevention policies and reduction of NPS-related harms.

Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The views expressed here reflect only the authors' views. The authors would like to acknowledge the help of Dr Richard Szydlo from the Faculty of Medicine at Imperial College for assisting with statistical analyses, the survey respondents for contributing their time to this research and www.bluelight.ru for their help in advertising the survey.

Author Contributions

E.D., O.D. and L.A.L conceptualized the online surveys, methodology and extracted and analysed the data. E.D. and L.A.L wrote the first draft of the paper; E.D., F.S., J.M.C. and L.A.L then critically revised subsequent drafts.

Data Availability:

Research data are not shared. The data are not publicly available due to privacy / ethical restrictions.

Conflicts of Interest:

No conflicts of interest are declared here that may have influenced the interpretation of present data. Please note the following: F.S. is one of the editors of this special issue of Brain Science, was a full member of the UK Advisory Council on the Use of Drugs (ACMD) and a member of the ACMD's NPS and Technical Committees; J.C. is also a co-opted member of the NPS and Technical Committees. The views expressed here are solely those of the authors and do not necessarily reflect those of the Home Office or the ACMD.

Accepted Article

References

1. United Nations Office for Drugs and Crime (UNODC). Early Warning Advisory on New Psychoactive Substances. 2018. Accessed 10th August 2018
<https://www.unodc.org/LSS/Page/NPS>
2. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA-Europol). Annual Report on the implementation of Council Decision 2005/387/JHA. 2017. Accessed 18th October 2018.
http://www.emcdda.europa.eu/publications/implementation-reports/2017_en
3. Beltgens MT. Legislative Measures' Impact on the New Psychoactive Substances Market. In: Savona E., Kleiman M., Calderoni F. (eds) Dual Markets. Springer, Cham. 2017.
4. European Commission Report: Flash Eurobarometer 401: Young people and drugs. Luxembourg: TNS Political & Social. 2014. Accessed 18th October 2018.
http://ec.europa.eu/public_opinion/flash/fl_401_present_en.pdf
5. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) Legal approaches to controlling new psychoactive substances. 2014. Accessed 18th October 2018. <http://www.emcdda.europa.eu/topics/pods/controlling-new-psychoactive-substances>
6. Global Drug Survey 2016. Accessed on 10th August 2018.
<https://www.globaldrugsurvey.com/past-findings/the-global-drug-survey-2016-findings/>
7. Home Office Review of Psychoactive Substances Act. 2018. Accessed on 15th May 2019. <https://www.gov.uk/government/publications/review-of-the-psychoactive-substances-act-2016>

8. Office of National statistics. Deaths related to drug poisoning in England and Wales. 2013. Accessed on 10th August 2018
<https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2014-09-03>
9. Office for National Statistics. Deaths related to drug poisoning in England and Wales: 2017 registrations. Accessed on 10th August 2018 from
<https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2017registrations>
10. Wood DM, Ceronie B, Dargan PI. Healthcare professionals are less confident in managing acute toxicity related to the use of new psychoactive substances (NPS) compared with classical recreational drugs. QJM. 2016; 109:527-9.
11. Home Office Psychoactive Substances Act 2016, The Stationery Office Limited, 2016. Accessed on 10th August 2018
<http://services.parliament.uk/bills/2015-16/psychoactivesubstances.html>
12. Wadsworth E. Drummond C, Deluca P. The adherence to UK legislation by online shops selling new psychoactive substances. Drugs Educ. Prev. Policy. 2018; 25, 97–100.
13. Acreman DJ and Smith JC. Increased prevalence of high potency substances – an inadvertent effect of legislative control. Vth NPS conference 2017.
14. Van Buskirk J, Griffiths P, Farrell M, Degenhardt L. Trends in new psychoactive substances from surface and “dark” net monitoring. Lancet Psychiatry 2017; 4, 16–18.
15. Global drug survey 2018. Accessed on 10th August 2018
<https://www.globaldrugsurvey.com/gds-2018/>

16. McElrath K, O'Neill C. Experiences with mephedrone pre- and post-legislative controls: Perceptions of safety and sources of supply. *International Journal of Drug Policy*, 2011; 22(2), 120–127.
17. Corazza O, Simonato P, Corkery JM, Trincas G, Schifano F. “Legal highs”: safe and legal “heavens”? A study on the diffusion, knowledge and risk awareness of novel psychoactive drugs among students in the UK. *Riv Psichiatri*. 2014; 49(2): 89-94
18. Sutherland R, Bruno R, Peacoc, A, Lenton S, Matthews A, Salom C, Barratt MJ. Motivations for new psychoactive substance use among regular psychostimulant users in Australia. *International Journal of Drug Policy* 2017; 43, 23–32.
19. Soussan C, Kjellgren A. The users of Novel Psychoactive Substances: Online survey about their characteristics, attitudes and motivations. *International Journal of Drug Policy* 2016;32, 77–84.
20. Soussan C, Andersson M, Kjellgren A. (2018) The diverse reasons for using Novel Psychoactive Substances - A qualitative study of the users' own perspectives *International Journal of Drug Policy* 2018; 52, 71-78.
21. King LA (2014) New phenethylamines in Europe. *DTA drug testing and analysis*. 2014; 6(7-8), 808-818.
22. Deligianni E, Corkery JM, Schifano F, & Lione LA. An international survey on the awareness, use, preference, and health perception of novel psychoactive substances (NPS). *Human Psychopharmacology*, 2017; 32(3).
23. Deligianni E, Corkery JM, Schifano F, Lione LA. Impact of the UK Psychoactive Substances Act on awareness, use, experiences and knowledge of potential associated health risks of NPS. VIth NPS conference, *Research and Advances in Psychiatry* 2019; 6(1):1-71.

24. Home Office Drug Misuse: Findings from the 2017/18 Crime Survey for England and Wales London: Home Office. Accessed on 5th June 2019
<https://www.gov.uk/government/statistics/drug-misuse-findings-from-the-2017-to-2018-csew>
25. Wood DM, Hunter L, Measham, F, Dargan PI. Limited use of novel psychoactive substances in South London nightclubs. QJM 2012; 105(10), 959–964.
26. The Student Beans survey. Drug culture at UK universities. 2012; Accessed 10th August 2018
<https://www.theguardian.com/education/interactive/2012/oct/12/university-drug-culture-survey>
27. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (2018) UK Drug Report. 2018. Accessed 18th October 2018.
<http://www.emcdda.europa.eu/system/files/publications/8894/united-kingdom-cdr-2018-with-numbers.pdf>
28. Barratt MJ, Cakic V, Lenton S. Patterns of synthetic cannabinoid use in Australia. Drug Alcohol Rev. 2013; 32(2):141-6.
29. Lloyd AK, Shafi A, Mitchell K, Mayordomoaranda A, Martinotti G, Corazza O. NPS misuse in children and adolescents: a study among a sample population in North London accessing acute and community mental health services. Vth NPS conference, 2017.
30. Ramsey J, Dargan PI, Smyllie M, Davies S, Button J, Holt DW, Wood DM. Buying 'legal' recreational drugs does not mean that you are not breaking the law. QJM. 2010; 103(10):777-83.

31. Sande M. Characteristics of the use of 3-MMC and other new psychoactive drugs in Slovenia, and the perceived problems experienced by users. *International Journal of Drug Policy* 2016; 27:65-73.
32. Global Drug Survey 2017. Accessed on 10th August 2018
<https://www.globaldrugsurvey.com/gds2017-launch/results-released/>
33. Home Office New psychoactive substances review: Report of the expert panel. London: 2014. Accessed on 10th August 2018
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/368583/NPSexpertReviewPanelReport.pdf
34. Beharry S, Gibbons S. An overview of emerging and new psychoactive substances in the United Kingdom. *Forensic Sci Int.* 2016; 267:25-34.
35. Zawilska JB. "Legal Highs"--An Emerging Epidemic of Novel Psychoactive Substances. *Int Rev Neurobiol.* 2015; 120:273-300.
36. Corazza O, Schifano F, Simonato P. et al. Phenomenon of new drugs on the Internet: the case of ketamine derivative methoxetamine. *Hum Psychopharmacol.* 2012. 27:145-9.
37. Singh S. Adolescent salvia substance abuse. *Addiction* 2007; 102: 823-4. 24.
38. González D, Riba J, Bouso JC, Gómez-Jarabo G, Barbanoj MJ. Pattern of use and subjective effects of *Salvia divinorum* among recreational users. *Drug Alcohol Depend* 2006; 85: 157-62.
39. Tracy DK, Wood DM, Baumeister D. Novel psychoactive substances: identifying and managing acute and chronic harmful use. *BMJ*; 2007; 356.
40. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). European Drug Report. Trends and Developments; EMCDDA: Lisbon, Portugal, 2017. Accessed 18th October 2018. <http://www.emcdda.europa.eu/system/>
41. Papanti D, Schifano F, Botteon G, et al. "Spiceophrenia": a systematic overview of

“spice”-related psychopathological issues and a case report. *Hum Psychopharmacol.*

2013;

28:379-89.

42. Reuter P, Pardo B. New psychoactive substances: Are there any good options for regulating new psychoactive substances? *International Journal of Drug Policy* 2017; 40:117-122.

43. Penney J., Dargan PI, Padmore J, Wood DM, Norman, IJ. Epidemiology of adolescent substance use in London schools. *QJM.* 2016; 109(6), 405–409.

44. DfE and ACPO drug advice for schools: Advice for local authorities, headteachers, school staff and governing bodies. London: Department for Education. 2012; Accessed 18th October

2018. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/270169/drug_advice_for_schools

45. Hargreaves P. School-based drug education and prevention: The impact of inspection and curriculum provision. *Drugs and Alcohol Today.* 2016; 16(2), 131–141.

46. Home Office New Psychoactive Substances (NPS) Resource pack for informal educators and practitioners. 2017; Accessed 18th October 2018

<https://www.gov.uk/government/publications/new-psychoactive-substances-nps-resource-pack>

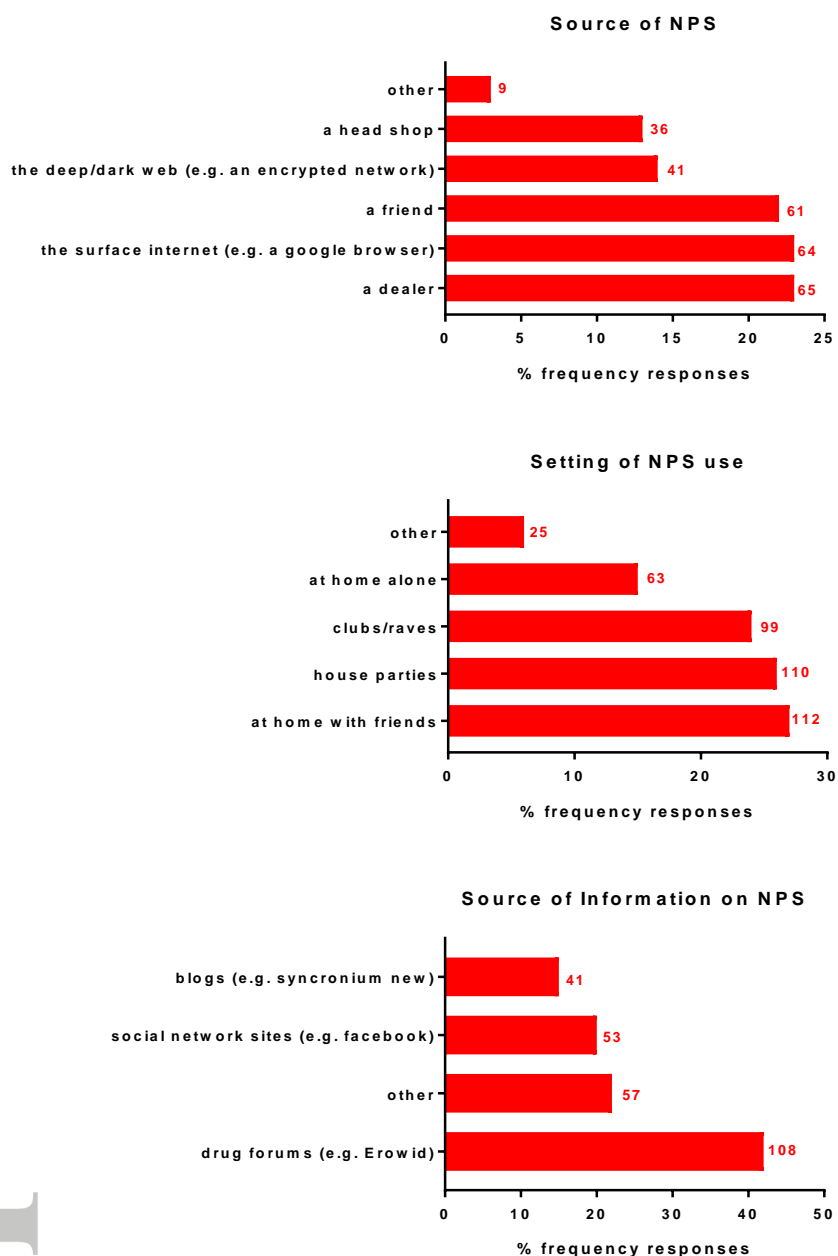


Figure 1. Source of NPS (a) setting of NPS use (b) and NPS information (c) in 2017 UK survey respondents. Data is expressed as % frequency responses of the 134 UK 2017 users. Absolute n number of responses denoted on histogram. Other sources of information on NPS (c) included friends, PubMed, ScienceDirect, medical case reports or simply trying them.

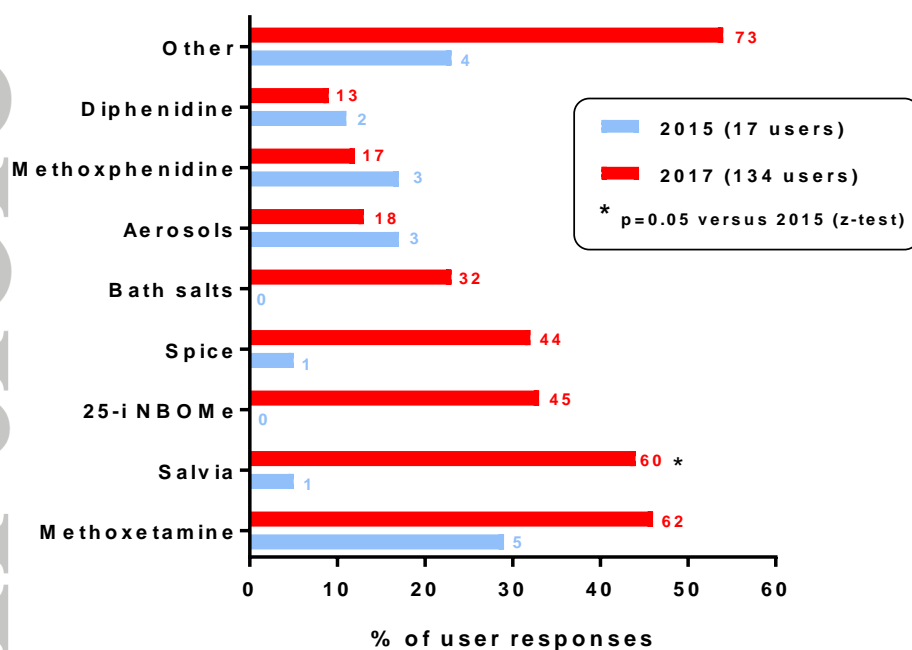


Figure 2. Types of NPS Used by 2015 and 2017 UK survey respondents. Data is expressed as absolute number of responses (on histogram) and % of user responses. Significant population proportional change $*p < 0.05$ (z-test). The total number of responses is higher in 2017 users (354 responses, 3-4 NPS per user) compared with 2015 users (19 responses, 1-2 NPS per user). ‘Other’ NPS reported included stimulants, hallucinogens, dissociatives, sedatives and opioids. 2017 Other included kratom, ‘shrooms, 5-MeO-dimethyltryptamine, dimethyltryptamine, etizolam, pyrazolam, mescaline, butyr-fentanyl, furanyl-fentanyl, diclazepam, ephenidine, clonazolam, diclazepam, methiopropamine, thiopropamine and entheogens. 2015 Other included kratom, Alpha -Methyl - Tryptamine, methylphenidate.

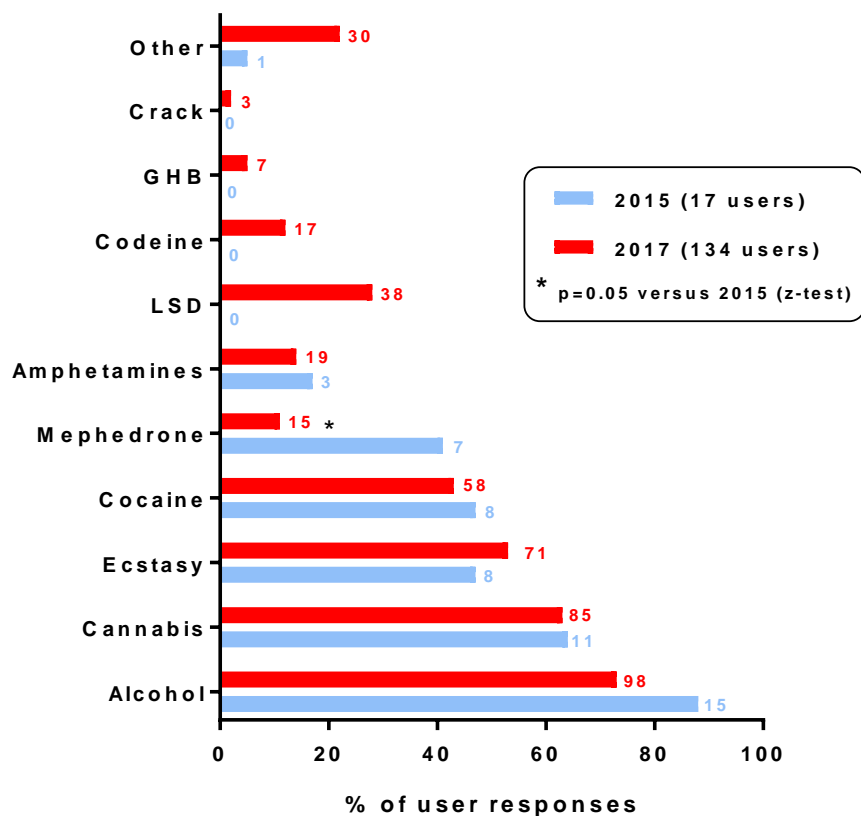


Figure 3. Preference for other substances used in combination with NPS in UK 2017 and 2015 respondents. Data is expressed as absolute number of responses (on histogram) and % of user responses. Significant population proportional change * $p < 0.05$ (z-test). Polydrug use is similar in both survey samples (2017, 441 total responses, 3-4 drug per user; 2015, 54 total responses, 3-4 drug per user).

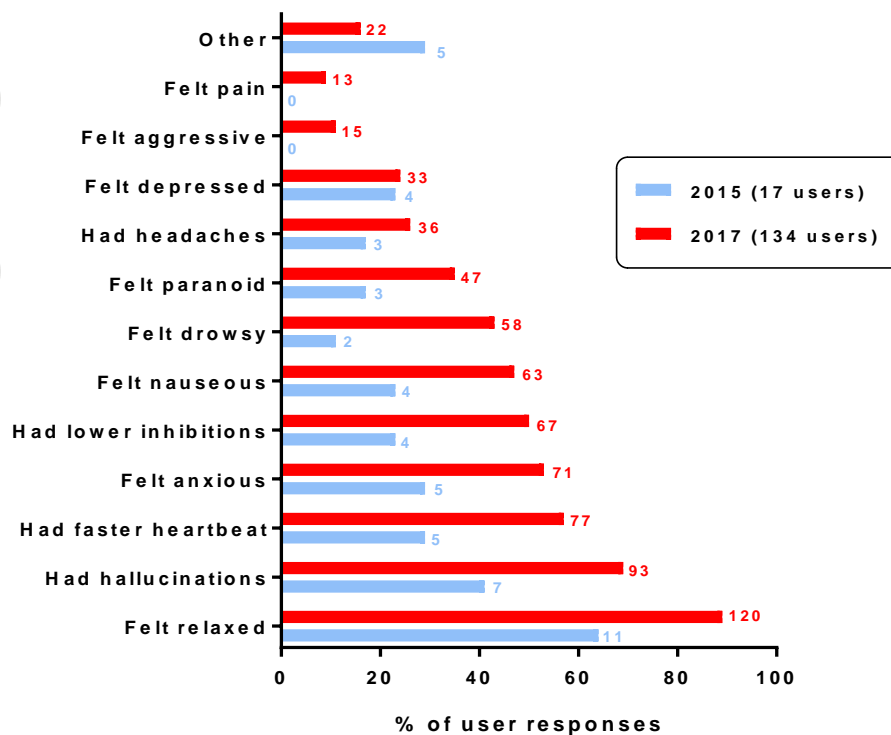


Figure 4: Subjective effects of NPS use. Data is expressed as absolute number of responses (on histogram) and % of user responses. Similar trends in subjective effects of NPS use in both survey samples ($p > 0.05$, z test).

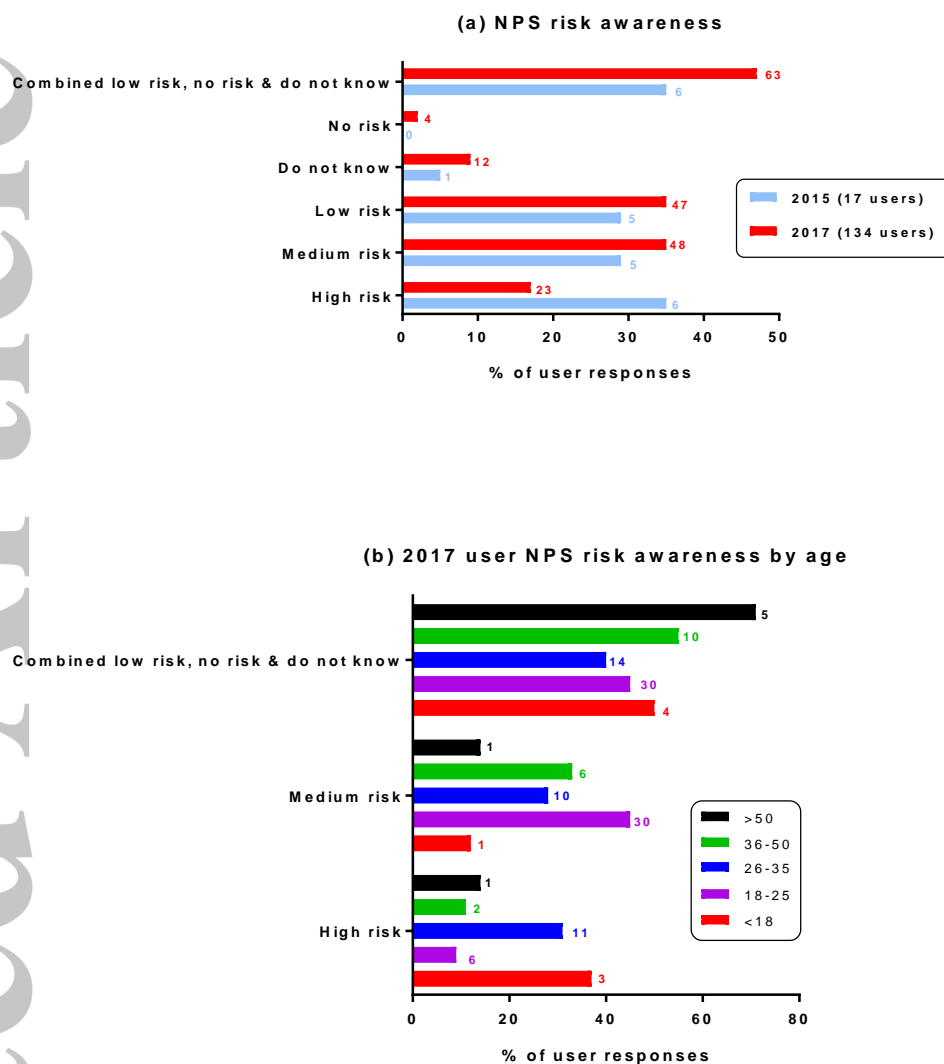


Figure 5. (a) User perception of health risks associated with NPS use and (b) 2017 user risk awareness by age. Data expressed as absolute number of responses (on histogram) and % of user respondents. There is a decreased trend ($p>0.05$) in health risk perception in 2017 survey sample compared with 2015 sample. There is no age group effect on risk awareness of the 2017 NPS users ($p>0.05$)

Table 1. Demographics of UK respondents (absolute n number and %) in the 2015 and 2017 survey sample.

Characteristics	2015		2017		p value (z-test, 2015 vs 2017)
	Total respondents (n=98)		Total respondents (n=500)		
	n	%	n	%	
Gender					
Male	34	34.7	197	39.4	>0.05
Female	64	65.3	303	60.6	>0.05
Age (years)					
<18	1	1	13	2.6	>0.05
18-25	87	88.8	269	53.8	#<0.05
26-35	5	5.1	90	18	>0.05
36-50	5	5.1	73	14.6	>0.05
>50	0	0	55	11	>0.05
< 25 combined	88	89.8	282	56.4	#<0.05
Sexual orientation					
Straight/heterosexual	88	89.8	447	89.4	>0.05
Homosexual	5	5.1	20	4	>0.05
Bisexual	5	5.1	29	5.8	>0.05
Other ~	0	0	4	0.8	>0.05
Highest level of education					
High School	4	4.1	31	6.2	>0.05
College	9	9.2	63	12.6	>0.05
Undergraduate studies	71	72.4	266	53.2	>0.05
Postgraduate studies	13	13.3	137	27.4	>0.05
Combined HE	84	85.7	403	80.6	>0.05

1

¹ Other ~ denotes asexual, asexual, pansexual or preferred not to say. Significant population proportional difference #p<0.05 (z-test) in <25 and 18-25 age group between 2015 and 2017 survey sample.

Table 2. NPS Awareness (absolute number and %) of 2015 and 2017 UK survey respondents

	NPS Awareness						p value (z-test, 2015 vs 2017)
	2015			2017			
	Number of responses (%)		p value (Chi- Squared)	Number of responses (%)		p value (Chi- Squared)	
	Yes	No		Yes	No		
	71 (72%)	27 (28%)		434 (87%)	66 (13%)		>0.05
Demographics							
Gender			0.637			0.223	
Male	26 (76%)	8 (24%)		176 (89%)	21 (11%)		>0.05
Female	45 (70%)	19 (30%)		258 (85%)	45 (15%)		>0.05
Sexual orientation			0.33			0.626	
Straight/ heterosexual	62 (70%)	26 (30%)		386 (86%)	61 (14%)		>0.05
Homosexual	4 (80%)	1 (20%)		18 (90%)	2 (10%)		>0.05
Bisexual	5 (100%)	0 (0%)		27 (93%)	2 (7%)		>0.05
Other ~	-	-		3 (75%)	1 (25%)		nd
Employment			*0.031			0.076	
Full time	19 (90%)	2 (10%)		169 (86%)	28 (14%)		>0.05
Part time	22 (71%)	9 (29%)		134 (91%)	13 (9%)		>0.05
Not employed (looking for work)	9 (50%)	9 (50%)		37 (77%)	11 (23%)		>0.05
Not employed (not looking for work)	16 (84%)	3 (16%)		72 (85%)	13 (15%)		>0.05
Other ~	5 (56%)	4 (44%)		22 (96%)	1 (4%)		#<0.05
Education			*0.031			0.176	
High school	3 (75%)	1 (25%)		30 (97%)	1 (3%)		>0.05
College	4 (44%)	5 (56%)		58 (92%)	5 (8%)		##0.01
Undergraduate studies	57 (80%)	14 (20%)		229 (86%)	37 (14%)		>0.05
Postgraduate studies	6 (46%)	7 (54%)		114 (83%)	23 (17%)		#<0.05
combined High school/College	7 (54%)	6 (46%)		88 (94%)	6 (6%)		##0.01
Other ~	1 (100%)	0 (0%)		3 (100%)	0 (0%)		>0.05
Age			0.131			0.191	
<Under 18	0 (0%)	1 (100%)		13 (100%)	0 (0%)		###<0.001
18-25	65 (75%)	22 (25%)		228 (85%)	41 (15%)		>0.05
26-35	2 (40%)	3 (60%)		81 (90%)	9 (10%)		#<0.05
36-50	4 (80%)	1 (20%)		61 (84%)	12 (16%)		>0.05
>Over 50	-	-		51 (93%)	4 (7%)		nd

2

² Other ~ refers to: Sexual orientation - asexual, pansexual, preferred not to say. Employment - semi voluntary, freelancer, out of work due to injury, disabled, long term sick, study-based practice. Education - qualified accountant ACCA, diploma, vendor qualifications. Significant difference *p<0.05 Chi-Squared test; #p<0.05, ##p<0.01, ###p<0.001 population proportional difference between 2015 and 2017 (z-test).

Table 3. NPS Use (absolute number and %) of 2015 and 2017 UK survey respondents

	NPS Use						
	2015			2017			
	Number of responses (%)		p value (Chi-Squared)	Number of responses (%)		p value (Chi-Squared)	p value (z-test, 2015 vs 2017)
	Yes	No		Yes	No		
	17 (17%)	81 (83%)		134 (27%)	366 (73%)		0.248
Demographics							
Gender			0.27			***<0.001	
Male	8 (24%)	26 (76%)		95 (48%)	102 (52%)		0.12
Female	9 (14%)	55 (86%)		39 (13%)	264 (87%)		>0.05
Sexual orientation			0.572			0.319	
Straight/heterosexual	16 (18%)	72 (82%)		115 (26%)	332 (74%)		>0.05
Homosexual	0	5 (100%)		6 (30%)	14 (70%)		>0.05
Bisexual	1 (20%)	4 (80%)		12 (41%)	17 (59%)		>0.05
Other ~	0	0		1 (25%)	3 (75%)		>0.05
Employment			*0.008			**<0.01	
Full time	9 (43%)	12 (57%)		56 (28%)	141 (72%)		>0.05
Part time	5 (16%)	26 (84%)		28 (19%)	119 (81%)		>0.05
Not employed (looking for work)	1 (6%)	17 (94%)		16 (33%)	32 (67%)		>0.05
Not employed (not looking for work)	2 (11%)	17 (89%)		22 (26%)	63 (74%)		>0.05
Other ~	0 (0%)	9 (100%)		12 (52%)	11 (48%)		#<0.05
Education			0.473			***<0.001	
High school	1 (25%)	3 (75%)		18 (58%)	13 (42%)		>0.05
College	2 (22%)	7 (78%)		33 (52%)	30 (48%)		0.15
Undergraduate studies	14 (20%)	57 (80%)		62 (23%)	204 (77%)		>0.05
Postgraduate studies	0 (0%)	13 (100%)		20 (15%)	117 (85%)		>0.05
combined High school/College	3 (23%)	10 (77%)		51 (54%)	43 (46%)		0.13
Other ~	0 (0%)	1 (100%)		1 (33%)	2 (67%)		>0.05
Age			0.717			***<0.001	
<Under 18	0 (0%)	1 (100%)		8 (62%)	5 (38%)		0.11
18-25	16 (18%)	71 (82%)		66 (25%)	203 (75%)		>0.05
26-35	1 (20%)	4 (80%)		35 (39%)	55 (61%)		>0.05
36-50	0 (0%)	5 (100%)		18 (25%)	55 (75%)		>0.05
>Over 50	0	0		7 (13%)	48 (87%)		>0.05
combined <25	16 (18%)	72 (82%)		74 (26%)	208 (73%)		>0.05

3

³ Other ~ refers to: Sexual orientation - asexual, pansexual, preferred not to say. Employment - semi voluntary, freelancer, out of work due to injury, disabled, long term sick, study-based practice. Education - qualified accountant ACCA, diploma, vendor qualifications. Significant difference *p<0.05, ** p<0.01, *** p<0.001, Chi-Squared test; #p<0.05 population proportional difference between 2015 and 2017 (z-test).

Table 4: Reasons and motivations for NPS use (absolute n number of responses and %) of 2015 and 2017 UK survey respondents

	2015		2017		p value (2015 vs 2017)
	Total responses (n=54)	Total users (n=17)	Total responses (n=481)	Total users (n=134)	
Reasons	n	% of user	n	% of user	
Friends have taken them	14	82.4	92	68.7	>0.05
I was able to buy them online	8	47.1	57	42.5	>0.05
I know I was not against the law	7	41.2	36	26.9	>0.05
They are cheaper than other drugs	6	35.3	47	35.1	>0.05
I was able to buy them easily in head shops (stores that specialize in paraphernalia)	-	-	36	26.9	nd
They are safer than other illegal drugs	-	-	18	13.4	nd
Motivations					
Give me a good high	10	58.8	102	76.1	>0.05
Make a night out much better	6	35.3	51	38.1	>0.05
Make me more confident to socialise	3	17.6	42	31.3	>0.05

Accepted