



Research Paper

No prescription? No problem: A qualitative study investigating self-medication with novel psychoactive substances (NPS)



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ABSTRACT

Background: The proliferation of Novel Psychoactive Substances (NPS) presents a challenge for global drug policy. The ease of online drug purchase and the emergence of the dark web have created new avenues for the growth of NPS. Despite the global nature of this issue, limited research has examined motivations of use. These include perceived safety or convenience, an interest in novel pharmacology and self-exploration. Recent evidence has suggested individuals may be self-medicating with NPS, however this phenomenon has yet to be thoroughly explored. This study aims to investigate the occurrence of NPS self-medication, identify the specific NPS involved, and understand the motivations behind their use.

Methods: Discussions surrounding self-medication using NPS were collected between October 2022 and February 2023 via a content analysis of a Reddit community. Ninety-three threads, comprising 182,490 words and 5023 comments, were collected and cleaned. A frequency analysis was conducted to identify the NPS discussed, and data was analysed systematically through the process of iterative categorization (IC).

Results: Our study revealed frequent discussions about the self-medication with several NPS, notably etizolam, clonazepam, diclazepam, flualprazolam, 2-FMA, 4F-MPH, 3-FPM and 3-MeO-PCP. Individuals were mainly self-treating ADHD, anxiety and depression. Motivations for choosing NPS included access, cost, legality and a dissatisfaction with conventional healthcare. Substances were often chosen based on a profile of "Functionality" and outcomes varied. The use of clonazepam was highlighted as particularly problematic.

Conclusion: The current study provides insight into the phenomenon of self-medication with NPS within an internet demographic, exploring the motivations behind why individuals choose NPS for a variety of disorders. The easy access to NPS and lack of scientific data pose a significant challenge for drug policy. Future policies should focus on improving healthcare providers knowledge of NPS use, removing barriers to adult ADHD diagnosis and rebuilding trust between individuals and addiction services.

Introduction

Novel psychoactive substances (NPS) are defined by the United Nations Office on Drugs and Crime (UNODC) as 'substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat (United Nations Office on Drugs and Crime, 2013). NPS are subject to a rapid rate of market introduction, meaning that the pharmacological profiles of emerging substances are poorly understood, and therefore, pose a significant challenge for public health authorities and legislators (Baumeister et al., 2015). Whilst described as 'novel' or 'new', this is not necessarily because that they have just been discovered but

can instead refer to their recent availability on the drug market, however some have argued this definition to be counterproductive given the highly heterogeneous nature of NPS substances and a lack a clear definition (Potter & Chatwin, 2018). Several different classes of NPS exist, often mimicking classic street drugs (Shafi et al., 2020). This can include synthetic cannabinoids, cathinones, opioids, psychedelics and benzodiazepines. Recently, the misuse of novel benzodiazepines has represented particular concern (Advisory Council on the Misuse of Drugs, 2016; Høiseith et al., 2016; Jolliff, 2020; Moosmann et al., 2015; Pendkar et al., 2018).

Currently, NPS use presents a challenging issue for authorities. In 2021, the European Monitoring Centre for Drugs and Drug Addiction (European Monitoring Centre for Drugs and Drug Addiction, 2022)

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identified 52 novel compounds, bringing the total number of currently monitored NPS to more than 880. Throughout the last decade governments have been playing a game of “cat-and-mouse” with those producing new substances, banning newly emerging chemicals when they arise (Seddon, 2014). Several countries have opted to introduce a research chemical ‘blanket ban’, such as the UK and Poland (Neicun et al., 2018). Research reviewing the effectiveness of the UK’s 2016 Psychoactive Substances Act (PSA) has been mixed (Deen et al., 2021; Deligianni et al., 2020; Humphries, 2022; Office, 2018; Reuter & Pardo, 2017; Webb et al., 2019) and more broadly the picture of NPS use is complex (Sedefov et al., 2013). The issue remains global in nature and a recent propensity for the online purchase of drugs and the rapid evolution of the dark web means that NPS now have an alternative route to flourish (Hill, 2020).

Whilst the estimated prevalence of NPS use is low (Palamar et al., 2015), there is evidence suggesting use is growing disproportionately in those who are young, and experiencing mental health issues (Neicun et al., 2021). Therefore, understanding the behaviors and motivations of those that use NPS is extremely pertinent. Self-reported reasons for NPS use can be varied, including perceived safety or convenience, a curiosity or interest in novel pharmacology, self-exploration, self-medication, to improve social bonding or purely for recreation or pleasure (Andersson & Kjellgren, 2017; Martin & Anette, 2016; Soussan et al., 2018a; Soussan & Kjellgren, 2016).

Initial evidence has suggested that there is a considerable group of NPS users defining their use as self-medication (Martin & Anette, 2016; Mason & Kuypers, 2018; Soussan et al., 2018b) however, currently there is a paucity of research focusing on this topic. Self-medication is a global phenomenon and can be defined as ‘choosing and using substances to treat self-diagnosed symptoms and diseases without consulting a doctor’. To free up resources many governments are beginning to encourage self-medication practices for minor ailments (Porteous et al., 2005), emphasizing the active role individuals have in their own healthcare (Bennadi, 2014). Self-medication brings with it risks of potential costs to the healthcare system, such as the risk of adverse effects or increased antibiotic resistance, which is a particular problem for developing countries where antibiotics are available without prescription (Pagán et al., 2006).

Estimates for the prevalence of self-medication vary considerably (2–92%) (Shehnaz et al., 2014), with self-medication encompassing the use of non-prescribed medication, supplements, illicit substances and the misuse of prescribed medication. Self-medication practices are often higher in young people (Fetensa et al., 2021) and use of illicit drugs has been shown to increase in those with unmet mental health care needs (Harris & Edlund, 2005; Smith et al., 2021). The self-medication of psychiatric symptoms with drugs or alcohol is commonplace in the general population (Bolton et al., 2009; J. Robinson et al., 2009; J. A. Robinson et al., 2009), with estimates around 24% for those suffering from mood disorders and even higher in those suffering from bipolar disorder (41%) (Bolton et al., 2009). Higher rates of NPS use in individuals with eating disorders and other psychiatric comorbidities has also been shown (Jones et al., 2016; Martinotti et al., 2014), which could be explained through the self-medication hypothesis (SMH) (Khantjian, 1985, 1997, 2003).

Many studies have indicated the value of online research and the ability to provide rich insight into areas often hard to explore (Davey et al., 2010, 2012; Deluca et al., 2012; Soussan & Kjellgren, 2014a, 2016). Online resources have been utilized effectively to monitor drug trends, including NPS (Catalani et al., 2021; Deluca et al., 2012). Utilizing internet forums as a method of analysis is becoming increasingly popular (Proferes et al., 2021; van Hout & Hearne, 2017) with sites such as Reddit (Pestana et al., 2020), Twitter (Tassone et al., 2020) and YouTube (Andersson & Kjellgren, 2019; Prevete et al., 2021) all being subject to investigation for emerging drug trends. Internet forums and social media remain valuable sources to unveil harm reduction practices and NPS knowledge (Davey et al., 2012; Kaló et al.,

2017; Miliano et al., 2018; Natter & Michel, 2020; Rolando & Beccaria, 2019; Soussan & Kjellgren, 2014a). Additionally, Reddit discussions shown to be a predictor of increased NPS-related exposures (Barenholtz et al., 2021). Currently, observations from forums such as reddit (www.reddit.com) or bluelight (<https://bluelight.org>) indicate an abundance of discussion surrounding the use of various NPS for the self-medication of conditions such as anxiety, treatment-resistant depression, ADHD (Reddit Forum, 2023), cognitive deficit and pain that is currently not represented in the literature.

The primary aim of this paper is to understand why individuals may choose to self-medicate with NPS. Our secondary aims are to establish the occurrence of NPS self-medication within an internet demographic and identify the range of NPS used.

Methods

We used text mining to evaluate posts made on Reddit, a self-organized platform where users can interact within and across subcommunities (i.e., subreddits). Reddit has over 138,000 active subreddits, each with unique norms, cultures and moderation practices. Whilst posts made by users are linked to their account, most have no personally identifiable information and therefore maintain a large degree of anonymity. Posts made on reddit are subject to user upvoting/downvoting, dictating the visibility of the post. Subreddits are user-created and user-moderated (Proferes et al., 2021). We used the R package ‘RedditExtractor’ (Rivera I., 2019) in R studio to extract relevant thread data using the Reddit API. In Reddit, “post” means the first content shared by a user (e.g., questions, thoughts, tips, experiences, pictures) and “comment” defines any eventual reply to this specific post.

Ethics

King’s College London research ethics committee approved the study (LRS-22/23-33941), and data collected between October 2022 and February 2023. In line with the British Psychological society’s ethics guidelines for internet-mediated research (Hewson & Buchanan, 2019) direct quotes were altered slightly to protect subject anonymity. Data was collected in accordance with Reddit’s Terms and conditions.

Workflow

Fig 1 illustrates the workflow for the current study. All processing and analysis took place on R Studio software 2022.07.1 + 554 “Spotted Wakerobin” Release for Windows.

Data collection

An NPS-specific subreddit consisting of 158,000 users at the inception of the study was identified using the ‘find_subreddits’ (“novel psychoactive substance”) command (Rivera I., 2019). This subreddit is described as ‘for the discussion of synthetic psychoactive research chemicals a.k.a. Novel Psychoactive Substances (NPS)’. Data collection took place between October 2022 and February 2023.

We then used the ‘find_thread_urls’ and ‘get_thread_content’ functions to retrieve the text (original post and comments) of threads containing “self-medication”, “self-medicate”, “self medicate”, “self-treatment” and “self-prescribe”. Pilot searches on the Reddit browser were used to determine which search terms may elicit new results. Still, there was a large degree of overlap for these terms and the package limited threads retrieved to 100 for each search term. Irrelevant threads were then excluded. Ninety-three threads were extracted in total, comprising of 5023 comments and 182,490 words. Our text corpus was cleaned using the text mining package ‘tm’ v0.7-6 (Feinerer et al., 2008). This process involved 1) removing punctuation 2) removing white space 3) converting all text to lower case 4) removing all non and “stop words” (e.g., “the”, “is”, “at”, “which”, “on”). We also manually adjusted drug

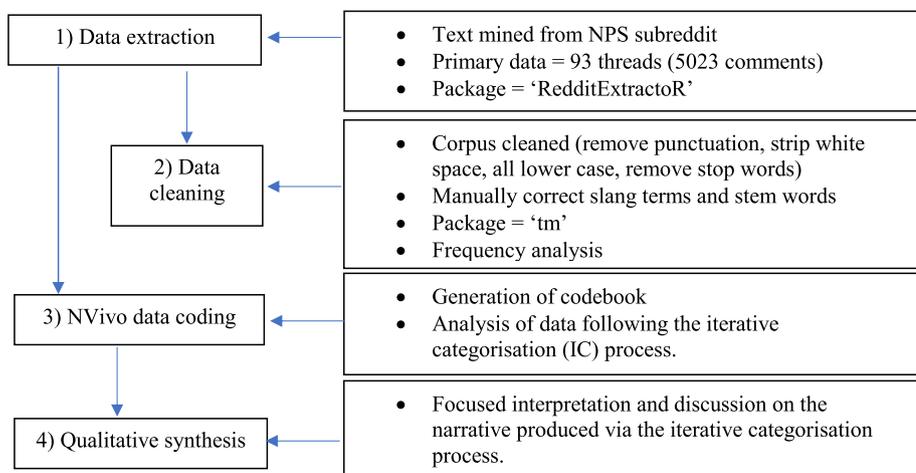


Fig 1. Box diagram highlighting the project workflow.

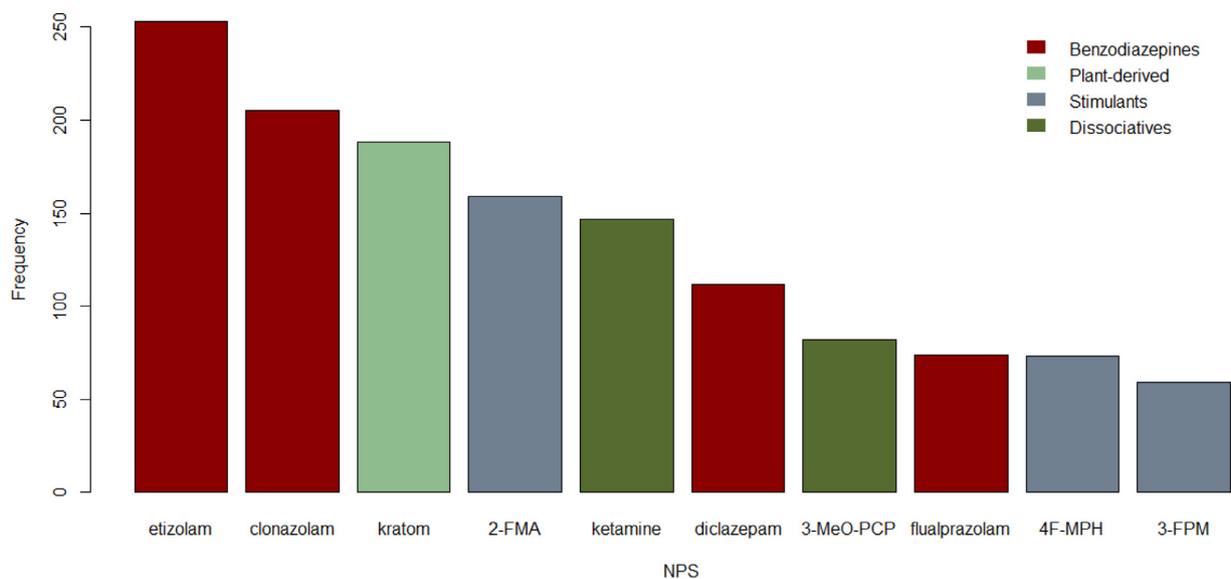


Fig 2. Frequency of NPS substances mentioned within the Reddit content analysis. Ninety-three threads, including 5023 comments were examined from the NPS specific subreddit. Number of mentions tabulated using R studio.

slang for any terms that referring to the same substance (e.g., “Etizolam” and “Etiz”). During this we also corrected obvious misspellings and international differences in spelling, retaining original meaning.

Data analyses

First, we tabulated the number of mentions for NPS within the text corpus. Relevant substances are presented in Fig. 2. Next, thirteen codes were generated *a priori* based on previous research (Smith et al., 2021). Following an iterative process, any unexpected NPS themes were then added to the *a priori* codeset. Data management and analyses were based on Iterative Categorisation (IC) (Neale, 2016,2021). First, all thread data was read with key issues noted. Coding was then done using NVivo 12 (QSR International Pty Ltd, 2020). After coding our code tree consisted of 4 overarching categories: drug information, individual information, self-medication discussion and professional health-care discussion. Textual data was coded in multiple destinations, and we include the resulting code tree (S1). Next, data from each category was exported back into MS Word, allowing for line-by-line analysis, generating inductive themes and patterns which were then grouped into a broader structure. Findings are reported below, supported by quotations.

Results

Data collection took place between October 2022 and February 2023. All substances in Fig. 2 are mentioned in the results, however kratom, and its use in self-medicating opioid use disorder is not discussed at depth. This is due to a large body of literature existing already and its categorization as a plant-derived substance separating it from the synthetic NPS discussed here. Ketamine is discussed, but not as an NPS substance. Instead, it is included to demonstrate how individuals are basing dosing regimens for novel dissociatives on current research with ketamine.

1) Why use NPS to self-medicate?

Our analysis revealed the use of NPS to self-medicate a multitude of disorders such as anxiety, ADHD and depression. The motivations to self-medicate are discussed by substance type.

Benzodiazepines

Benzodiazepines were used mainly for the treatment of anxiety related disorders: “Clonazolam is so alluring because my social anxiety disappears. [...] I’m free from feeling like everyone hates me, from being shy.”

There were examples of use being prompted by a life event such as bereavement. Others were substituting a substance that had run out. Some individuals had been drawn in by online advertisements on NPS websites or had purchased after being refused a higher dosage of prescription medication.

Benzodiazepines were also commonly used as sleep aids: *“For 2 years now I’ve been doing the frustrating trials of sleeping medications that do not work effectively, and etizolam has far exceeded anything my doctor given me in the past (anxiety is my main reason for bad insomnia).”*

“I am a big fan of flualprazolam, but I also have insomnia issues and that is what I use it for.”

Other uses for benzodiazepines included pain and substance withdrawals. Their use for substance withdrawals was seen as problematic given the lowered inhibitory control: *“The last time I overdosed I was blacked out on Clonazepam. At the time I wasn’t doing dope and had no intention of getting dope. But that is what I ended up doing, [...] 3 days later I woke up in a hospital.”*

Legality was often a motivation for use and individuals would express annoyance at changes in scheduling requiring them to look for an alternative, not wanting to be caught on the wrong side of the law: *“I tried getting etizolam first [...]. It is now unfortunately a scheduled substance in my area, I am considering going for metizolam since that a much less potent alternative, do you have any experience with metizolam?”*

One issue commonly raised was that some specialist services would be unwilling to help those on high benzodiazepine dosages, leaving them little option other than to purchase their own benzodiazepines: *“Ironically, I’ve ended up using flubromazolam as the compound to taper with after getting rejected by local healthcare/addiction “specialists” because they weren’t willing to take me on once they made a benzo conversion”*

Some individuals hoped that their NPS use would provoke a response from their healthcare professional: *“I reached out to etizolam in the first place because of the lack of care towards the issue I’m facing, but maybe seeing that I’ve had to reach out will provoke a conclusion.”*

Discussing NPS use with a doctor was often seen as problematic. Individuals described how they thought that being transparent with doctors would impede their chances of getting a future prescription, or that doctors would be less willing to help: *“Has anyone here spoken to their doctors about etizolam usage? How does it generally go? [...] I’m about to face it on Tuesday.”*

Some believed doctors did not care or want to cooperate with them. This extended to being judged or stigmatised in the view of some: *“I’ll take self-medication and the advice of knowledgeable strangers over the look of disgust on the face of a doctor and the ‘here’s 800mg of ibuprofen, ya scumbag.”*

Stimulants

Stimulants were predominately used for the self-treatment of ADHD. Some felt as though they couldn’t function without: *“Same here. I need stimulants like 4f-mph to help me function...”*

Financial issues appeared a more prominent motivation for using novel stimulants, including medication, diagnosis, and insurance costs. These seemed to be especially relevant to the US demographic: *“So, to start off I have ADHD and due to crappy insurance, I cannot afford monthly doctor visits plus the medicaid, also I don’t think it would even cover the meds so what is one to do...”*

“I will no longer have access to Adderall for at least 3 months while I wait for open health insurance enrollment to begin at the company I work at. [...] I’m worried about my lack of medication affecting my work, so I’m investigating into RCs (research chemicals), specifically 3-FPM...”

Some of those with a prescription were looking to supplement their current medication: *“I’ve got pretty severe ADHD, and after self-medicating for a bit with the 4f-mph, I managed to get a Vyvanse prescription. Only*

issue is, the Vyvanse doesn’t last ALL day and I cannot really get anything else done on a day that I work...”

Avoiding side effects of prescription medication was a motivation for some: *“I quit taking Wellbutrin and have been self-medicating with 2-FMA for the last few days. My memory started working again and I can study for my exams.”*

In European countries prescriptions for adult ADHD were perceived as hard to obtain if you hadn’t been diagnosed as a child. In one case using 2-FMA led them to seek a diagnosis for ADHD: *“We tried 2fma and she suddenly felt like a normal person. That led us to trying to get an assessment but also prepare in case she’s not gonna get diagnosed. Here in DK/Europe I heard there is reluctance (to diagnose) especially when you do it as an adult as some line of thought says you must have it (ADHD) as a child to have it as an adult.”*

“I’ve been abusing 2-FMA quite heavily the last three/four months or so to self-medicate my ADHD (given that no psychiatrist will prescribe me anything more potent than bupropion to treat my ADHD; being an adult ADHD’er here in Europe sucks)...”

Dissociatives

Novel dissociatives were mainly used for self-medicating depression, but there were also indications of using to help with anxiety, fibromyalgia, chronic pain, ADHD and brain fog: *“I suffer from treatment-resistant depression and find that even a dose once per two weeks (3-MeO-PCP) sees my depression suppressed to the point that it is an annoyance at worst most days.”*

“Deschloroketamine obliterates my depression for two days after using.”

“I’m 37 and have been self-medicating by microdosing 3-MeO-PCP since May 2017. I’ve had low self-esteem all my life from lots of social rejection, which in hindsight might probably be blamed on my ADHD that was diagnosed at 35!”

Like the use of novel benzodiazepines, there was evidence of traumatic life events: *“I have had some traumatic events happen in my life recently, which has spurred an episode of depression which coupled with my ADHD has left me struggling to motivate myself to get anything done lately.”*

Often, the motivation to purchase dissociative NPS was influenced by research with ketamine, with users looking to replicate findings with a structurally similar substance: *“From my understanding of the ketamine trials, a low dose of around 30mg was administered and patients showed a rather substantial decrease in depressive symptoms [...] I would like to attempt something like this. Which of the dissociatives currently available would you consider the best for such an experiment?”*

This option was viewed as more favorable than SSRI use: *“I am considering purchasing one of the available research chemical dissociatives to take a low dose of once per week to help deal with my issues. I understand this is self-medicating, but I would much prefer this then go to a psychiatrist and be put on an SSRI.”*

Prescription medication was perceived as addictive, with many side effects such as extreme weight gain. Individuals expressed a desire to not be on antidepressants forever and saw NPS as a way out: *“Last year I decided to visit a doctor for my struggles with depression. I began taking Prozac which actually helped me a lot but after a while I decided I did not want to be medicated forever.”*

Dissatisfaction and stigma towards SSRIs were apparent, which fed into a distrust of medical institutions more generally. This distrust was a key factor in discourse, with individuals routinely discussing the corruption of the medical system: *“I don’t trust the medical psychiatric institution to provide any solutions. They are still in witch doctor stage and don’t have any real answers for unresponsive depression and mood disorders.”*

The misunderstanding of some disorders even went as far as causing offence, with some left feeling frustrated with the lack of options: *“I stopped looking for professional help because of my bad experience with it. They will not go outside of their protocol and will not go out of their way*

to help you. For bipolar they'll give you some dopamine antagonists or other dysphoric drugs with tons of side effects and send you off. Same with unipolar depression, they can prescribe SSRIs and other crap that doesn't work instead of something that actually does like ketamine"

Practical issues were evident, such as long waiting times or having to travel a large amount of distance to obtain a prescription, rendering self-medication an easier option. Like with ADHD, obtaining a diagnosis, or even a consultation was sometimes seen as too expensive, and individuals from the US described how NPS could be used if medication was not covered by their insurance: "If you cannot get insurance to pay for those, you can replicate this concept with intranasal ketamine / 2FDCK powder. I have not tried this, but there are posts about it, essentially a small dose amount of ketamine, chopped into sixths, snorted 10 minutes apart, three days a week, for two weeks."

Legality continued to be a motivation with individuals paying attention to changes in law: "I sought out research chemicals due to their legality and novel effects. Mainly as a functional study aid and antidepressant."

"I'd love to hear information on this topic, especially with Deschloroketamine and ephedrine, as I don't think 3-meo-pcp is legal in the UK anymore? Very tempted to try the research chemical dissociatives for relief of depression"

The prior discussed factors all fed into individual motivations to self-medicate. Novel benzodiazepines were mostly used for anxiety, novel stimulants for ADHD and dissociatives for depression. Legality, access and cost were often motivating factors. Cited reasons for choosing to self-medicate included not wanting to see a psychiatrist, the view that it was possible to responsibly self-medicate, the view that you can self-medicate better than a doctor could help you and the view that the drugs available were better than those available to professional healthcare. Self-medication was broadly viewed as a good option for those with less medical access, a poor doctor or if they had exhausted treatment options: "If you've tried several antidepressants and none of them help you, then experimenting with ketamine or another dissociative might save your life."

2) NPS effects

Benzodiazepines

Novel benzodiazepines differed in their duration of action, with some being more appropriate for abating panic attacks and others more suited to long term anxiety: "For me etizolam lasts 4–6–8 h, I want something that lasts 8–14 h for all day anxiety relief. I like etizolam's quick hitting properties. Great for Anxiety / Panic attacks."

However, some individuals required a benzodiazepine with a longer half-life, to avoid having to redose in the day or wake up with anxiety during the night: "...that half-life is so short, I can wake up feeling stressed during the night and whatnot."

"diazepam was the Goldilocks of the benzodiazepines for me. It lasts long enough to let me sleep through the night. I didn't feel like re-dosing [...], but effective enough to kill anxiety attacks."

Side effects experienced included blackouts, memory loss, delusions of sobriety, suicidal thoughts, seizures upon cessation and strong rebound anxiety: "If I knew how devious Clonazolam was, I would never have taken it. [...] Random withdrawal times, blackouts, memory loss..."

Clonazolam demonstrated numerous side effects and represented a poor choice for therapeutic use. Individuals were constantly surprised by the strength and long half-life, with most being unable to control their use. Additionally, pills appeared to be dosed unevenly, making use even harder to control. Blame for high dosages was often ascribed to vendors: "Told myself I would use it for two weeks, but now am on day 35 at a consistent dose of 0.7–1 mg/day (but who knows what the hell is in them)."

Compounding the issue of dose variability was the inability to test and distinguish between novel benzodiazepines with drastically varying active dosages: "I have like 1500mg of suspected Pyrazolam [...]. I have reagent test kits but idk I feel like there would be zero reaction with all 4 of my reagent tests kits if it was a diazepam, but I just wouldn't know which one."

Benzodiazepine discussion commonly focused on potency equivalents between different benzodiazepines, which represented integral information when attempting to taper: "According to tripsit.me, metizolam should be around half as potent as etizolam and has a 60% longer half-life.". Individuals often recommended volumetrically tapering using a powder solution.

Stimulants

With stimulant use, euphoria was a key consideration, with more euphoric substances being harder to use responsibly. 4F-MPH was seen as more euphoric than 2-FMA or Isopropylphenidate, other popular options for self-medicating: "Isopropylphenidate is the best option, it is way less addictive than 4F-MPH and also way less euphoric."

Side effects varied from person to person but included appetite suppression, anxiety, paranoia and residual stimulation: "Ritalin and 4f-mph cause me anxiety and have you tried 2-FA?"

Effects on anxiety were sometimes mixed and often unpredictable: "My problem with 2-FMA is sometimes it is a nice clean stimulation, but other times it turns into anxiety."

Some individuals claimed that 2-FMA in fact had anti-anxiety properties: "2-FMA can actually have anti-anxiety effects. Would recommend, I also find caffeine too much."

Hyper focus was sometimes an issue, making it difficult to prioritize tasks: "Workwise my only concern is hyper focusing, especially my first weeks on NEP I was absolutely loving my job and everything around it, but I could not discern between minor tasks and major ones."

Since medicating ADHD required daily dosing, user often debated the safety of daily stimulant dosing. Some users thought daily use would be safe, given the way Ritalin etc. are prescribed, although this was contested: "For the 4f-mph it (Psychonautwiki) actually states that it can be used daily for extended period of times (as analogue to Ritalin and Concerta)".

"I suggest you look into 2-fma, 2-fa, 4f-mph or maybe low dose 3-fa, they **should** be safer stims, and you shouldn't use them daily, twice a week max should be 'acceptable' ... be safe".

Some users outlined supplement regimens to take with stimulants, to offset toxicity. Vasodilators such as propranolol were discussed as being used to counter stimulant induced cardiotoxicity: "Niacin, arginine and citrulline (these three are strong vasodilators, vasodilators being from what I've read are the most important form of cardio protection when it comes to 2-FMA...)"

Oral dosing was advised over insufflation, and a small starting dose measured with a good scale was advised. There was evidence of prolonged stimulant use, in one case this was at between 20–40mg of 2-FMA daily, for approximately a year. This individual allegedly reported no side effects: "Today I am celebrating my first full year since starting my adventure with 2-FMA, [...] Let say, like three weeks off once, three times one week off and some 'days in between' but besides that, I've been taking 2-FMA daily"

Individuals were surprised when substances outperformed their prescribed counterparts: "I hated Ritalin, but Isopropylphenidate works wonderfully IME. It doesn't make sense, but it is what it is. If you're really prone to anxiety, get a beta blocker."

Dissociatives

The effects the novel dissociatives were more varied than those of stimulants or benzodiazepines, with mixed reports on efficacy: "It is hit or miss (3-MeO-PCP). Some days, especially on the comedown / after effect

stage, it would give me motivation, wittiness, talkativeness and confidence. When I dosed too much, I'd experience mild speech impediment, sluggishness and trouble finding the right words.

Some saw the symptoms of the disorder they were self-medicating return when the drug wore off, whereas others saw the 'hangover' effects or 'afterglow' as part of the therapeutic profile, although this was debated: "3-MeO-pcp is not like ketamine. It recreational to a point then the afterglow has been reported to be beneficial. I've seen people say their depression and anxiety has been temporarily lifted."

"I would advise against 3-meo-pcp as there is not really much therapeutic value at all, with zero after glow."

Mania was a common side effect for 3-MeO-PCP, making it a precarious substance for self-medication: "I tried to self-medicate bipolar and ADHD with low dose daily 3-meo-pcp and had a really manic episode [...]. Memantine saved me and now I'm stable using only lamotrigine."

In one post an individual was heavily warned to not cease his use of a mood stabilizer, with many believing him to be in a manic state: "I really strongly recommend against doing 3-meo-pcp alone without a mood stabilizer. If you do taper off of lamotrigine please try adding memantine on first as it will help keep mood stable while giving many of the benefits of 3-meo-pcp."

3-MeO-PCP was used in a variety of different dosing patterns, with long term use evident: "I've been microdosing 3-MeO-PCP every day for 7+ months to battle my ADHD, mild depression, social anxiety and low self-esteem."

Individuals opted for a normal dose (10–15 mg) or a microdose (1–3 mg). Daily use was warned against, with it hypothesized to build up in the system more than other dissociatives: "Not advocating daily use of 3-MeO-PCP though, it is too long acting and (I guess) it builds up in the system more than other dissociatives available on the market"

Some used in conjunction with other psychiatric medications such as Lamotrigine, others intentionally made the switch from medication such as Wellbutrin and Vyvanse: "First option for me was 100mg Wellbutrin and 20mg Vyvanse. It worked for a week and then I was all fucked up. [...] It was still too much so I eventually quit that and found 3-MeO-PCP was doing a good job of controlling my ADHD, anxiety and depression."

Functionality

"Functionality" was a key theme which emerged throughout the study. This encapsulates the idea that individuals were aiming for a substance that allowed them to function better in daily life, but with minimal impeding side effects. Potential options for self-medication were all viewed through this prism of "functionality". This need for a functional substance was evident across substance types:

"A ton of people use kratom as maintenance. It way healthier and more functional than say suboxone or methadone."

"1P-LSD and 1CP-LSD will always be some of the most perfect substances known, period. They have everything!!! visuals, headspace, euphoria, stimulation, recreational and spiritual value...and is even functional at microdose levels!!!"

When considering novel benzodiazepines, substances that were overly hypnotic or euphoria inducing were the least functional: "I don't tend to enjoy the effects of Clonazepam, I think the hypnotic affects outweigh the anxiolytic benefits (for now). [...] Looking strictly for medicinal use."

A lack of euphoria meant a lower compulsion to redose: "One thing that I especially like about flualprazolam is that I am never tempted to redose perhaps because there is little if any euphoria."

Some preferred benzodiazepines with a longer half-life: "I recommend diclazepam to be honest. Really functional benzodiazepine with great medicinal effects and it lasts absolutely ages."

"Pyrazolam typically is also very light and functional, without much of a limitation in all day life."

Etizolam was considered one the most "functional" benzodiazepines: "I would say etizolam is vastly superior in treating anxiety. Of course, I am biased, and I strongly prefer functional benzodiazepines. I just don't have the time to be non-functional."

Like benzodiazepines, stimulant functionality was dictated by euphoria and associated side effects: "4f-mph has worked better for me than any other medication I have tried for adhd. I can retain an appetite, don't get stim stutters, I fall asleep on it quite easily, and it is amazingly functional."

Overall, 2-FMA, 4F-MPH, Isopropylphenidate and 3-FPM were all popular "functional" options for treating ADHD: "Have you tried 2-fma? Least euphoric stimulant ever!!!!"

"4F-MPH is pretty functional. It is potent, long lasting and not that euphoric."

"3-fpm is a fantastic functional stimulant if you keep your doses relatively low. 2-fma is also a great functional stimulant that lasts longer than 3-fpm."

"Isopropylphenidate feels really underappreciated here in my opinion. I think it an ideal functional stimulant. There has been a study showing its improved safety profile over methylphenidate (Ritalin)."

However, there was not unanimous agreement: "...I purchased some 2-FMA from a well-known vendor. I did this to self-medicate ADHD and I had read about how 2fma was clean and non-euphoric and shit. However, [...] I found it to be one of the most fiendish stimulant highs I have ever tried."

For stimulants, oral dosing was recommended to avoid the "rush" associated with other routes of administration (ROA): "For functionality, maybe a small dose (with an ROA that doesn't give that extreme rush) can do the trick for you, but probably just as well as other, much safer substances."

Despite being a dissociative, 3-MeO-PCP was seen to be largely functional, possibly due to the stimulant like properties: "Most people that like 3-meo-pcp enjoy the fact that it is functional. 3-meo-pcp really is more of a stimulant than it is a true dissociative imo."

"3-MeO-PCP is my only crutch [...] I eat healthy and feel like I'm taking functional doses."

With dissociatives, functionality appeared to be more closely linked to dose: "Dissociatives are pretty effective at handling benzodiazepine withdrawals (in lower doses to stay functional). They'll get rid of the anxiety at least."

3) Perceived outcomes

When considering outcomes, the effects of novel benzodiazepines appeared to be overwhelming negative. A common pattern of benzodiazepine use became evident; with many individuals describing the short-term improvement in anxiety symptoms, followed by long-term addiction and negative life impact: "Have had crazy social anxiety my entire life so I started using it more and more [...] soon I was taking probably 50mg of etizolam a day, my usage just kept climbing higher and higher [...], right after my birthday last year I got a DUI."

The effectiveness of novel benzodiazepines was often praised: "I struggle pretty bad with social anxiety and depression and used to see a Doctor for it. They had me on 30mg of lorazepam a month, [...] but I've recently began ordering etizolam and I'll tell ya, from a medicinal standpoint I've never felt better."

However, there was also an acknowledgement of the potential for dependence: "Pyrazolam, etizolam and diclazepam saved me from a total breakdown more than once. One episode of extreme stress and insomnia around 2 years ago forced me into dependence, though."

One factor contributing to dependence was the development of tolerance, leading to progressively higher doses or the individual switching to a more potent benzodiazepine. Prolonged low dose use was greatly admired: "As you say, the etizolam will slowly become less effective so I may have to consider using clonazepam just to make it last during working hours"

Once tolerance and addiction took hold, withdrawal would increase the likelihood of seizures. In one case, the closure of a company prompted seizures: *"I also use kava, [...]. It even stopped my awful seizures when I quit clonazepam cold turkey due to the shutdown of a well-known company."*

Individuals were commonly warned of addiction: *"There are a couple of lines in here that scream to me you've slipped down the benzodiazepine hole [...], if there was even a CHANCE you had a problem with etizolam, the clonazepam will take you."*

After developing addiction a significant volume of discussion focused on tapering. The 'Ashton manual' was routinely referenced as a guide for helping others set a tapering schedule: *"I'm kind of new to this whole thing and have fallen down the rabbit hole. I'm trying to find the best way to taper off Clonazepam"*.

When it came to depression, outcomes were mixed: *"Dissociatives worked ok for a while but for consistent results, 3 years now, mushrooms have been a godsend."*

Effects from substances such as MXE appeared to be dose-dependent: *"I seem to find that if I take more than a certain dose (40 mg or more) it makes me feel worse, not better. Below that, it helps lift the depression."*

Novel psychedelics, often used in a microdose regime, lacked the addiction risk posed by benzodiazepines, however still had varying results: *"Personally, I found research psychedelics didn't help my depression, but mushrooms made a huge difference. I still take .35g every other day."*

"I microdosed both shrooms and 4-aco-dmt [...]. I found both to be highly effective, 4-aco-dmt a little more though."

Some spoke of the benefits acquired through NPS use: *"I just recently reduced my antidepressants by a third because 4AcODMT and ald52 are curing my depression [...]. Cannot wait to see how it feels after reducing further the SNRI that I've been on for over half my entire life."*

4) Individual reflections:section-title>

Benzodiazepines

Upon reflection numerous users expressed that they wish they had never started self-medicating with a novel benzodiazepine: *"Clonazepam has left me working at a call center, living with my 58-year-old dad who forces me to go to AA meetings. I am so embarrassed about my life and have no driver license, meaning that I cannot really make friends."*

Interestingly, many users outlined clonazepam as being particularly hard to avoid addiction with: *"How fascinating it is that *this chemical in particular* is one which is singled out by this community of educated drug users as an apparent and indisputably dangerous inebriate."*

Some justified their use by the fact that other benzodiazepines are prescribed legally: *"if certain people like me didn't require these drugs they wouldn't be available by prescription"*

Overall, despite some positive discourse, those that had never used benzodiazepines were routinely dissuaded against use: *"I'm going to recommend against etizolam, [...] it certainly has its place and its use, but you don't want to accidentally start your girlfriend down a path of addiction / dependency."*

Stimulants

Upon reflection, the amphetamine and phenidate analogues were greatly favored over the pyrovalerones: *"4f-mph has worked better for me than any other medication I have tried for adhd, [...] it is extremely functional. It is a serious life saver for me"*

Despite this, most agreed that using unstudied substances everyday was dangerous. Many described using as a last resort, dancing a fine line between self-medication and developing addiction: *"I need stimulants like 4f-mph to help me function but at the same time I have to make myself take breaks because I can clearly see how susceptible to dopamine addiction I am."*

Also, I will not buy anything more potent than this because I am very afraid I will not be able to stop. ADHD sucks..."

The key to responsible use was seen to be sticking to a dose: *"It works well but she needs to stick to a medium dose regimen and not use it for recreation."*

Stimulants such as 2-FMA were seen as safe by most, however there was still a reticence to use every day, for fear of unknown side effects. More broadly, there was a dissatisfaction that individuals had to self-medicate in the modern age: *"Using a relatively mild stimulant to function every day is brave. But brave in a super fucked up way because in a civilized, science-savvy world you would have access to the treatment of choice for your condition."*

Often, the potential of addiction was finely balanced with the dysfunction the individual was experiencing in their daily life: *"I can see I'm addicted to it, but I don't plan on stopping. You see, we must walk this very thin line between, on the one hand, having to self-medicate because, having no access to genuinely effective medication, we're rendered completely dysfunctional and unproductive if we don't, and, on the other, having to battle the addiction issues that [...] are pretty much guaranteed to manifest if you decide to self-medicate *every day* with extremely addictive substances"*

There were safety concerns with many of the substances unstudied, and research had suggested that prolonged use of fluorinated amphetamines could potentially result in a build-up of toxic metabolites: *"2fa and 2fma are both more like classic stimulants. But it is probably not good to take fluorinated amphetamines daily."*

Individuals were constantly emphasizing that the aim of these substances should be to give positive benefit to your life: *"stick to a firm plan / dosing schedule and keep making sure that you are really using the substance to continue getting a positive benefit in your life, and not just chasing the high"*

Experimentation was encouraged to find a substance that matches with individual brain chemistry: *"experimenting with other compounds is important as some will work better than others depending on her brain chemistry."*

Dissociatives

Despite the side-effects there were individuals who appeared to benefit from the use of 3-MeO-PCP: *"3-MeO-PCP is the only drug that medicates me by fighting my everyday blues and keeps me looking forward. Again, all the while feeling threshold effects."*

"Yeah, 3-meo-pcp saved my life, I would be dead right now without it."

For some however, self-medication led them down the path of addiction: *"Started by self-medicating, turned into recreational use, became addicted, tried to self-medicate out of that with horrible ups and downs and mixed results, realized I am an addict [...], this started about 3 years ago and involves a list of over probably 20 research chemicals."*

It was sometimes hard to spot the damage the substance was doing until after they had finished using the substance, this was especially true of the mania induced by 3-MeO-PCP: *"I thought I was self-medicating on 3-meo-pcp but it turns out I was actually completely crazy."*

Overall, there was a real sense of a 'last resort' for those choosing to self-medicate with NPS. Some believed, fundamentally, that disorders such as anxiety or depression could not be cured through drug use, although using NPS could be a catalyst for change: *"What if I told you that depression can be so bad that you want to die, and maybe a substance like Deschloroketamine or ALD-52 can remind you what it is like to be happy. Something to live for - a break from self-hatred is all I needed to get out and improve my life."*

Discussion

The current research presents four key points. Firstly, we outline evidence suggesting there is a subset of NPS users who are utilizing NPS to self-medicate for a multitude of disorders. Secondly, we highlight

that those self-medicating aim for a functional substance (i.e., one that won't impede their daily functioning). The idea of functional substance use is not new (Boys et al., 2001; Lende et al., 2007), and other research has demonstrated that individuals may replace one substance with another to fulfill an explicit purpose (Boys et al., 1999). However, this is the first study to suggest that functionality may be a key theme for NPS use. In addition, many of those choosing to self-medicate are using it as a last option. This "last resort" profile of NPS use could be seen as separate to the 'e-psychonauts' (O'Brien et al., 2015; Orsolini et al., 2016; Schifano et al., 2021), who focus on substance investigation and 'mind exploration'. Albeit both these groups appear to demonstrate high levels of pharmacological knowledge. Thirdly, we demonstrate that participants choosing to self-medicate often outline a dissatisfaction with professional healthcare, manifesting with a stigma against modern pharmaceutical medication for affective disorders such as depression and anxiety. Social stigma has previously been shown to be a motivation for prematurely ending antidepressant medication (Maxwell, 2005) and taken together this suggests that improving confidence in professional healthcare could reduce NPS use. Finally, we highlight how some individuals choose to use NPS because of reduced costs in comparison to professional healthcare. It appeared that this was largely a US phenomenon, with some choosing to use NPS when their healthcare insurance would not cover doctor visits or medication costs. For those individuals there may be an economic benefit that outweighs the associated risks. It is unsurprising that there are many references to the US given that almost half of Reddit users are Americans (Shatz, 2017), and our data demonstrating poor access, issues with affordability, and complexities with insurance are echoed in the literature (Emanuel et al., 2017; Osborn et al., 2016) with some suggesting US healthcare to be in crisis (Himmelstein et al., 2018).

Our research confirms that novel benzodiazepines are being used for the self-medication of anxiety disorders, as suggested by others (Advisory Council on the Misuse of Drugs, 2016; Bohnenberger & Liu, 2019; Jolliff, 2020; LaCasse et al., 2021; McNamara et al., 2019; Moosmann et al., 2013; Reeves et al., 2022) and we add to the limited human data available (Abouchedid et al., 2018; Zawilska & Wojcieszak, 2019). Motivations for benzodiazepine use included a dissatisfaction with professional healthcare, with some individuals stating that specialist services were unwilling to help if their current dose was too high. This highlights a need for healthcare services to be more prepared to help those stuck on a high benzodiazepine dose. Additionally, we outline the issue of users being unable to distinguish between novel benzodiazepines with drastically different dosages and half-life's (Bohnenberger & Liu, 2019). We highlight Clonazepam as a particularly dangerous substance which represents significant concern given its appearance in Xanax counterfeits (Lucie, 2022) and the recent increase in the nonmedical use of benzodiazepines (Hockenull et al., 2021), especially in younger people (Vice, 2023). This is exemplified by the recent death of a 14-year-old with a positive toxicological finding for clonazepam, who believed he was using Xanax (Moore, 2022). In the current research, inconsistent dosing was confounded by the underlying worry that doctors were being pushed to limit benzodiazepine prescriptions, following an over-prescription crisis (US) (Kahle, 2020; Zhang, Mohliver, & King, 2022). In this sense, an overt attempt to reduce prescription benzodiazepine use could push individuals towards self-medication with NPS, potentially a more dangerous outcome than keeping them within the medical system. Given the negative view of professional healthcare in this study, we recommend the rebuilding of trust between individuals and healthcare providers as a way of countering addiction, with this recommendation likely to be most effective in the US.

The nature of benzodiazepine withdrawal, including the possibility of seizures and the pharmacological need for a taper makes self-medication using novel benzodiazepines particularly dangerous. With increased potency, novel benzodiazepines may be harder to control than classic benzodiazepines and we echo other authors concerns surround-

ing the challenges of treating patients with novel benzodiazepine use (Reeves et al., 2022). Our research suggests that the 'slippery slope of addiction' was relatively common when attempting to self-medicate, which is at odds with research into flubromazolam (Andersson & Kjellgren, 2017). This may be explained by the nature of the forum Reddit, which highlights more impactful posts (positive and negative) through an upvote system. Finally, our research suggests that blackouts caused by novel benzodiazepines use may play a role in the overdose of other substances. This finding warrants further research.

Further, we demonstrate that there is a subset of the population using novel stimulants to self-treat ADHD and we build on the limited findings available for several substances (Karinen et al., 2014; Kosciuk et al., 2019; Menard et al., 2018; Potocka-Banaś et al., 2020; Purtschert Baquerizo, 2019; Shoff et al., 2019). Financial issues such as medication, diagnosis and insurance costs appeared to be a more prominent motivation for individuals using novel stimulants. Additionally, there was an unwillingness from some healthcare specialists to diagnose ADHD in adults and these barriers to adult treatment are evident in the literature (Matthys et al., 2014). This suggests that undiagnosed adults suffering from ADHD may be particularly at risk to novel stimulant use. Previously, studies have highlighted a link between ADHD and increased cigarette and substance use (Sousa et al., 2011; Whalen et al., 2003; Wilens et al., 2007), often viewed through the lens of self-medication hypothesis (SMH) (Hall & Queener, 2007; Khantzian, 1997, 2003; Odell et al., 2017). SMH posits that it is not the psychiatric diagnosis that is being self-medicated, but instead the psychological suffering described by the diagnosis (Mariani et al., 2014). Our findings appear to contradict this with individuals selecting NPS structurally closest to ADHD medication and opting for "functional" substances, with little or no euphoria. However, it could also be that the motivation to alleviate suffering may be operating unconsciously.

Moreover, we suggest that novel dissociatives are being used for the self-medication of depressive disorders. We supplement the limited case report data for 3-MeO-PCP (Allard et al., 2019; Arbouche et al., 2021; Bäckberg et al., 2015; Bakota et al., 2016; Berar et al., 2019; Bertol et al., 2017; de Jong et al., 2019; Frison et al., 2021; Gomila et al., 2019; Grossenbacher et al., 2019; Helander et al., 2015; Johansson et al., 2017; Krotulski et al., 2018; Lecinena et al., 2019; Thornton et al., 2017; Zidkova et al., 2017), including the first fatal intoxication in the UK (Copeland et al., 2022). Of note, a recent case study describes a 25-year-old with schizophrenia and bipolar disorder who "was trying to find a cure to his illness using chemical products bought by himself" (Castro et al., 2022), demonstrating the potential risks in self-medicating with NPS. When attempting to self-medicate depression, motivations to use novel dissociatives appeared to be linked to a negative view of SSRI's and antidepressant medication. In contrast, emerging research with ketamine (Walsh et al., 2022) was perceived positively, and many individuals were basing their self-medication regimes off study protocols. Currently, we live in an era where individuals are incredibly self-aware. Whilst this is celebrated, it is also likely that this may contribute to individuals identifying symptoms of physical and psychological disorders, and subsequently seeking substances to self-medicate. This can appear particularly worrying when we acknowledge the growing technological connectivity, instances of advertising leading to the inception of use and the fact that NPS are often perceived as safer than other substances (Deligianni et al., 2020; Soussan & Kjellgren, 2016).

Our data, derived from internet discussion, is not without weakness. Some have stated self-report internet data to be unreliable or biased (Wood & Dargan, 2012), however others have demonstrated a high degree of congruence between online data and clinical data (Soussan & Kjellgren, 2014b). In the current study, our findings may be limited by the scope of the specific subreddit used. Since not all of those who are self-medicating with NPS will be on Reddit our findings may only be generalizable to this internet community. Despite this lack of generalizability, the data suggests that the experiences of those self-medicating with NPS are similar between those in different countries, with indi-

viduals citing similar motivations for use. It could be postulated that the online nature of NPS procurement creates a more globalized profile for NPS use. Additionally, outcomes and experiences appear to be separated more by substance type than demographic or severity of mental health condition. Another limitation of the current study is that subreddits are self-governing through an upvote system and subject to moderation by the moderators, which may influence which posts appeared in the subreddit and were subsequently captured using the *R studio* package. Particularly impactful posts rise whereas less interesting posts can be downvoted by the community and lost. Whilst this introduces a degree of selection bias, it is also likely that this self-governing structure could benefit data collection, allowing upvoted posts to reflect what the community believe to be relevant and eradicating potentially misleading or false information. Moreover, anonymity of posts is integral for reddit use and this is a positive, allowing users to express themselves honestly. Conversely, this anonymity means we cannot determine user location, although textual indications suggest individuals to be largely from the US, UK and areas of Europe. Whilst we are unable to make any assertions concerning prevalence, we note that during the study and write up period (October 2022–June 2023) the subreddit grew by 25,000 members (16%). However, it is important to note that overall site membership also grew, with the number of active daily users estimated to increase by 11.57% between 2022 and 2023 ([Reddit User Data, 2023](#)). Lastly, the current data only provides a snapshot of use. From the user perspective they would be interpreting each post within the context of other subreddits. This interrelationship of different subreddits could affect the context of the discussion. This snapshot of data also means it is not possible to discern use over a longer timeframe. Given the above limitations we can make no assertions on the efficacy of any substance. Nonetheless, the data highlights a previously unstudied phenomenon which would benefit from further investigation.

Conclusions

Our research demonstrates that there is a subset of the population using NPS to self-medicate a multitude of disorders. These individuals are using NPS as a last resort and searching for a “functional” solution to their disorder. Individuals often indicate feeling let down by professional healthcare, which may be leading them to search for other options online. The ease of access to NPS, abundance of information online and scarce availability of scientific data makes them a precarious class of substances. Currently, it is unclear how prevalent self-medication with NPS is. It is assumed to be a minor phenomenon, however one which has the potential to worsen. Future policies should aim to rebuild trust between the individual and the healthcare provider as a way of preventing NPS use. Finally, healthcare providers should be actively considering harmful NPS interactions and be aware that denying a patient medication could lead them toward a more dangerous NPS substance.

Ethics approval

The authors declare that they have obtained ethics approval from an appropriately constituted ethics committee/institutional review board where the research entailed animal or human participation. A university (KCL) research ethics committee approved the study (LRS-22/23-33941) and data were collected between October 2022 and February 2023.

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Declarations of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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