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"Becoming Your Own Psychologist": Novel Psychoactive Substances (NPSs) for Mood and Anxiety Disorder Self-Medication

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Abstract

Numerous individuals suffer from mental health issues including depression and anxiety, resulting in substantial societal burden. Data suggests individuals are choosing to self-medicate with Novel Psychoactive Substances (NPS); however, this phenomenon is poorly understood. We aimed to investigate which NPS are being used to self-medicate, evaluate their perceived effectiveness and examine influencing factors. Data from respondents (n = 274) (Mean Age [SD] = 29.8 ± 9.1, Male = 71%, Female = 18%, non-binary 5%) were collected via an online survey, with five participants (male = 2; nonbinary = 3) undertaking further semi-structured interviews and the data examined using a Framework analysis. NPS used included bromazolam, etizolam, clonazolam, 1P-LSD and 2-FDCK. Individuals perceived self-medication to be more effective than conventional treatment ($p < 0.001$). A Framework analysis identified the following themes surrounding mood and anxiety disorder self-medication: (1) depression being chronic, treatment resistant and often comorbid; (2) individuals attempting to mimic existing treatments; (3) individuals having high levels of pharmacological knowledge; (4) difficulties in controlling benzodiazepine self-medication. This study brings important insight into self-medication practices with NPSs, adding to data demonstrating an increase in bromazolam use. Data suggests self-medication follows conventional treatment and, therefore, we outline the importance of affordable emerging treatment options for depression and anxiety.

Keywords: novel psychoactive substances (NPSs); self-medication; anxiety; depression; bromazolam

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1. Introduction

A significant portion of the global population suffer from mental health challenges, primarily manifesting as anxiety and mood disorders [1,2]. Both depression and anxiety exhibit escalating prevalence rates, posing a critical public health concern [3,4]. The treatment gap for mental disorders exceeds 50% worldwide, reaching a staggering 85% in low and middle-income countries [5]. Treatment-resistant depression (TRD), defined as failing to respond to two or more antidepressants, affects 12–40% of individuals [6–8] and anxiety disorders (AD) impact between 0.9 and 28.3% [9], with both disorders resulting in substantial societal and economic burden. In 2010 anxiety disorders were estimated to contribute to 26.8 million disability adjusted life years [10], and data demonstrates TRD and anxiety both correlating with adverse life outcomes including low employment, impaired social

functioning, comorbid conditions, heightened suicide risk and compromised educational attainment [11].

Pharmacological intervention is often the first choice for depression and anxiety, including the use of antidepressants [12] and benzodiazepines [13] alongside behavioural treatments such as cognitive behavioural therapy (CBT) [14]. These are considered first-line and have demonstrated efficacy [15]; however, they remain ineffective for some [16]. A recent editorial by Fiorillo et al. (2025) highlights the clinical challenges faced regarding the management of TRD. The editorial demonstrates the advances in therapeutic innovation including brain stimulation therapies, novel pharmacological agents and new treatment-delivery modalities; however, this clearly illustrates a significant prevalence (30–40%) of individuals remaining treatment resistant to antidepressants [8]. These clinical issues provide consideration for the broader role of self-medication behaviours. Recently, there has been a renewed academic interest in the investigation of illicit psychoactive substances as treatment options, such as ketamine for the treatment of depression [8,17,18]. Moreover, psychedelics have indicated positive effects in a myriad of areas such as end-of-life anxiety [19–22], depression [23–25] and addiction [26,27].

Furthermore, data suggests that when faced with insufficient treatment options individuals may attempt to self-medicate [28]. Self-medication, defined as 'using substances to address self-diagnosed or professionally diagnosed symptoms without consulting a doctor', can provide benefits, but also poses significant risks including misdiagnosis, use of excessively high dosages, prolonged duration of use and adverse effects [29]. Many individuals practice some form of self-medication, such as the use of over-the-counter (OTC) medication [30]. Additionally, rates of self-medication are often higher in younger populations, including students [31]. Self-medication has also been posited as a general theory of substance use [32,33] and correspondingly, evidence shows that self-medication with drugs and alcohol is higher in those suffering from mood and anxiety disorders [34,35]. This intersection of mental health issues and substance use, particularly novel psychoactive substances (NPS), has garnered attention more recently [28,36–39].

NPS, also referred to as 'research chemicals' or 'legal highs', are by definition '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' [40]. NPS often mimic classic illicit substances such a cocaine or MDMA [41] and the category consists of a heterogenous variety of substances including synthetic cannabinoids, cathinones, opioids, psychedelics and benzodiazepines. Despite their namesake, these substances are not necessarily 'novel' or 'new' but instead may have recently become available on the drug market. This transient and unclear definition of NPS has received criticism from some which question its usefulness [42]. Regardless, NPS remain a persistent issue for authorities [43] and recently, the misuse of novel benzodiazepines has represented particular concern [44–48]. Often available online and perceived by many as legal, the NPS class represents an appealing option for self-medication. Previous data from forums such as Reddit (www.reddit.com) has shown that individuals are using novel benzodiazepines for anxiety, novel dissociative analogues for depression and stimulant analogues of prescription medication such as Ritalin or Adderall for ADHD [28]. This rational or intentional NPS use suggests significant parallels with the previously researched "psychonaut" profile of NPS use [49–51], whereby a high degree a pharmacological knowledge is often present. However, the extent to which the motivations and behaviours of self-medicators and psychonauts overlap is not fully understood.

The use of NPS to self-medicate a variety of conditions such as anxiety, TRD and ADHD is evident in the literature. Prior research has focused on ADHD [52] illustrating

that novel stimulants can be used as a stopgap between prescriptions and that their use is often motivated by poor access to treatment. However, no such study has been conducted exploring the motivations and outcomes of those attempting to self-medicate mood and anxiety disorders. Currently, comprehensive data investigating the experiences of those that self-medicate and exploring which NPS are being used are lacking.

Therefore, the aims of the following research are to investigate which NPS are being used to self-medicate mood and anxiety disorders, evaluate their perceived effectiveness compared to conventional treatment options and explore the experiences of those self-medicating.

2. Materials and Methods

We launched an online cross-sectional convenience between June 2023 and January 2024, including participants that were ≥18 years old. The survey was conducted using Qualtrics, with participants recruited from the following websites which had previously been associated with NPS discussion: Reddit (https://www.reddit.com/r/researchchemicals, accessed on 10 July 2025), Bluelight.org, partyvibe.org and Drugs-forum.co.uk.

The survey initially asked which disorder participants suffered from and allowed the individual to declare whether this was diagnosed by a medical professional. Participants were able to declare up to two disorders, which could be chosen from a list of indicated disorders or by using a free text box. Participants could then rate the effectiveness of NPS self-medication and their conventionally offered treatment (medication, therapy, etc.) for each disorder. This was performed using a 100-point slider scale. Participants could choose from a list of 28 NPS highlighted by previous research [28], as well as having the option to use a free text box. There were no limits on the number of NPS that could be chosen. Participants were then asked to state whether their diagnosis or NPS use came first. In addition, demographic questions included level of education, history or drug use, income, country of origin, ethnicity, gender and age. A copy of the survey is included (Supplementary S1). Post hoc, answers that mentioned generic category terms such as 'amphetamines' were discounted. This was performed to aid one of our main aims, which was to categorise and measure the specific NPS being used to self-medicate. Overall, the discounting of responses was limited and in most cases individuals that included free text generic responses also responded using the provided NPS list, limiting information loss.

Following completion of the survey, participants were offered the opportunity to participate in the interview part of the study. Twenty-two of the participants responded and consented to participate. Ten of the participants completed the interview process with five interviews focusing on mood and anxiety disorders and data focusing on ADHD published separately [52]. Prior to interviews a pilot was conducted to ensure validity and question comprehension. Notably, saturation was not reached in the interview research undertaken and therefore the data provided should not be seen as representative and instead exploratory only. Our previous research has suggested that eight interviews could be sufficient to reach data saturation [52]; however, this level was not researched in the current study. Prior to the data collection, a semi-structured interview guide was constructed focusing on four topics: (1) the history of NPS use; (2) views on NPSs; (3) self-medication practices; (4) perceptions of conventional healthcare. The interview data were recorded using Microsoft Teams and transcribed using KCL software (Kaltura Version 1), with all identifiable information discarded after the interview process and participants referred to by their identification codes. We include a copy of the codetree (Supplementary S3) and interview guide (Supplementary S2).

Interview data was then analysed qualitatively, using a Framework analysis [53]. This methodology has strengths in its ability to facilitate comparative techniques through the review of data across a matrix. In line with Gale et al. [53] the initial stages of analysis took place by creating verbatim transcripts of each interview, with notes on emergent themes written down in a notebook. KCL software was used for transcription, with subsequent amendments made by the researcher to correct errors. This process allowed an opportunity to become immersed in the data. The second stage of Framework analysis involved an in-depth familiarisation with the data. Audio recordings were re-listened to while analytical notes on thoughts or general impressions were made in the margin of the transcript. Stage three then involved line-by-line coding of the data using the software NVivo 14. The initial codetree (Supplementary S3) was based on previous NPS research [28,52] and updated in an iterative fashion as we proceeded with the coding process. Once completed NVivo contained five coded transcripts focussing on mood and anxiety self-medication, allowing data from various files under the same code to be compared efficiently. Throughout the coding stage the working analytical framework was applied iteratively, making use of 'other' categories to make sure no useful data was omitted. Finally, the data was charted into Framework matrices, represented as a spreadsheet in Microsoft Excel [54]. An effort was made to reduce text volume without losing meaning. Once data had been charted and summarised, connections or relationships between participants or parts of the data can be explored. At this stage reference was made to a working file where notes were kept throughout the analysis and used to prompt ideas for the interpretation of the data. Data regarding the Framework analysis are available upon request.

Data processing was conducted using Microsoft Excel [54], SPSS 27.1 [55] and NVivo 14 [56]. Means (±SD) are presented for self-rated effectiveness score and age demographic data. Furthermore, frequences are reported for demographic information. The effect of income was analysed using an ANOVA, with paired-sample T-tests used to compare conventional treatment and NPS self-medication scores.

3. Results

3.1. Survey Data

Overall, 496 participants opened the survey. It was completed by 274 participants, with individuals excluded for not using an NPS to self-medicate (n = 29), not suffering from a mood or anxiety disorder (n = 62) and not finishing the survey (n = 131).

The median survey completion time was 7 min and 42 s. No incentives were offered for completion. We note that the sampling strategy is convinced base and internet focused, limiting generalisability. These limitations are acknowledged further in the discussion section. Participants were mostly male (74.5%), with 54 female (17.9%) and 17 non-binary (5.4%). Individuals (Mean Age [SD] = 29.8 ± 9.1) were largely from the USA (48%), Netherlands (11.3%) and Germany (8.3%). Most respondents were white (83.1%) and earned between USD 10,000 and USD 24,999 (24.5%). A large portion had achieved a College (University) education (41.1%) and high levels of non-NPS were evident with cannabis (93%), alcohol (92%) and nicotine (83%).

One hundred and sixty-two individuals declared themselves to suffer from one disorder and 112 individuals declared to be suffering from two disorders, resulting in 386 overall declared disorders. Generalised Anxiety Disorder (GAD) was most common (28.2%) (Table 1). When asked, most declared to have been diagnosed by a medical professional (78.0%).

Table 1. Disorders being self-medicated.

Disorder	*N* (%)
Generalised anxiety disorder (F41.1)	109 (28.2)
Post-traumatic stress disorder (PTSD) (F43.1)	46 (11.9)
Panic disorder (F41.0)	23 (6.0)
Obsessive–compulsive disorder (OCD) (F42)	19 (4.9)
Social phobia (F40.11)	6 (1.6)
Agoraphobia (F40.0)	5 (1.3)
Recurrent depressive disorder (F33)	69 (17.9)
Depressive episode (F32)	38 (9.8)
Bipolar affective disorder (F31)	24 (4.9)
Borderline Personality Disorder (F60. 3)	9 (2.3)
Cyclothymia (F34.0)	3 (0.5)
Emotionally Unstable Personality Disorder (F60.3)	2 (0.5)
Attention-deficit hyperactivity disorder (F90.9)	13 (3.6)
Non-ICD-10 Disorder	4 (1.0)
Substance addiction (F19.2)	2 (0.5)
Chronic Pain (G89.2)	2 (0.5)

Table includes disorders mentioned by more than one person.

3.2. Treatment, Self-Medication and Healthcare Perceptions

A majority (52.3%) had received both therapy and medication. Some had received either medication (21.5%) or therapy (10.4%), and 15.3% had received no treatment. Sixty-seven percent declared that their medical diagnosis preceded their NPS use. Ratings of perceived effectiveness of conventional treatment and self-medication, as well as perceptions of healthcare are included below (Table 2).

Table 2. Table of perceived effectiveness.

Question	Mean Score (±SD)
"On a scale of 1–100, how well do you feel the treatment worked?"	
Conventional treatment	43.6 (27.0)
NPS self-medication	69.3 (22.2) *
"On a scale of 1–100, how much did your symptoms improve?"	
Conventional treatment	41.4 (27.5)
NPS self-medication	66.9 (24.7) *
"On a scale of 1–100, how much did your quality of life (QOL) improve?"	
Conventional treatment	42.2 (29.4)
NPS self-medication	62.8 (27.6) *
Healthcare perceptions	
How competent do you view professional healthcare?	37.1 (24.9)
How well-supported are you by the medical healthcare and mental health system?	32.9 (27.4)
How do you rate your access to healthcare needs?	51.3 (32.0)

* Paired Sample *T*-Tests showed a significant in self-medication scores for all three measures ("Did it work" = $p < 0.001$, Cohen's $d = 0.76$; "Did symptoms disappear" = $p < 0.001$, Cohen's $d = 0.72$; "Did QoL increase?" = $p < 0.001$, Cohen's $d = 0.54$.).

3.3. Most Used NPSs

When looking to self-medicate, the most used NPS were bromazolam (37.1%), etizolam (35.5%), clonazolam (26.7%), 1P-LSD (1-propanoyl-lysergic acid diethylamide) (25.9%) and 2-FDCK (2-Fluorodeschloroketamine) (25.9%). Differences in type of substance used were apparent between mood disorders (MD) and anxiety disorders (AD), with the biggest

difference apparent for benzodiazepine use: psychedelics (MD = 14%, AD = 11%), dissociatives (MD = 40%, AD = 35%), benzodiazepines (MD = 26%, 42% = AD) and stimulants (MD = 13%, AD = 8%). A table of most used substances is included below (Table 3) with a comprehensive list of substances used for each disorder also available (Supplementary S4).

Table 3. NPSs used.

Substance	Total (%)
bromazolam	37.1%
etizolam	35.5%
clonazolam	26.7%
1P-LSD (1-propanoyl-lysergic acid diethylamide)	25.9%
2-FDCK (2-fluorodeschloroketamine)	25.9%
dextromethorphan (DXM)	23.1%
deschloroketamine	22.5%
flualprazolam	21.5%
4F-MPH (4-fluoromethylphenidate)	19.4%
pyrazolam	18.7%
O-DSMT (O-desmethyltramadol)	17.6%
2-FMA (2-fluoromethamphetamine)	16.6%
O-PCE (2′-oxo-PCE)	16.1%
4-AcO-DMT (O-acetylpsilocin)	15.5%
flubromazolam	14.3%
3-MeO-PCP (3-methoxyphencyclidine)	13.7%
flubromazepam	13.7%
1CP-LSD (1-cyclopropionyl-d-lysergic acid diethylamide)	12.2%
diclazepam	12.2%
methoxetamine (MXE)	10.6%
3-MeO-PCE (3-methoxyeticyclidine)	10.4%
3-HO-PCP (3-hydroxyphencyclidine)	8.0%
isopropylphenidate (IPPH)	6.7%
3-HO-PCE (3-hydroxyeticyclidine)	6.0%
FXE (fluorexetamine)	5.7%
nitrazepam	4.2%
4-HO-MET (4-hydroxy-N-methyl-N-ethyltryptamine)	3.4%
U-47700	3.1%
2-BDCK (2-bromodeschloroketamine)	2.6%
phenazepam	2.3%

3.4. Income and Self-Medication

To obtain an overall perception of the effectiveness of NPS self-medication, scores regarding each measure ("Did it work", "Did symptoms disappear", "Did QoL increase?") were integrated. These data were then split by the level of income to explore the relationship between income and self-medication effectiveness.

A multiple regression analysis was conducted to examine the relationship between income categories and the total perceived self-medication effectiveness score. The overall model accounted for 8.8% of the variance in total score (R^2 = 0.088) and an adjusted R^2 of 0.068. Assumption testing indicated no violations of multiple regression requirements (Residuals were approximately normally distributed, homoscedasticity was observed, multicollinearity within acceptable limits).

The model's constant indicated a baseline effect (B = 150.652, SE = 13.205, t = 11.408, $p < 0.05$) with the \$0 group used as the reference category. When compared to the 0\$ category all income groups demonstrated statistical significance other than the \$100,000–\$149,000 group ($p = 0.137$).

3.5. Interview Data

Qualitative interviews were conducted with five participants that had previously taken part in the survey research. The following quotes are data which has been analysed using a Framework analysis and focus on the self-medication of depression, anxiety and PTSD. The participants were male (n = 2), non-binary (n = 3). The locations of participants included Netherlands, France, United Kingdom and the United States with the ages ranging from 20 to 39. The participants demonstrated significant comorbidity, including ADHD, anxiety, post-traumatic stress disorder (PTSD), anhedonia and autism spectrum disorder (ASD). The interviews revealed the following themes surrounding NPS use: (1) depression being chronic and/or treatment resistant and often comorbid, with NPS as a last option; (2) attempts to mimic emerging treatments; (3) evident pharmacological knowledge; (4) difficulties in controlling benzodiazepine use.

3.5.1. Chronic and/or Treatment Resistant Depression

Individuals using NPS to self-medicate often described their depression as chronic or treatment resistant. Additionally, cases appeared complex, with most presenting comorbid disorders like anhedonia, ASD, anxiety and PTSD:

> *"I feel like I'm quite a fringe case because of my complex problems, my ASD, the onset of depression. [. . .] I've been dealing with depression for 17 years now"*—N24

> *"I've been depressed for since 2017. [. . .] at this point I believe that I have chronic depression, and I have to deal with it for the rest of my life. . ."*—M39

> *"I was struggling with anxiety too around like school and socializing and all kinds of stuff"*—N20

Some participants outlined that the prescription medications they were getting were not substantially helping:

> *"I was not finding much help in the prescription medication that I was getting, specifically SSRIs."*—N20

> *"I have had multiple prescriptions for antidepressants throughout my life that haven't really worked. [. . .] 1P-LSD felt like the only thing that really helped. Or at least like it did what I felt like normal antidepressants would do. . ."*—N24

3.5.2. Academic Knowledge

Individuals displayed a high level of knowledge regarding pharmacology and mood disorders, engaging with academic research. Exposure to these sources appeared to influence their willingness to try specific NPS or formulate self-treatment plans:

> *"I follow a lot of researchers on Twitter and ResearchGate. [. . .] I get like 20 emails with new research papers, and I'll come across reports for example about the 2-FDCK that did a mouse study, and they found that it has longer aftereffects than ketamine, so that convinces me that perhaps it's a better way of treating depression than ketamine"*—M39

> *"You know I've looked at literature for depression in children, and chronic depression in children that lasts into adulthood. . ."*—N24

3.5.3. Rational Substance Use

The decision to self-medicate appeared to be a conscious, rational choice in response to persistent low mood and a lack of other treatment options:

> *"I was really sort of planning to kill myself, and as a last-ditch effort [. . .] I had access to LSD at the time, but I thought I wanted to try these, you know, Hawaiian Baby Woodrow seeds that I'd heard about."*—N24

"I think it was 2020 when I like seriously with the mindset of 'okay I'm going to take this because I'm feeling depressed, and I think this will help me.'"—M39

3.5.4. Mimicking Treatments

Most individuals referenced ketamine, either trying ketamine itself or outlining attempts to "mimic" the treatment with other arylcyclohexylamines like 2-FDCK. This was to varying degrees of success, with one participant suggesting that NMDA antagonists were of no benefit to them:

"I tried to DIY ketamine treatment on myself when I came off SSRIs, but I found that NMDA receptor antagonists of any kind are extremely harmful to my body somehow, at least my body perceives them as a threat."—N24

"I was interested in dissociatives, some different arylcyclohexylamines to mimic ketamine, which I had some interest in for antidepressive effects, as well as like psychedelics. . . The goal with that [self-medication] was to treat it similar to a ketamine infusion, like by prescription, to just take some time to reflect and maybe gain new perspectives on my life"—N20

"So, as you probably know, ketamine is used for treating depression. And I occasionally use 2-FDCK because I know I'll have like an afterglow for a few days and that helps."—M39

3.5.5. NPS Used

Participants described using a range of NPS including arylcyclohexylamines like deschloroketamine or 2-FDCK, lysergamides such as 1P-LSD, phenethylamines including the 2C-X substances, novel opioids and the amphetamine substance 4-FMA:

"Deschloroketamine, that had a nice afterglow. I used 1P-LSD, but I find that actual LSD has a better after effect than most of the research chemical alternatives. . ."—M39

"Phenethylamines. I think that those might have been the most overall helpful and interesting ones that I tried. I tried [. . .] 2CB, 2CD, 2NBOH, mescaline. [. . .] I think that those were helpful for achieving more of what I was looking for than the dissociatives."—N20

One individual highlighted the use of a substance mixture known colloquially as Borax, which is a combination of 5-MAPB, 2-FMA and 5-MeO-MiPT. This appeared to be used in a similar way to MDMA therapy:

"I've also tried [. . ..] borax molly, which is basically a mix of three different research chemicals that replicate the effects of MDMA and I usually have like a huge boost of confidence and it feels very nice for a couple of days afterwards"—M39

3.5.6. Complementary Treatments

Some individuals outlined utilising alternative treatments in addition to their medication; however, others opted to cease their prescription medication:

"I was on antidepressants for the period when I was using all this stuff. And I would combine those with these dissociatives, like as you said, FXE and more recent times, or like 2FDCK was another one for a little bit."—A20

"My mental health was really suffering so that's when I kind of stopped taking my medications and that's when I felt inclined to start trying anything else because I was really, really, really not functioning."—N24

3.5.7. Reflections

Broader discussion elicited individuals' reflections on their self-medication, with one participant suggesting that you can "become your own psychologist" or achieve a fresh perspective, promoting motivation:

> *"It's as if you're not with a psychiatrist or a psychologist, but you become your own psychologist in that moment [of self-medication]. [. . .] "Because you can see your life and yourself from a different perspective. And that really helps in finding what's missing in your life or finding what's causing problems, [. . .] actually convincing you somehow in a natural way like 'hey, maybe I should actually do a sport, find a football club and just become a member' [. . .] and yeah the motivation comes like instinctively and it's not like a chore. . ."*—M39

Upon reflection, one individual thought that their attempts to self-medicate could have had more impact had they focused more on learning from the experiences, and had not been on their antidepressant medication:

> *"Overall, I don't think that they [NPS] really had as large of an impact as they might've if I was doing more work to like intentionally to integrate those experiences. And maybe also if I wasn't also on antidepressants and the other stuff."*—N20

As with previous self-medication research, the line between recreational use and self-medication was blurry at times:

> *"Yeah, for me the lines are blurred a little bit because while I was using it recreationally, [. . .] it definitely felt like self-medication, in that with the depression specifically I was struggling so much to find anything else that would help."*—N20

3.5.8. Anxiety and Benzodiazepines

Participants also outlined the self-medication of anxiety, usually with novel benzodiazepines such as clonazolam, flualprazolam, flubromazolam, bromazolam and pyrazolam:

> *"For anxiety specifically, I was looking at a lot of those novel benzos that you were talking about [. . .]. I was messing with some slightly stronger stuff like clonazolam, flualprazolam and flubromazolam."*—N20

These were often described as particularly cheap, with one participant indicating they were a "guaranteed addition" when making an order:

> *"If I was doing my order, they [benzodiazepines] were a guaranteed addition, like for sure I'm adding because it was so cheap in the Netherlands, you add bromazolam and pyrazolam [. . .] if you ordered enough, it was like 50 cents per dose"*—M21

> *"It was very cheap and easy to get a lot of them [benzodiazepines]. And of course, I'm sure you know a bunch about the compulsive redosing as well"*—N20

3.5.9. Side Effects

Many individuals outlined issues with benzodiazepines being easy to overdose and demonstrating amnesic episodes or "blackouts":

> *"Benzos are not something you want to dose incorrectly. . . I don't like the memory reduction, like the amnesia you get from it is really strong. So, I just don't like that at all. I try and do any dose below amnesia level."*—M21

> *"I remember one time I, my first experience with clonazolam, I got a dropper bottle of the stuff and did a dose and then came to like a month later and didn't really remember much."*—N20

As ever with benzodiazepines, despite their perceived efficacy, issues surrounding withdrawal, tolerance and rebound anxiety arose eventually:

> *"Oh, the tolerance is immediate. It's so noticeable. I can take like a quarter for like the first two days and feel something, but after that, it just becomes like the normal [dose], [. . .] and then you have to go up from that."*—M21

> *"I definitely think that they worked well for managing anxiety when I was on them, but I never wanted to be on them all the time because I've always been wary of withdrawal"*—N20

> *"Especially for bromazolam that has like really bad withdrawal, like you're okay for the first two, three days. But then if you go longer than that, you get like this rising anxiety, but because it slowly comes on, you don't notice that you're like fully withdrawing."*—M21

3.5.10. Reflections on Anxiety Self-Medication

When asked, participants acknowledged that the use of benzodiazepines was not curative, although upon reflection one participant suggested that this thought is hard to resist. Individuals also appreciated that it was complicated without the oversight of a doctor:

> *"I have like that. . . a little bit of like you know remnant [of thought] like 'oh yeah you can fix your anxiety with benzos'"*—M21

> *"It's maybe more complicated than doing it with a doctor and like you don't have someone who's there to see if it's becoming problematic"*—M21

3.5.11. PTSD Self-Medication

One participant suffering from comorbid PTSD attempted to self-medicate with 1P-LSD. He outlined using psychedelics as a microdose first, before using a higher dose to achieve a therapeutic effect:

> *"For PTSD, I am playing with the analogues of LSD right now. So, I have 1P-LSD, and also trying to find proper goals for this PTSD situation"*—M38

> *"I tried the microdose, I think 10 microgram pellets. And then I wanted to have some fun, and I put slightly more on. I dropped 50 µg I think, and it turned to soul therapy, actually."*—M38

He suggested that the use of 1P-LSD facilitated a regression back to a traumatising point in childhood, emphasising that he was not looking to 1P-LSD for recreational or visual effects, but purely as a therapeutic agent:

> *"I actually regressed back to my childhood under the influence of 1P-LSD. and I saw some two or three very traumatizing situations in my childhood, and I relived it actually just like I was above my head and cried and cried. Yes, that's what's really helping for me."*—M38

> *"I don't want to hallucinate here I don't want to see any fractals or just visual visuals. I just want to open myself to myself"*—M38

3.5.12. Reflection on PTSD Self-Medication

The participant outlined the inadequacy of treatment available in Germany for PTSD, suggesting it was a last resort for him; however, changes in legislation would make him more reticent to explore these options:

> *"The point why I started with this therapy [1P-LSD] or also with MDMA, is that the conventional therapy in Germany is useless for this kind of situation, and I feel in my internal self, I feel if I don't do something [. . .] then my life will be probably no longer be very long. . ."*—M38

4. Discussion

We conducted, to the best of our knowledge, the first study analysing the self-medication of mood and anxiety disorders with NPSs within an internet population. The current study aimed to conduct a cross-sectional survey supplemented with qualitative analysis to determine a comprehensive account of the NPS used to self-medicate mood and anxiety disorders, evaluate their perceived effectiveness and examine the experiences of those choosing to self-medicate anxiety and depression.

The above study extends the findings of previous research suggesting the most used novel substances for anxiety and depression were bromazolam, etizolam, clonazolam, 1P-LSD (1-propanoyl-lysergic acid diethylamide) and 2-FDCK (2-Fluorodeschloroketamine. Supplementary interview data then suggests that individuals seeking to self-medicate mood disorders are usually suffering from chronic and/or treatment-resistant conditions which are often comorbid. Further, the use of NPS is usually a last option, with many basing their use on emerging therapeutic treatments with ketamine or MDMA, and some even considering psychological factors such as post-substance integration, a technique often included in the prescribed ketamine treatment protocols [57]. Finally, individuals display evident pharmacological knowledge, and the findings echo the difficulties in controlling benzodiazepine use outlined in prior research [28].

The survey data indicate that most individuals (54%) were choosing to self-medicate anxiety disorders, specifically Generalised Anxiety disorder (GAD) and Post-Traumatic Stress Disorder (PTSD) and predominately using novel benzodiazepines (Supplementary S4). Notably, 11.9% of individuals were self-medicating PTSD, an area currently lacking in research [58,59]. We confirm the use of the novel benzodiazepines etizolam and clonazolam for anxiety disorders [27] and additionally highlight the use of bromazolam. This use is consistent with our previous research [28] and we extend our findings on varying novel benzodiazepine pharmacodynamics and dependence, whereby fast acting benzodiazepines, such as etizolam, are favoured for their short-term effects in abating panic attacks or anxiety; however, they can also be liable to compulsive redosing and have a higher potential for tolerance development. In this sense, designer benzodiazepines with a high potency and short duration of action may be more prone to the dependence, tolerance and withdrawal effects outlined in the qualitative data above. It is worth noting that etizolam is a licenced medication in some countries, including Italy, India and Japan [60]. Whilst these countries only represent a small portion of participants in the survey at 2%, 0.25% and 0.5%, respectively, there is a chance that their use could have been prescribed and therefore may more correctly represent clinical malpractice [61]. Recently, bromazolam has been detected in both the UK [62] and internationally [63]. Further, the temporal nature of our findings is notably similar to wider literature [64] and recent data from Australia [65], highlighting the international nature of the NPS problem. Correspondingly, the Welsh Dug Checking service (WEDINOS) 2022–23 report outlined bromazolam as the most identified substance in 2023, and of concern, also the substance most likely to be mis-sold under the belief that the buyer was buying another substance, usually diazepam [66]. Together, these findings suggest an increase in availability of bromazolam within the drug market and demonstrate a need for healthcare providers to be aware of its novel pharmacological profile and the possibility of its appearance as an adulterant

Furthermore, 39% of individuals were self-medicating mood disorders and the novel psychedelic 1P-LSD, and dissociative 2-FDCK emerged as common choices for self-medication; however, we exercise caution in generalising these findings given the internet-based sample. The appearance of 1P-LSD is unsurprising given its implications in microdosing [67,68] with purported mental health benefits illustrated in previous self-medication surveys [69] and the increased investigation of psychedelic treatment for depression and anxiety [70,71]. Limited data exists on the safety of 1P-LSD; however, it may act as a prodrug to LSD and therefore share a similar safety profile [72]. Moreover, almost half (45.5%) of the current sample declared the use of ketamine to self-medicate, reflecting the emergence of ketamine and esketamine as treatment options in depression [73,74]. It is likely that the emergence of these treatment options may be contributing to a public perception of arylcyclohexylamines as entirely safe compounds and these data suggests that 2-FDCK may be used as a substitute for ketamine, in lieu of treatment options. Additionally, a recent review by Di Vincenzo et al. (2024) suggests that there may be a discrepancy between the facts surrounding esketamine for treatment-resistant depression and the perception of the treatment from the patient or clinician [75]. Taken together, this suggests that individuals self-medication behaviours may be shaped by what they read or see in the media, but that this is likely to incomplete or distorted. There is scarce information surrounding 2-FDCK; however, reports suggest it is easy to obtain online [76] and that it may possess a similar abuse potential to ketamine [77]. It has been detected in various countries [78] and with increasing frequency at festivals [79]. Data from the United Nations Office on Drugs and Crime indicates 2-FDCK to be the second-most prevalent dissociative, behind ketamine, in all reporting countries since 2020 [80].

These disorder-based NPS preferences reflect conventionally offered pharmacological treatments and imply a degree of informed intent when self-medicating [81]. Further, our findings align with broader research suggesting that individuals who are self-medicating desire a "functional" substance. Indeed, others have observed active substance substitution [36] in situations where treatment options may remain out of reach due to geographical or financial constraints [28]. More broadly, our data lends support to the self-medication hypothesis [32,33] with 67.2% declaring their NPS use to follow their diagnosis. Despite the above findings, the qualitative data in the current study demonstrates that in some cases the line between therapeutic and recreational use is blurred. It is most likely difficult for individuals to reflect on substance use that is both recreational and therapeutic, and more research is needed on the duality of these motivations and whether they can co-exist. Finally, it is interesting to consider the near complete absence of synthetic cannabinoid use in the current study, despite synthetic cannabinoids appearing in large quantities internationally [82] and within the prison [83,84] and homeless populations [85]. We suggest that the behaviours and motivations of these populations differ, despite a shared 'desire to cope' with life through NPS use.

The qualitative analysis unveiled four key themes: (1) individuals seeking to self-medicate are suffering from chronic and/or treatment-resistant disorders which are often comorbid; (2) the mimicking of emerging therapeutic treatments with ketamine or MDMA; (3) high levels of pharmacological knowledge; (4) difficulties in controlling benzodiazepine use.

The finding that those who are facing treatment resistant disorders may search for alternative medications is not necessarily novel and strongly aligns with the finding of our previous research whereby NPS remain a 'last resort' [27]. However, the above study extends this finding, suggesting that individuals may attempt to mimic novel treatments using illicit substances. Previous research by Jilka et al. [86] utilised a focus group of depressive patients demonstrating that patients thought self-medication with ketamine

would be more likely if they could not access ketamine through the NHS or if the treatment was too expensive, particularly if they were desperate. Given ketamine's increasing popularity in both the recreational and therapeutic fields, a comprehensive understanding of its non-medical use is warranted, as is ensuring that emerging treatments become affordable and accessible [87].

Furthermore, the NPS users in the current study indicate high levels of pharmacological knowledge, and we suggest that the psychonaut [88] profile of NPS user is more likely to be willing to self-medicate, with a knowledge base that facilitates the mimicry behaviours outlined above. These notions are corroborated by a case report by Brown et al. (2017) [89] and wider research indicating that physicians and psychiatrists appear to demonstrate a willingness to self-medicate their own depression in treatment-resistant cases [90].

In addition, the analysis of income levels suggested a possible effect on perceived self-medication effectiveness (Figure 1). This could portray the fact that individuals with a higher income have better access to healthcare or are likely to be in better health generally and therefore may be more resistant to the potential adverse effects of self-medication. The influence of demographic and socioeconomic factors on self-medication is complex [34], with research suggesting that being younger, male and Caucasian are factors that are linked to an increased likelihood to self-medicate anxiety and depression [35,91–93]. Previous research has demonstrated that self-medication is practiced by those of low and high incomes [94], providing value to both [95]. Broadly, however, research has suggested that those who self-medicate mood and anxiety disorders with drugs or alcohol are more likely to be in lower income categories [35], and so this income relationship could be specific to NPS, as research has outlined differences between NPS users and other substance user populations [96]. Notably, we highlight that a large degree of the sample reported polydrug use making it difficult to examine the relationship between disorder and substance effectiveness.

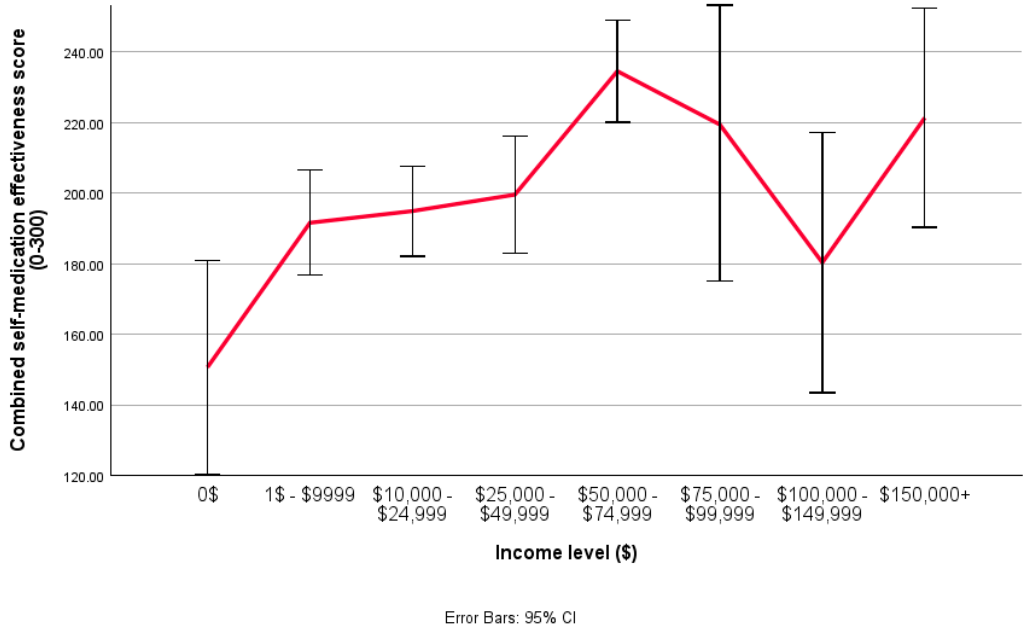

Figure 1. Line graph comparing the mean total score (0−300) for the perceived effectiveness of NPS self-medication across different income levels. Made in SPSS.

Finally, we corroborate wider research highlighting the issues of benzodiazepine self-medication [28,39] and demonstrate that outcomes tend to be worse compared to dissociatives or psychedelics, with amnesic episodes and the development of tolerance

evident. We note the remarks of one individual suggesting that without a doctor it is difficult to see when self-medication has become problematic. Clearly self-medication carries significant risk, and medical oversight would likely improve outcomes for the individuals in the current research. Therefore, we highlight the need for effective, affordable and accessible mental health treatments.

While the current research has strengths in its novelty, it is not without limitation. Data suggests that drug use self-report data can be reliable [97]; however, we make no assertions of causation given the convenience sample. Further, we cannot rule out the possibility that the self-medication outlined here could be addiction maintenance, where individuals may be using NPS to alleviate their addiction and withdrawal symptoms. This point is particularly relevant to those using benzodiazepines given their addiction profile and the need to taper off GABA agonists [98]. Additionally, we recognise the possibility of social desirability bias [99] and acknowledge that individual stigma towards antidepressant medication and conventional healthcare in drug forums may have influenced the declared effectiveness ratings. Moreover, perceived effectiveness ratings may have been influenced by expectancy effects and lack of blinding. Further, it is likely that individuals within these forums will be against stricter regulation of the substances they use, and therefore, may attempt to describe these novel substances in a positive light, hoping that a positive academic reflection could result in less legislative control. This may operate either consciously or unconsciously and could influence responses.

In addition, the current study design only allowed one effectiveness rating per disorder, regardless of the amount of NPS used to self-medicate. Due to this we were unable to establish whether any specific NPS were perceived as effective or non-effective and it may be that patterns or outcomes of substance use become clearer with a focus on a specific substance or substances class. In the future this could be altered; however, from our sample it appeared that the most users were polysubstance users. Finally, the current data is unable to provide a long-term perspective, and it is likely that a longitudinal study may uncover increasing negative side effects as use becomes more prolonged. Indeed, it is difficult to rate effectiveness in self-medicating a disorder that is ongoing, such as anxiety or depression, where ebbs and flows are likely. Similarly, it is difficult to evaluate the effectiveness of a substance that may elicit a tolerance and increasing negative side effects over time, and during this study there was an instance of an individual reaching out to request a change in their scores after a period of reflection had elapsed. Despite these caveats, our study demonstrates a clear willingness to attempt self-medication within an internet population of NPS users.

5. Conclusions

Overall, these findings provide novel insight into the phenomenon of self-medicating mood and anxiety disorders with NPS. Our data extends previous research, suggesting that individuals that have exhausted treatment options will be more willing to explore self-medication, and may attempt to mimic existing treatment protocols. Particularly, we highlight the dangers of benzodiazepine self-medication and recommend that health professionals be aware of the increase in novel benzodiazepine use, particularly bromazolam and its appearance as an adulterant. We highlight the need for further research, especially that which can confirm substance use and examines self-medication over time; however, we suggest that the behaviours demonstrated here in most cases represent informed intent and therefore, that developing effective legal treatment options for anxiety and depression should reduce self-medication.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/psychoactives4030028/s1. S1: Survey copy, S2: Interview guide, S3: Codetree, S4: Drug use table.

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Abbreviations

The following abbreviations are used in this manuscript:

MDMA	Methylenedioxymethamphetamine
ADHD	Attention Deficit Hyperactivity Disorder
TRD	Treatment-resistant depression
GAD	Generalised anxiety disorder
WHO	World Health Organisation
ACMD	Advisory Council on the Misuse of Drugs

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