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Perspectives on psychedelic treatment and research in eating disorders: a web-based questionnaire study of people with eating disorders

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Approximately 1.25 million people in the UK suffer from an eating disorder, yet the treatment options show limited efficacy, warranting the need for novel approaches. This study aimed to investigate the perspectives of people with eating disorders on the use of complementary therapies and psychedelic research and treatment. Two hundred participants with eating disorders took part in this web survey study. The majority of participants (70%) had used a complementary treatment to manage their eating disorder. Participants believed that psychedelic research was worthwhile in the context of a moderate level of concern. The most popular solutions to meet these concerns included providing education around psychedelics and their effects and use in psychiatry and experiencing endorsement from professionals in the area. Moreover, participant responses emphasized the need for a safe, monitored environment and the patient-therapist rapport in the context of psychedelic treatment. The findings are explored concerning future trials of psychedelics as a treatment for eating disorders.

Keywords

Anorexia nervosa; Binge eating disorder; Bulimia nervosa; Complementary therapy; Eating disorder; Pharmacotherapy; Psychedelics; Treatment

1. Introduction

An estimated 1.25 million people in the UK suffer from an eating disorder [1]. Eating disorders are associated with high levels of morbidity and mortality across all eating disorder types, with lifetime anorexia nervosa (AN) having a standardized mortality ratio of 4.37 [2]. Furthermore, approximately a third of individuals with AN develop a chronic course of the illness [3]. This can contribute to secondary issues such as a hyperactive stress response and neuroinflammation, contributing to comorbidities such as depression and anxiety [4]. Currently eating disorders are predominantly managed with psychological programs such as Cognitive Behavioral Therapy (CBT), the Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA), specialist supportive clinical management (SSCM) or eating-disorder-focused focal psychodynamic therapy (FPT) [5]. Several psychiatric medica-

tions are also used, most commonly selective serotonin reuptake inhibitors, such as fluoxetine, as well as atypical antipsychotics [6]. However, meta-analyses and systematic reviews have shown that psychological treatments [7, 8] and pharmacotherapy [9] have limited efficacy for AN, warranting a need for novel approaches.

Furthermore, patients with AN tend to be reluctant to take medications that lead to weight gain and do not perceive the low body weight as their core problem. Nonetheless, the primary outcome criterion in most randomized controlled trials (RCTs) in AN is an increase in body mass index (BMI). Thus, patients might feel that psychopharmacological treatment leading to an increase in BMI is just a way to speed up weight gain for the clinician's benefit, rather than to help their state of mind, depression and anxiety, which patients often see as their main problems [10]. Because of this discrepancy, recruitment into clinical trials for AN has been a challenge. It has been shown previously that high dropout rates, high levels of non-compliance and patients' reluctance to enter pharmacological trials, are likely due to fear of weight gain. Thus, it has been challenging to conduct randomized controlled trials looking into the pharmacological management of eating disorders [11]. In order to respect the patients' perspective and to be more successful in clinical trials, the patients' perspective on new psychopharmacological treatments is vital. Patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) are helpful tools in assessing care from a patient perspective. Unfortunately, they have not yet been used in the pharmacological management of eating disorders. Still, they may be a vital aspect of further research to try and reduce dropout rates and increase compliance.

Strategies for managing treatment-resistant AN show limited efficacy [7]. Individuals with treatment-resistant AN have a poor prognosis; at 20 years of illness, the mortality rate is 20% [12, 13]. This patient group is the most challenging amongst the psychiatric disorders to treat, which is thought

to be due to their ambivalence towards recovery, and secondary neurological changes associated with chronic stress and extended periods of malnutrition [4]. Given this treatment resistance patients are therefore likely to be more willing to try newly available treatments. The proposed neurological alterations seen in AN throughout the illness are paralleled in other psychiatric disorders that often show high comorbidity with the disorder [14]. Interestingly, psychedelic drugs are now considered in treating such psychiatric disorders, emphasizing their use for treatment-resistant depression [15]. Psychedelics are defined as psychoactive substances that can alter mood, perception, and cognitive processes [16]. They exert their effects primarily by an agonist (or partial agonist) action on brain serotonin 5-hydroxytryptamine (5-HT) 2A receptors [16]. There is evidence of longstanding psychedelics such as ayahuasca and psilocybin in tribal and religious ceremonies. Some depictions of mushroom effigies on prehistoric rock paintings date from over 1000 years ago [17–19]. In 1943 Albert Hofmann self-administered lysergic acid diethylamide (LSD), which led to large-scale psychedelic research [20]. However, progress in the use of this group of substances has been limited since the 1970s due to cultural stigma and legislation [21]. For example, some psychedelics, such as psilocybin, are classified as Class A under the UK's Misuse of Drugs Act 1971. This has made using these substances within research controversial [21], despite studies showing positive outcomes regarding mental health and general well-being compared to conventional treatments [22, 23].

Psychedelics such as LSD, psilocybin, ketamine and dimethyltryptamine (DMT) are beneficial in a wide range of psychiatric conditions, such as depression, anxiety, obsessive-compulsive disorder and substance abuse [24, 25]. Ketamine is a medication used primarily for initiating and maintaining anesthesia, although it has been categorized as an atypical psychedelic with NMDA receptor antagonist properties. It has shown particular promise to treat major depressive disorder and bipolar depression [26]. Moreover, esketamine, an isomer of ketamine, was approved in 2019 for the treatment of treatment-resistant depression via intranasal administration.

There is a lack of evidence for psychedelics in treating eating disorders, and no RCTs. The first published work examining psychedelic treatment in eating disorders was in 1998, where 16 individuals with eating disorders were given ketamine infusions to reduce their compulsive behaviors [27]. A relatively large dosage was given for an extended duration (20 mg/hour for 10 hours) compared to new trials [28]. Nine patients were categorized as “responders” and showed a clinical reduction in compulsive behaviors. Other investigations of psychedelics in eating disorders comprise retrospective interview studies into their experiences during an ayahuasca ritual. Participants in these studies have suggested that ayahuasca treatment has led to a reduction or cessation in their eating disorder symptoms and thoughts [29], together

with allowing participants to heal painful memories and generate self-love and acceptance [30]. Many individuals who choose to engage in psychedelic experiences plan this process. One cohort study of 28 patients self-reporting a lifetime diagnosis of an eating disorder capitalized on this phenomenon by taking prospective measures of wellbeing and depression (but not eating disorder symptomatology) 2 weeks before the experience and 2 weeks after [31]. Results showed profound reductions in depressive scores and increased well-being by using psychedelic drugs which included ayahuasca, DMT, psilocybin, LSD and the San Pedro cactus. At present there are several clinical trials registered to investigate psilocybin as a treatment for AN, and one investigating ketamine, also for AN.

Given that many of the common psychiatric comorbidities seen with AN have had promising results with psychedelics, there is current interest in their use in treating AN [32]. Clinical trials examining the safety and effectiveness of psychedelics in eating disorders are of particular interest. An essential step in the progression of trials of these substances is to elicit the views of patients themselves. We utilized a web survey to examine the views of a large sample of people with eating disorders on complementary and emerging treatments, focusing on the use of psychedelics.

2. Methods

2.1 Study design and participants

A total of 332 participants from the general population consented to participate in this cross-sectional, web-based survey from 24 April 2020 to 27 June 2020. Participants were included if they were: (i) adults (over the age of 18), (ii) self-reported as having a diagnosis of eating disorder and (iii) living in the UK.

Participants were recruited through the social media channels of BEAT (the UK eating disorder charity) and The Psychedelic Society, as well as departmental and academic-led social media accounts. Respondents clicked on a link that took them to the online web survey. The web survey was delivered using the secured online Qualtrics system [33] and took up to 15 minutes to complete. Two prizes of £50 were offered as incentives for participation. Approval for the study was granted by King's College London Ethics Committee [ethics number: HR-19/20-14805].

2.2 Measures and procedure

The questionnaire was co-developed with professionals working in eating disorders and patients with eating disorders. In addition, we utilized contacts within the research team to identify 3 patients with eating disorders, of which 2 have previously had experiences of psychedelics, to participate in the survey design. The questions were piloted with the assistance of these 3 patients to ensure that the questions conveyed the intended meanings and the responses available captured their views. The web survey consisted of six components, including demographics information, clinical information, current use of complementary/alternative treatment

to manage eating disorders and views on psychedelics as a treatment option.

2.2.1 Demographic and clinical characteristics

The demographic questionnaire included age group, education level, current relationship status, and current employment status. Clinical data collected included eating disorder diagnosis, psychiatric comorbidities, year of first eating disorder symptoms, and eating disorder diagnosis. In addition, information on current and past psychological and pharmacological treatment was recorded.

2.2.2 Use of complementary treatments for eating disorders

To explore participants' direct experience of complementary treatments in managing their condition they were asked questions regarding their use of these treatments and their perceived usefulness. Responses to questions on drug use were recorded on Likert scales ranging from "effective" (1) to "ineffective" (3) and "unsure" (4) for drug efficacy, and from "severe complications" (1) to "no complications" (4) for side effects.

2.2.3 Perspectives on psychedelic treatments for eating disorders

The survey also contained questions regarding attitudes towards psychedelics as a treatment option for eating disorders. This included their opinions on the importance of psychedelic research, their likelihood to take part in psychedelic research, levels of concern and types of concerns. Questions were presented as a sliding scale from 0–100 with the cursor centered in the middle. To yield further information on respondents' concerns regarding psychedelic treatment for eating disorders, they were allowed to specify their concerns with a text-entry response. Similarly, the opportunity to give a full written answer on their perspectives on psychedelic research generally, was facilitated by providing another text-entry box. Additionally, participants were asked their level of concern in the following parameters: safety, side effects, stigma, long term psychological/physical effects, negative psychedelic experiences, weight gain, addiction and loss of control. Participants responded to these questions as (1) "no concerns", (2) "some concerns, but would not stop me from participating", (3) "some concerns and would stop me from participating" and (4) "highly concerned and would stop me from participating". Participants were then asked to select which factors from the following would make participating in psychedelic research more appealing: a safe monitored environment, temporary psychological relief, long term psychological benefit, confidentiality, trying something new, the treatment being a last resort, trust in the research team, regular follow-up from the research team, more information about psychedelic research, and monetary reimbursement for participation. Finally, participants were informed that esketamine was recently licensed for use in treating depression in the UK, US and Europe and were asked whether this information changed their level of concern, using a 4-point scale ranging from "more concerned" to "unsure".

2.2.4 Additional measures

Participants also completed the Brief Illness Perception Scale [34]. The BIPS is a 9-item questionnaire assessing cognitive and emotional beliefs about their illness. The questionnaire was adapted for use in this study, by replacing the word "illness" with "eating disorder symptoms" within items.

2.3 Statistical analysis

The questionnaire yielded both qualitative and quantitative data which was analyzed separately. For all quantitative variables, results are reported as descriptive statistics; frequencies and percentages for categorical variables and means and standard deviations for continuous variables. To examine associations between personality factors and a participant's views on psychedelic treatment, participants were sorted into "minimal concern" and "extreme concern", as well as "open to participate" and "would never participate". Quantitative data were analyzed using R [35].

The qualitative data were reviewed independently by two researchers who analyzed the data by thematic analysis. Themes were discussed with the broader research team, and areas of particular interest were identified. Direct patient quotes were utilized in the results and discussion to illustrate the content of themes.

3. Results

3.1 Demographics and clinical information

A total of 332 participants consented to participate in the survey. Two hundred participants met the eligibility criteria and completed the survey in full. Thus, the results are based on data from 200 participants. Of the 200 participants, the majority were females (94.5%, $n = 189$), with a mean age of 28.9 (SD = 8.9). Over half (54.5%, $n = 109$) completed tertiary education and were in full-time/part-time employment (51.5%, $n = 103$). AN was the most common diagnosis (52.5%, $n = 105$), although over a quarter had more than one eating disorder diagnosis, reflecting the diagnostic complexity of eating disorders. The mean age at which eating disorders were first diagnosed was 21.0 (SD: 7.2), with an average five-year gap between first eating disorder symptoms and diagnosis. In addition, over 70% of the participants reported depression ($n = 145$), and 71% reported anxiety either currently or in the past ($n = 142$; see Table 1).

Over 80% ($n = 162$) have received or are receiving psychological therapy for their eating disorders, with cognitive-behavioral therapy being the commonly endorsed ($n = 152$), followed by the Maudsley Model of Anorexia Nervosa Treatment for Adults ($n = 35$) and cognitive analytical therapy ($n = 27$). Regarding prescription medication, 71% ($n = 142$) of respondents were either currently or previously receiving prescribed medication. Antidepressants were the most commonly prescribed ($n = 138$), followed by sedatives (such as benzodiazepines or promethazine; $n = 74$) and then antipsychotic/mood stabilizers ($n = 45$).

Table 1. Demographic and clinical characteristics of the sample (n = 200).

Variable	N (%) or M (SD)
Age	28.9 (8.9)
Sex	
Female	189 (94.5%)
Male	10 (5%)
Other	1 (0.5%)
Education	
Mandatory education	27 (13.5%)
Higher education	63 (31.5%)
Tertiary education	109 (54.5%)
Other	1 (0.5%)
Employment	
Full-time	71 (31.5%)
Part-time	32 (16%)
Self-employed	10 (5%)
Unemployed	33 (16.5%)
Student	53 (26.5%)
Retired	1 (0.5%)
Eating disorder diagnosis	
AN or a-typical AN	105 (52.5%)
Bulimia nervosa	19 (9.5%)
Binge eating disorder	13 (6.5%)
EDNOS	6 (3%)
OSFED	1 (0.5%)
Multiple diagnoses/other	56 (28%)
Age of first eating disorder symptoms	16.0 (4.8)
Age when symptoms first diagnosed	21.0 (7.2)
Comorbidities	
Depression	
Current	99 (49.5%)
Past	46 (23%)
Anxiety	
Current	120 (60%)
Past	22 (11%)
OCD	
Current	32 (16%)
Past	14 (7%)

*SD, Standard deviation; AN, anorexia nervosa; EDNOS, eating disorder not otherwise specified; OCD, obsessive compulsive disorder; OSFED, otherwise specified feeding and eating disorder.

3.2 Brief illness perception scale

Overall, respondents were ambivalent about whether their current pharmacological or psychological treatment was helping with their eating disorder symptoms with a mean score of 49.2 (SD = 27.2). In addition, there was a high level of hopelessness, as respondents scored highly when asked, "How long do you think your eating disorder symptoms will continue?" with higher scores representing a longer time frame (79.3, SD = 21.7). The perceived consequence and impact of an eating disorder was also severe, with respondents scoring highly on "How much do your eating disorder symptoms affect you emotionally?" (75.8, SD = 24.2) and "How much do your eating disorder symptoms affect your life?"

(73.8, SD = 22.5). Participants also reported a high level of understanding of their eating disorder symptoms (70.5%, SD = 25.4). However, participants reported moderate control over their symptoms (47.2, SD = 25.0), the severity of their symptoms (55.4, SD = 23.0) and concern about their eating disorder symptoms (51.8, SD = 26.9).

3.3 Complementary therapies and psychoactive substances for managing eating disorders symptoms

Nearly 70% (n = 139) of respondents had previously used complementary treatment to manage their eating disorders. The four most popular complementary treatments were yoga meditation, relaxation techniques and hypnosis. Only 6.5% (n = 13) had ever obtained medication that had not been prescribed to them to manage their eating disorder symptoms. This included medication to control weight (n = 6), stimulants (such as modafinil and amfepramone; n = 4), sedatives (n = 3) and analgesia (such as buprenorphine; n = 1).

In terms of legal psychoactive substances, 52% (n = 104) of respondents had previously used them to help with their eating disorders. Caffeine was the most commonly used legal substance from the list provided. This was followed by alcohol, nicotine and cannabidiol. 13.5% (n = 27) reported using substances to manage their eating disorder in terms of illegal substances. The majority of these participants had a diagnosis of AN (n = 23). Cannabis use was reported as the most frequent, followed by cocaine. Other illegal substances used included ketamine, magic mushroom and stimulants such as ecstasy and speed. See Table 2 for a summary of alternative therapies, legal substances and illegal substances stratified by diagnosis type.

3.4 Perspectives on psychedelic treatment for eating disorders

When asked their perspectives on psychedelic research for eating disorders, participants considered the research moderately valuable, albeit they were also moderately worried about participating (see Table 3 for item descriptions by eating disorder diagnosis). Only 29.5% of respondents (n = 59) felt that they would never participate in a clinical trial using psychedelics.

Exploring their concerns further, nearly three-quarters (74%, n = 146) chose weight gain as a concern that would stop them from participating. This was followed by addiction (61%, n = 121), long term psychological effects (61%, n = 119), negative psychedelics experiences (60%, n = 118), long term physical health effects (55%, n = 107) and side effects (54%, n = 104). However, nearly half of the respondents were not concerned about the potential stigma associated with psychedelics (46%, n = 90). In addition, knowledge on how psychedelics, such as ketamine, have been licensed for other mental health conditions reduced concerns in over half of respondents (54.3%, n = 107).

In terms of how to improve participation in psychedelic research for eating disorders, from the options given, most participants chose a safe monitored environment, in that drugs are given in the presence of a doctor and nurse, with regular monitoring throughout the experience (n = 127).

Table 2. Use of complementary therapies, legal substances and illegal substances by participants for management of their eating disorder. The use of each treatment is stratified by diagnosis.

Response	Type of eating disorder					Total
	AN/atypical	Bulimia nervosa	Binge eating disorder	Other	Multiple diagnoses	
N (%) of group	AN (n = 109)	(n = 19)	(n = 14)	(n = 10)	(n = 48)	(n = 200)
Complementary treatments						
Yoga/pilates	51 (47%)	11 (58%)	6 (43%)	2 (20%)	20 (42%)	90 (45%)
Meditation	36 (33%)	8 (42%)	5 (36%)	1 (10%)	16 (33%)	66 (33%)
Relaxation techniques	35 (32%)	8 (42%)	4 (29%)	3 (30%)	13 (27%)	63 (32%)
Hypnosis	11 (10%)	2 (11%)	2 (14%)	0 (0%)	2 (4%)	17 (9%)
Legal substances						
Caffeine	49 (45%)	11 (58%)	6 (43%)	6 (60%)	23 (48%)	95 (48%)
Alcohol	32 (29%)	8 (42%)	3 (21%)	5 (50%)	14 (29%)	62 (31%)
Nicotine/e-cigarettes	25 (23%)	6 (32%)	4 (29%)	2 (20%)	11 (23%)	48 (24%)
Cannabidiol	9 (8%)	1 (5%)	1 (7%)	0 (0%)	4 (8%)	15 (8%)
Illegal substances						
Cannabis	11 (10%)	0 (0%)	2 (14%)	1 (10%)	5 (10%)	19 (10%)
Cocaine	4 (4%)	0 (0%)	1 (7%)	0 (0%)	2 (4%)	7 (4%)
Ketamine	1 (1%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	3 (2%)
Psilocybin	3 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (2%)
Stimulants	3 (3%)	0 (0%)	1 (7%)	0 (0%)	1 (2%)	5 (3%)

Table 3. Respondents' perspectives of psychedelic research, stratified by type of eating disorder.

Question (response option)	Type of eating disorder					Total
	AN/atypical	Bulimia nervosa	Binge eating disorder	Other	Multiple diagnoses	
	AN (n = 97)	(n = 16)	(n = 9)	(n = 8)	(n = 42)	
How worthwhile do you think it is to conduct research in psychedelic drugs for eating disorder? <i>Score (SD) from 0 "Not at all valuable" to 100 "Very valuable"</i>	65.7 (30.8)	74.3 (31.2)	59.1 (36.2)	52.6 (30.7)	60.6 (34.3)	62.1 (32.6)
How worried would you be about participating in psychedelic research for patients with eating disorder? <i>Score (SD) from 0 "Very worried" to 100 "Not worried at all"</i>	49.7 (34.9)	53.5 (31.5)	65.3 (35)	51.8 (29.1)	46.1 (35.4)	47.7 (35.1)
How likely would you take part in psychedelic research in eating disorder? <i>Score (SD) from 0 "Very unlikely" to 100 "Very likely"</i>	49.1 (36.8)	63.4 (38.6)	37.0 (37.5)	33.4 (31.7)	48.5 (36.9)	48.2 (37.0)

^a A total of 28 participants did not respond to these questions.

Other critical areas of importance include regular follow-up and support from the research team (n = 114), long-term psychological benefit (n = 112), more knowledge about psychedelics (n = 109) and trust in the research team (n = 100).

3.5 Qualitative results

In the analysis of participants' responses, they could be categorized into several broad themes: those that (a) perpetuated their eating disorder symptoms or those that, (b) improved their eating disorder symptoms. Positive influences included lifestyle strategies (e.g., meal planning, getting sufficient sleep, alternative/complementary therapies) and engaging in positive mental health strategies (e.g., engaging with mental health services, distraction, social interaction and reducing work/education stress). Negative influences on eating disorder symptoms included social influences (e.g., dieting culture on social media/television, neg-

ative impacts of others, social comparison, social isolation, arguments with peers), psychological influences (comorbidities, negative self-thoughts, eating disorder-related behaviors, stress) and a lack of self-care (poor sleep and lack of, or over-exercising). When being asked their perspectives on existing treatments, psychological therapy was most frequently mentioned as being the most useful in managing their eating disorders (n = 65). Many participants reported that their current treatment met their needs (n = 45). However, a significant portion of respondents reported openness to try a new treatment to manage their eating disorders (n = 28), indicating support for novel treatments:

"I think everybody responds different to all sorts of treatment for eating disorders. I think it is essential to be open minded in regards to treatment."

"I feel that my ED has ruined my life and made it extremely difficult. Any research into a possible treatment is so welcome and,

as long as the good effects outweigh the bad, I would be more than willing to help with the research. If I can help others too that will feel amazing.”

“Anything that helps, as long as it is safe to do so, should be considered in using to treat eating disorders.”

Participants were asked about their general concerns about research into psychedelic drugs in eating disorders, which produced variable results. Interestingly, only two people raised weight gain as a specific concern, which contrasts with the quantitative data whereby 74% reported this as a concern when presented to them. Fifty-four participants did not have any concerns about this research. However, 14 participants were opposed to psychedelic research in eating disorders. In addition, 32 participants reported concerns over side effects. Other thematic concerns included fear of the drug effects (e.g., on thoughts, adverse events, “bad trips”, dependence, losing control, mental health), stigma (e.g., fear of judgment, perception of the word “psychedelic” as dangerous), skepticism regarding medication and insufficient information on psychedelics. Additionally, a reluctance to participate in the research but a general interest in results was another theme.

We were most interested in the difference between those who expressed minimal concern about research into psychedelics and the group with extreme concerns over this area from the many themes identified. Examples of these contrasting views are below:

“As long as proper ethics processes are followed, I have no worries about the research.”

“Not worried at all. If drugs have been okayed through research, I'd be happy to take.”

“I would worry about safety and risks in medically vulnerable patients.”

“I would be worried about side effects and the feeling of no control.”

Of note, in many responses that reported concerns, potential strategies to address these worries were reported, which may be addressed by a focused research team:

“I think it's so worthwhile to research any possibility because if you can help even a few people to recover then that's worthwhile. Of course, I would be worried because I've never taken any drugs so I have no idea what it would feel like and that would scare me. But, if the medical use of illegal street drugs (like marijuana) becomes more widely accepted in society, this fear will slowly go away and people will be able to see the drugs as medicine rather than something that should be illegal. Also, if I felt I had sufficient medical supervision from doctors that I trusted then I wouldn't be too worried.”

“I would not be concerned as long as I trusted the therapist I was working with.”

“I wouldn't be concerned taking these drugs in a supervised environment when I know safety is assured.”

4. Discussion

To our knowledge, this is the first study examining the views of people with eating disorders on psychedelic drugs as a potential treatment option. Approximately half of the participants reported that they would take part in psychedelic research, which is slightly higher than a similar study assessing patient's views towards psychopharmacology [36]. Over 60% of participants believed that it is a worthwhile research area to pursue, in the context of moderate level of concerns. Specific concerns were evident, as well as strategies for reducing these concerns. Crucially, many participants emphasized the need for a safe, controlled and professional setting during the psychedelic treatment, with trust in the research team/medical professionals emerging as a pivotal solution to concerns. These findings, combined with the poor quality of life and high mortality rate in relation to eating disorders, further highlight the importance of conducting trials examining emerging treatments in this complex patient group.

Empirical findings can alleviate many of the concerns stated by respondents in this survey. For example, over two-thirds of participants reported that weight gain is a concern in the context of psychedelic treatment. This association is likely derived from perceptions of increased appetite with cannabis use [37], whereas loss of appetite is a more likely transient side effect in psychedelic treatment [38]. Comparatively, 90% of participants in a survey assessing views towards psychopharmacological treatment reported concerns about weight gain [36]. This may be problematic for using some psychiatric medications, as some are associated with increases in appetite and weight gain (e.g., antipsychotics). In addition, the addictive potential of these substances and their effects on long-term physical health was an additional concern. However, psychedelics produce little, if any, dependence and have effectively treated substance use disorder in many cases [39]. Similarly, no long-term physical adverse effects have been reported, with adverse reactions such as increases in blood pressure and heart rate, gastrointestinal discomfort, anxiety and psychotic-like symptoms being transient, resolving after the cessation of the substance [25]. However, regarding ketamine specifically, some are concerned that it may be addictive and that some physical side effects such as ulcerative cystitis can occur [40]. Therefore, for substances that have specific concerns, additional monitoring to ensure participant safety would be necessary.

Unsurprisingly, participants reported concern regarding adverse side effects and negative psychedelic experiences (i.e., “bad trips”). Our patient group reports many concerns that are also shared by the general population. Only 1–2% of the general population have experienced psychedelic drugs recreationally [41].

However, there is an overrepresentation of people with prior experience of psychedelic drugs in clinical trials [42, 43], likely due to people feeling more comfortable to engage in the treatment if they already have some experience of it. Although there are limitations regarding recruitment bias

which will be later discussed, the population is comparable to the general population of previous psychedelic use (ketamine 2%, psilocybin 2%). This makes the group's reflections particular interest as it may be closer to the general population's views. A recent systematic review on the safety profile of common psychedelic treatments concluded that those administered in a clinical context have a good tolerability and safety profile [25]. Ayahuasca specifically has adverse reactions associated with administration in both ritual and clinical contexts, such as nausea, vomiting and diarrhea. However, these are considered by many to be integral to the therapeutic process [44]. In addition, individuals often experience transient anxiety and psychotic-like symptoms, but these effects are generally associated with the drug being administered in an unfavorable and uncontrolled context [21, 45]. The "set" and "setting" are crucial for avoiding unpleasant experiences, and this can be mitigated by the use of compassionate "guides" to accompany patients in trials [21], as well as a therapeutic alliance [46] and an appropriate environmental context. In terms of "set", a low readiness for the experience, no clear intention for it and low trust in the individuals accompanying participants is predictive of a "bad trip" [21]. Furthermore, it has been recommended that individuals with a personal or family history of psychosis be excluded from psychedelic research. Certain groups could be at more risk of adverse outcomes [25].

Hence, some of the solutions to these concerns proposed by the respondents included education regarding the effects of psychedelics and how they are used within psychiatry and being informed that professionals in the area endorse their use. Concurrently, informing participants of esketamine's licensing for the treatment of depression reduced concerns in half of the group, suggesting that increasing awareness about psychedelics as a treatment will be a valuable avenue to explore in reducing concerns about experimental medication. Presumably, underlying these solutions is the need to address the stigma associated with psychedelics, which is prevalent [47]. Similarly, their possible benefits over conventional treatment should be considered; standard pharmacological treatment involves patients taking medication daily for several years, whereas it is commonly found that psychedelic treatment is effective after a single dose, which is maintained for several weeks or months [25]. Patients may not be aware of psychedelic drugs' potential benefits, so highlighting this may help them make a more balanced decision about participation. Our findings suggest a pivotal role for the research team in supporting participants to become involved in psychedelics research. For example, co-developing information packs about psychedelics with patients who have previously received psychedelic treatment would address some of the concerns raised. Other essential design elements include the presence of medical professionals during psychedelic administration and building rapport and trust with the participants. A clinical trial co-designed with patients would potentially aid recruitment and retention. This is of great impor-

tance given the high drop-out rates observed in psychopharmacology trials in eating disorders [48].

In addition, participants expressed a high level of perceived difficulties associated with eating disorders. The plethora of positive and negative views about medication, psychological therapy and alternative treatment supports the idea that treatment for eating disorders must be personalized and tailored to the individual. No one treatment is effective for all. Indeed, a third of participants stated that they would never participate in psychedelic research. As aforementioned, the "set", or mindset entering the experience, of individuals is a crucial determinant of the psychedelic experiences [49]. This highlights the importance of the views of participants taking part in psychedelic research. Furthermore, evidence suggests that personality factors such as neuroticism are associated with challenging experiences during psilocybin dosing, emphasizing the importance of the "set" [50]. Therefore, participants in psychedelic research should therefore be carefully assessed for their suitability, based on these psychological factors and physiological factors.

4.1 Future directions

For future research, essential questions to be answered before psychedelics may be applied in well-defined groups of patients with eating disorders: (a) what are the most relevant outcome parameters for psychedelic treatment? (b) what are the framework conditions for its application? and (c) which safety measures must be in place?

The Core Outcome Measures in Effectiveness Trials (COMET) initiative [51] confirms that BMI is the established primary outcome measure in clinical effectiveness trials in AN. In contrast, for bulimia nervosa and binge eating disorder, the specific eating disorder psychopathology is the primary outcome. Secondary outcomes for clinical trials in eating disorders include anxiety, depression, bipolar disorder, suicidality and sleep problems [52, 53]. Therefore, PROMs and PREMs should be included in the outcome criteria for RCTs of psychedelic substances. PROMs and PREMs assess the effectiveness, safety, and experience of care from a patient's perspective. They have already been developed within the the United Kingdom (UK) NHS, for specific elective procedures [54]. An example of a PROM/PREM currently used in psychiatry is the DIALOG tool used in community mental health teams. Patients are asked to rate their satisfaction with different areas of their life [55]. However, there are currently no PROMs or PREMs for the psychopharmacological treatment of AN. If the main outcome criteria of an RCT were to include PROMs and PREMs such as anxiety and depression, the RCT would be of benefit from a patient's perspective and might improve their willingness to participate in the trial [10]. Thus, the development of PROMs and PREMs could be the next step in allowing patients to inform and shape the development of psychedelic treatment in eating disorders.

Concerning the setting in which psychedelic drugs are applied, treatment for eating disorders needs to be in contact with, or provided by, multidisciplinary specialist services and

involve psychotherapy, diet counseling and physical health monitoring [5]. Psychedelic therapy has been found to harness a therapeutic window opened up by the brain via the effects of the drugs to facilitate insight and emotional release [56]. Thus, its most sensible use may be to assist with psychotherapy. Recent work [57] of MDMA-assisted psychotherapy for treating eating disorders with comorbid post-traumatic stress disorder showed promising results. Additionally, psychedelic drugs might benefit from music as it plays a central therapeutic function in psychedelic therapy [58].

There are specific risks associated with different psychedelic drugs, including “bad trips”, dissociation, and suicidal ideation [21, 59]. Therefore, in addition to the usual physical monitoring of patients and using a broad general side effect scale, instruments to monitor specific hazards tailored to the particular drug must be applied.

4.2 Limitations

There are several limitations to the present survey study. Regarding the sample achieved, there is a possibility of bias due to the recruitment methods. Given the survey’s online nature, it may not have reached groups without regular social media or internet use. Furthermore, individuals with extreme views may have been more likely to complete the survey and thus be included in the results. We advertised the survey on social media platforms that are likely to have an interest in eating disorders and psychedelic drugs, introducing a recruitment bias and influencing the results. It was also noticed after the survey period that some of the questions involving visual analog scales may not have been laid out in the most intuitive format, although they were labeled clearly.

Although participants were provided with some explanation of the term “esketamine” it is possible that participants may have misinterpreted or held misconceptions about the term “psychedelic drugs”. However this is still of importance as the preconceptions of the group are of interest. Therefore, this is an area that we feel should be further studied.

While the demographic and diagnostic variation achieved reflects the patient group well [60], most respondents were female, and an exceptionally high level of education was reported. Similarly, AN was the most common diagnosis, with a high level of comorbidity with anxiety and depression. Thus, the sample may not represent all eating disorder diagnoses and genders and may be confounded by the presence of other psychiatric disorders. Nevertheless, this patient group is one of great complexity and comorbidities are common. However, we did not ask participants about the severity of their disorder, which could have been helpful when interpreting the results, although illness duration was collected.

As the survey was conducted during the COVID-19 pandemic there may be a possibility that respondents were under a great mental health strain and thus are more eager for treatment. It may also have affected their answers to the BIPS section of the survey. Finally, due to ethical requirements, participants who dropped out of the survey prematurely could

not be analyzed, thus adding a potential bias to the results.

5. Conclusions

In summary, this study provided evidence of support in the eating disorder community for research into psychedelics. Many concerns need to be addressed, but participants in the web survey support research into this area. Co-designing the survey with patients, providing comprehensive information about psychedelics before enrollment, and conducting the trial in a controlled and medically supervised environment would encourage participation and aid retention in this complex patient group.

Abbreviations

AN, anorexia nervosa; BEAT, the UK eating disorder charity; BIPS, Brief Illness Perception Scale; BMI, body mass index; CBT, Cognitive Behavioral Therapy; COMET, Core Outcome Measures in Effectiveness Trials; DMT, dimethyl-tryptamine; EDNOS, eating disorder not otherwise specified; FPT, eating-disorder-focused focal psychodynamic therapy; MANTRA, Maudsley Model of Anorexia Nervosa Treatment for Adults; NHS, National Health Service; OCD, obsessive-compulsive disorder; OSFED, otherwise specified feeding and eating disorder; PREMs, patient-reported experience measures; PROMs, patient-reported outcome measures; RCTs, randomized controlled trials; SSCM, specialist supportive clinical management.

Author contributions

FH, MS and CK designed and performed the research. JT and CK provided advice on the survey design. FH, MS, JK and CK analyzed the data. FH and JK wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This research received ethical approval from the King’s College London Ethics Committee [ethics number: HR-19/20-14805].

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Conflict of interest

The authors declare no conflict of interest.

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