

Patient perceptions of lisdexamfetamine as a treatment for binge eating disorder: An exploratory qualitative and quantitative analysis[☆]

Abanoub J. Armanious^{a,b}, Audrey Asare^{a,b}, Deborah Mitchison^c, Morgan H. James^{a,b,d,e,*}

^a Department of Psychiatry, Robert Wood Johnson Medical School, Rutgers University, Piscataway, NJ, 08854, USA

^b Rutgers Addiction Research Center, Brain Health Institute, Rutgers Health, Piscataway, NJ, 08854, USA

^c Discipline of Clinical Psychology, Graduate School of Health, University of Technology Sydney, Sydney, NSW, Australia

^d School of Psychology, Faculty of Science, University of Sydney, Sydney, NSW, Australia

^e Brain and Mind Centre, University of Sydney, Sydney, NSW, Australia

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ABSTRACT

Lisdexamfetamine (LDX) is the only medication to have gained FDA approval for the treatment of binge eating disorder (BED). LDX treatment is generally effective at reducing binge eating symptoms but is associated with several unwanted side effects. How BED patients perceive the therapeutic efficacy vs. associated side effects of LDX has not been explored. We carried out a thematic analysis of 111 online reviews posted to the website Drugs.com by persons prescribed LDX to treat BED. We also explored how qualitative themes were associated with perceptions of treatment efficacy on a quantitative (1–10 scale) scale. Themes associated with higher efficacy ratings included improved binge eating outcomes, enhanced focus/concentration, as well as weight loss (χ^2 tests, p 's < 0.05). Lower efficacy ratings were associated with themes that included tolerance to therapeutic effects of LDX, insomnia, return of binge eating in the evening, loss of energy in the afternoon/evening ('crashing'), and weight gain (χ^2 tests, p 's < 0.05). Limitations of the study include representativeness of the data and self-reported BED diagnosis. Together, these data provide novel insights into individual experiences with LDX as a treatment for BED and their association with perceived efficacy. The causal nature of these relationships should be tested in future studies, as well as any implications for medication adherence.

1. Introduction

Binge eating disorder (BED) has an estimated lifetime prevalence of 0.8–3.0% (Galmiche et al., 2019; Keski-Rahkonen, 2021; Udo and Grilo, 2018) and in 2019 accounted for 0.8 million disability-adjusted life years (DALYs) globally (Citrome, 2019; Santomauro et al., 2021). BED is defined by the *Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5)* as recurrent episodes of binge eating in the absence of compensatory behaviors and an accompanying sense of lack of control over eating (American Psychiatric et al., 2013). BED is associated with depression and anxiety, as well as obesity-related health conditions including Type 2 diabetes and insomnia, underscoring the importance of effective clinical interventions to treat BED (Yu and Muehleman, 2023). Moreover, the prevalence of BED across diverse body sizes emphasizes the significance of addressing this disorder beyond obesity alone (Kessler et al., 2013). In 2015, the United States Food and Drug

Administration (FDA) approved lisdexamfetamine dimesylate (marketed as 'Vyvanse®') for the treatment of moderate to severe BED in adult patients, making it the first (and only) medication specifically approved for BED. When taken orally, LDX is hydrolyzed in the blood to d-amphetamine, which readily crosses the blood-brain-barrier to increase central dopaminergic, noradrenergic and serotonergic transmission (Heal et al., 2013). Originally developed and approved for the treatment of ADHD in 2007, LDX was approved for BED based on a series of phase II and III clinical trials that collectively indicated that LDX reduced the number of binge eating episodes per week and improved several other clinical outcomes, including scores on scales that assess the behavioral, affective, and attitudinal components of binge eating (Hudson et al., 2017; McElroy et al., 2016a; McElroy et al., 2015). LDX is used both as a standalone treatment and as an adjunct to psychological interventions for BED (Guerdjikova et al., 2016).

Several studies support the overall efficacy of LDX for treating binge

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* Corresponding author. Office 164, 683 Hoes Ln West, SPH Building Piscataway, NJ, 08854, USA.

E-mail address: morgan.james@rutgers.edu (M.H. James).

eating symptomatology, particularly at higher doses (50–70 mg/d) (Citrome, 2015; Guerdjikova et al., 2016; McElroy et al., 2017; McElroy et al., 2016b). Like other stimulant medications, LDX is associated with a range of side effects, including dry mouth, insomnia, sleep disturbances, jitteriness, and upper respiratory tract infections (Adler et al., 2008; Fornaro et al., 2016; Wigal et al., 2010). In clinical trials, almost all (~85%) patients report at least one treatment emergent adverse event (TEAE) associated with LDX treatment, with some side effects (e.g. sleep disorder) being more prevalent at higher doses (McElroy et al., 2016a; McElroy et al., 2015). Moreover, although LDX has less abuse liability compared to other stimulants, high (non-approved) doses have similar likeability to d-amphetamine and other controlled substances, indicating a risk of abuse (Heal et al., 2013; Jasinski and Krishnan, 2009a, 2009b; Panagiotou et al., 2011). Despite these known unwanted outcomes associated with LDX treatment, to date there have been no published data about the subjective experiences of BED patients prescribed LDX and how these might shape their overall perception of LDX as a treatment and its efficacy. Understanding patients' perspectives of and experiences with specific medications in their own words is an important endeavor, as quantitative measures are constrained by the *a priori* hypotheses of researchers and may consequently miss important aspects of drug effects and patient adherence.

To this end, we conducted a qualitative analysis of patient attitudes towards LDX, with a focus on perceptions of treatment outcomes and associated side effects. To do this, we employed a thematic analysis approach to analyze anonymous reviews of LDX by self-identified BED patients posted to [Drugs.com](https://www.drugs.com), the largest, most-widely visited, independent drug information website on the internet ([Drugs.com](https://www.drugs.com), 2023). In addition to allowing patients to submit a qualitative review of medications, the site also allows respondents to submit a quantitative rating (scale 1–10) of LDX's efficacy; we thus explored how these ratings were related to qualitative themes. These exploratory analyses were expected to reveal novel, patient-centered insights relating to LDX as a medication for BED. These outcomes are important for guiding future hypothesis-driven research focused on improving treatment outcomes in BED patients.

2. Methods

2.1. Data collection - [Drugs.com](https://www.drugs.com) as a source

Patient reviews of LDX for BED on [Drugs.com](https://www.drugs.com) were included for analysis. [Drugs.com](https://www.drugs.com) is a free online source of drug information, which comprises peer-reviewed and independent data on over 24,000 prescription drugs, over-the-counter medicines & natural products (as of July 2023). Drug information is derived from several independent, leading medical-information suppliers, including the American Society of Health-System Pharmacists, Cerner Multum™, IBM Watson Micromedex, as well as the Food and Drug Administration ([Drugs.com](https://www.drugs.com), 2023). In addition to general information on medicines and products, [Drugs.com](https://www.drugs.com) allows individuals to submit a review of their experience with specific medications, including LDX. The clickstream to submit a review for LDX is as follows: [Drugs.com](https://www.drugs.com) > "Lisdexamfetamine" or "Vyvanse" > User Reviews & Ratings > Add your review. Respondents are first prompted to select the condition for which LDX was prescribed to them (e.g. BED, ADHD, etc) and to input a display name (respondents are instructed to avoid personal information, and to avoid using their full name or social media username). Patients are then prompted to "comment on your experience with LDX" and are encouraged to "describe how the medication helped (or why it didn't work); the benefits, side effects, dosage, ease of use" in a single text box. Patients can also rate the drug's efficacy on a scale of 1 (not effective) to 10 (most effective), input duration of medication use, as well as indicate whether insurance covered the drug and the out-of-pocket monthly cost incurred. The website administrators audit reviews and those that appear to be created by parties with a vested interest are not published. Users can also

report reviews they deem inaccurate, irrelevant, or potentially harmful because of their suspicious content.

Data were downloaded in October 2022. No retrospective time limit on reviews was imposed; the oldest review was from April 2015 and the most recent from May 2022. User reviews for both LDX and Vyvanse in which BED was listed as the primary indication were extracted, resulting in a total of 111 reviews.

2.2. Thematic data analysis

Reviews were imported into NVivo 14 software (Lumivero) which was used to assist with data analysis. The collected data were analyzed using a thematic analysis approach, as previously described (Braun and Clarke, 2006). Within this highly iterative framework, themes are generated from the collected data by reading, suggesting themes, re-reading, and comparing categories generated in several cycles of analysis. Two coders (AJA, AA) independently read the same 15 randomly selected user reviews at a time; excerpts relevant to the experimental question were coded and labeled according to a data-driven 'bottom-up' principle, thus avoiding any preconceived ideas that the reviewers may have had about patient perceptions of LDX. Some extracts were assigned multiple codes if deemed appropriate. After each set of 15 reviews, both coders met with a third-party noncoder (MHJ) to compare identified codes against the original data and each other, as well as to ensure that they were coherent, consistent, and distinctive. The process was predominantly inductive, in that the codes identified were strongly linked to the data themselves, and therefore were data driven. Also, the codes were semantic, in that they were identified within the explicit or surface meanings of the data, and the researcher did not attempt to infer anything beyond what a patient had written. This process was repeated until the point of thematic saturation, or where all three investigators agreed that further analysis was unlikely to result in additional unique codes. The initial round of analysis yielded 36 separate coding categories; these were then grouped into 7 main themes that related to patient perceptions of treatment outcomes associated with LDX. There were no predefined criteria for determining what would constitute a separate theme, rather, meaningful clusters of codes were identified, reviewed, and refined. Illustrative quotes were then selected to reflect and contextualize each theme.

Recognition must be made regarding the position and biases of each author and potential influences on identifying codes and meta-themes. At the time of coding, AJA (male) and AA (female) were undergraduate students, majoring in public health (AJA and AA) and cell biology and neuroscience (AJA), and were conducting laboratory research on the neurobiological basis of eating disorders. MHJ (male) is a researcher with expertise in neuroscience of motivation, including feeding, and psychiatric conditions more generally. The interpretations of the data by all three coders were likely influenced by their worldviews which included a thorough understanding of preclinical models of eating disorders and the neurobiological underpinnings of feeding, as well as the general literature on BED.

2.3. Quantitative analysis of user reviews

Of the 90 reviews that were analyzed prior to reaching thematic saturation (see Section 3.1), 89 users provided a rating LDX's efficacy on the 1–10 scale. We were interested in understanding how these scores might be associated with the qualitative themes identified via thematic analysis. Thus, we calculated the median rating score of participants whose reviews contributed to each theme; these median scores and associated median absolute deviation (MAD) values are presented alongside each of the subthemes in the *Results* section. We were also interested in whether some qualitative themes were associated with higher vs. lower efficacy ratings of LDX. To explore this, we split the data to create two groups either side of the median score (9); based on a frequency histogram of rating scores, this reflected a natural separation

of ‘higher ratings’ (n = 53) and ‘lower ratings’ (n = 36). We then plotted the frequency with which each subtheme was represented in each group, expressed as a proportion of all responses in that group. For the purposes of visualization, each subtheme was organized into ‘positive’ (e.g. reduced binge eating), ‘neutral’ (e.g. no side effects), or ‘negative’ (e.g. worsening of anxiety and depression symptoms) valance categories. We compared the frequency with which each subtheme was represented in respondents who gave ‘higher ratings’ vs. ‘lower ratings’ of efficacy using separate χ^2 tests (two-sided); a type-1 error rate of 0.05 was adopted for all analyses. A post-hoc power calculation indicated we achieved ~81% for detecting a medium effect size (0.3) between groups.

3. Results

3.1. Thematic analysis

Thematic saturation was reached after 90 reviews were analyzed. Seven major themes emerged from these analyses, each relating to patient outcomes and perceptions associated with LDX. For the majority of these, patient responses fell on a spectrum; that is, some patients reported a positive outcome, others reported a negative outcome (e.g. reduced vs. increased binge eating), and others indicated no change. In these cases, themes were organized into subthemes to highlight positive, negative, and neutral viewpoints. Below, we provide a description of each of the themes, including representative verbatim examples. For each subtheme, we also report the median (Mdn) score (1–10 scale) and median absolute deviation (MAD) of all participants who contributed to that theme.

3.1.1. Theme 1: binge eating and general appetite

Unsurprisingly, the majority of respondents made reference to the efficacy of LDX as a medication to reduce binge eating episodes. Many reviews indicated that LDX resulted in general appetite suppression rather than specifically reducing binge eating, *per se*. Overall, the majority of respondents (62%) indicated a perceived improvement in binge eating, food cravings, and general appetite (see Table 1; Subtheme 1a). The median efficacy rating of respondents in this theme was 10.0 (out of

10; MAD = 0.0). A smaller number of respondents (n = 8) reported that LDX had no effect on their binge eating (Subtheme 1b), which was associated with a lower median efficacy rating (Mdn = 4.5, MAD = 3.5). Interestingly, several respondents (n = 8) specifically indicated that LDX was ineffective at reducing binge episodes that occurred in the afternoon or evening, and in some cases increased propensity for bingeing later in the day when the medication wore off, making it challenging to identify the optimal time of day to take the medication (Subtheme 1c; Mdn = 7.5, MAD = 1.5). Finally, quite a few respondents (n = 19) indicated that although LDX was initially effective at reducing bingeing/appetite, its efficacy waned with prolonged use (Subtheme 1d; Mdn = 7.0, MAD = 2.0).

3.1.2. Theme 2: body weight

Many users also commented on their experience with weight loss associated with LDX treatment. This is notable, as LDX is specifically indicated for BED and has not been evaluated as a treatment to promote weight loss. Many users (n = 36) reported that they had experienced weight loss as a result of taking LDX (see Table 2; Subtheme 2a), and this theme was associated with high overall ratings (Mdn = 10.0, MAD = 0.0). A small number of respondents (n = 3) indicated that taking LDX had no effect on their weight (Subtheme 2b; Mdn = 10.0, MAD = 0.0), whereas a similarly small group (n = 3) indicated that they gained weight while taking LDX (Subtheme 2c; Mdn = 6.0, MAD = 2.0). Notably, the effect of LDX on body weight was not mentioned by approximately half (n = 48) of respondents.

3.1.3. Theme 3: sleep and energy levels

Several respondents (n = 11) indicated that they had trouble sleeping while taking LDX (see Table 3; Subtheme 3a; Mdn = 7.0, MAD = 2.0). Others (n = 6) reported that taking LDX in the morning (as directed) is associated with a loss of energy in the afternoon – a phenomenon that several users referred to as ‘crashing’ or ‘the Vyvanse crash,’ which was associated with lower overall ratings (Subtheme 3b; Mdn = 5.5, MAD = 2.5). Finally, some users (n = 4) indicated improved sleep outcomes while taking LDX (Subtheme 3c; Mdn = 8.0, MAD = 2.0) and several respondents (n = 13) indicated a general increase in overall

Table 1
Representative quotes for the Theme 1: “Binge eating and general appetite”.

Subtheme	n	Median (MAD) Efficacy Rating (0–10)	Examples of review comments
1a. Reduced bingeing/appetite	56	10.0 (0.0)	It is such a relief to not have to battle with food thoughts, cravings and compulsions! Food is no longer the first thing on my mind in the morning nor the last thing on my mind before I go to bed [Rating 10] Taking Vyvanse 50 mg helps me to never even think about food and plan binge evenings and weekends. In fact, I never want to eat large or small quantities of really bad foods at all anymore [Rating 10] The biggest thing for me is that I no longer obsess over food. I would think about food all day long and all night until I managed to fall asleep. I never knew what hunger truly was because I always used food to control my emotions. Vyvanse controls the compulsions and obsessions I once had over food [Rating 9] I can still eat, but I can't binge at ALL. Even if I am very stressed/bored and I emotionally feel like I want a binge, it's almost like Vyvanse is blocking my consciousness from entering that state [Rating 9] lifts the mental fog that usually clouds my judgement and leads to a binge, helps me understand my body's 'I'm full' cues [Rating 10] it did not suppress my appetite and it remained the same [Rating 3] It fails to address my main concern, the binges [Rating 3] I barely have an appetite but I always do late at night I guess when it wears off [Rating 8] Increases restriction and when it wears off, bingeing comes back. [Rating 1] If I took it too early, it wore off. I'd crash or cravings came roaring back at night (my worst time) [Rating 8] Some people find it actually makes eating issues more pronounced because when the effects wear off in the evening you end up stuffing your face [Rating 7] Unfortunately at almost 3 months in, I am having more urges to binge again [Rating 7] my medication worked less and less each year [Rating 6] the bingeing was starting to come back in phases [Rating 3] I noticed after two or so weeks the effects stop working [Rating 9] The medication did work at first to stop binges. At 30 mg, the starting dosage, it did not do anything. A week later at 50 mg, I had very little of an appetite for three days. After five days at 50 mg. I was binge free, but the binges started on the sixth day and continued until my doctor increase to 70 mg. I was binge free about five to 6 days at 70 mg, but then they started again and have continued [Rating 3] Doctor said I can increase my dose (I'm at 40 mg) but what happens when I get to the max dosage and my body gets used to that?? [Rating 8]
1b. No change in bingeing/appetite	8	4.5 (3.5)	
1c. Return of binge eating in evening	8	7.5 (1.5)	
1d. Reduced efficacy with prolonged use (tolerance)	19	7.0 (2.0)	

Table 2

Representative quotes for the Theme 2 “Body weight”.

Subtheme	n	Median (MAD) Efficacy Rating (0–10)	Examples of review comments
2a. Weight loss associated with LDX	36	10.0 (0.0)	I was able to lose 17lbs and plan on losing more [Rating 10] I've lost 24 pounds and plan to lose more [Rating 7] allows me to be in a calorie deficit and therefore LOSE WEIGHT [Rating 10]
2b. No change in weight associated with LDX	3	10.0 (0.0)	I didn't lose any weight [Rating 2] I would like to loose another 10 pounds, putting my BMI in the normal range, but have not restricted my calories, so (duh) no weight loss yet [Rating 10]
2c. Weight gain associated with LDX treatment	3	6.0 (2.0)	Every single time I tried it I ended up gaining weight. I know that many people do not have this experience, but for me, every time I've been on vyvanse I've gained weight ... even when exercising regularly and eating healthy [Rating 1]

energy associated with LDX treatment (Subtheme 3d: Mdn = 9.0, MAD = 1.0).

3.1.4. Theme 4: other physiological side effects

Many users (n = 24) reported that LDX was associated with a range of physiological side effects beyond sleep disturbances: dry mouth was by far the most common, along with increased blood pressure and increased frequency of headaches. Some users indicated that the side effects occurred with doses below the maximum approved dose of 70 mg/d (see Table 4; Subtheme 4a: Mdn = 9.0, MAD = 1.0). Others (n = 7) indicated that they did not experience unpleasant side effects, or that any initial side effects dissipated with ongoing treatment (Subtheme 4b; Mdn = 9.0; MAD = 1.0). Surprisingly, median reported efficacy scores for Subthemes 4a and 4b were identical.

3.1.5. Theme 5: psychiatric functioning

Many users indicated comorbidity of BED with a range of psychiatric conditions, most commonly depression, anxiety, and ADHD. A large proportion of the sample (n = 22) indicated that LDX increased anxiety and worsened their mood and overall productivity (see Table 5; Subtheme 5a: Mdn = 8.0, MAD = 2.0). Some respondents (n = 11) reported improvements in mood and anxiety (Subtheme 5b: Mdn = 10.0, MAD = 0.0). Consistent with the known efficacy of LDX as a treatment for attention deficit disorders, many users (n = 35) reported that LDX improved overall focus and attention (Subtheme 5c), which was interestingly associated with high median efficacy ratings with low variability (Mdn = 10.0, MAD = 0.0).

3.1.6. Theme 6: intention to discontinue medication

A substantial number of respondents (n = 15) indicated a strong desire to discontinue LDX treatment. Among these, many cited concerns with becoming dependent on LDX and identified a self-perceived risk of

abusing the medication (see Table 6; Subtheme 6a: Mdn = 8.0, MAD = 2.0). Some respondents (n = 6) indicated that the cost of LDX represents a barrier to treatment (Subtheme 6b; overall efficacy: Mdn = 8.5, MAD = 1.5).

3.1.7. Theme 7: LDX as an adjunct to psychotherapy

Several users (n = 6) commented on the need for a treatment plan that combines LDX with psychotherapy. Implicit in this is the notion that optimal outcomes cannot be achieved with a medication-based approach alone (see Table 7; Theme 7: Mdn = 7.5, MAD = 2.0).

3.2. Identification of themes contributing to higher vs. lower ratings of perceived LDX efficacy

Across the 89 participants who provided a quantitative rating of their perceived efficacy of LDX, the average rating was 7.89 out of 10 (SD = 2.76). Because the overall average of all 111 reviews available on the website was 7.9, we were confident that our sample of reviews used for thematic analysis was representative of all user reviews. Among the quantitative ratings analyzed, the most frequent rating was 10 (n = 37), followed by 9 (n = 16), indicating that a majority of the sample (59.6%) gave very high ratings of perceived efficacy (see Fig. 1a). The remaining respondents (n = 36; 40.4%) provided efficacy ratings between 1 and 8; among these ratings, the most frequent rating was 7 (n = 10), followed by 8 (n = 8), and then 3 and 1 (n = 5 each). Based on this distribution of ratings, we separated the data into two groups: ‘higher ratings’ (efficacy scores 9 or 10; n = 53) and ‘lower ratings’ (efficacy scores 1–8; n = 36; Fig. 1a).

To understand which qualitative subthemes might contribute to higher vs. lower quantitative ratings of LDX's efficacy, we used χ^2 tests to compare the frequency with which each subtheme was represented among ‘higher ratings’ vs. ‘lower ratings’ (Fig. 1b). Unsurprisingly,

Table 3

Representative quotes for the Theme 3 “Sleep and energy levels”.

Subtheme	n	Median (MAD) Efficacy Rating (0–10)	Examples of review comments
3a. Insomnia	11	7.0 (2.0)	I've been on this medication already and stopped taking it because of the trouble sleeping. It's a catch 22 because my bingeing happens at night. Taking the meds at night keeps me up [Rating 7] if you take to late in the day you won't be able to sleep [Rating 5] it has prevented me from sleeping at night for 4 nights straight. Scary [Rating 8]
3b. Loss of energy, particularly in the afternoon ('crashing')	6	5.5 (2.5)	I was crashing pretty early and couldn't function later in the day, so I started taking it at noon and incorporated a small coffee in the morning to get me by until noon and I haven't crashed since [Rating 9] I felt the Vyvanse crash (extremely fatigued, angry, hopeless, and “blah”) every day once I started moving up in dose (above 20 mg) [Rating 3] pretty severe crashes mid afternoon [Rating 8] I lost all my energy [Rating 3]
3c. Improvements in sleep or no change	4	8.0 (2.0)	The only thing I miss about the medication is that I've had some of the best sleep in my life on it [Rating 1] No more do I feel like I'm more tired after sleeping when I take this pill [Rating 10] I was prescribed 70 mg Vyvanse and had no problems from day 1. No problems falling asleep [Rating 10]
3d. General increase in energy	13	9.0 (1.0)	It gave me lots of energy [Rating 10] have energy and completely have increased my energy [Rating 10] My thoughts on the medication are that it gives me a much needed boost of energy [Rating 9]

Table 4
Representative quotes for the Theme 4 “Other physiological side effects”.

Subtheme	n	Median (MAD) Efficacy Rating (0–10)	Examples of review comments
4a. Physiological side effects	24	9.0 (1.0)	Only side effect is dry mouth [Rating 9] After about an hour I was cold and sweaty, I couldn't control what was coming out of my mouth, I fit 4–5 sentences into one breath I was talking so fast. My heart rate was 92 a minute, when I later checked after coming down it was 62 a minute [Rating 5] Honestly it was hard at first - it made me feel sedated and tired, and I had headaches and dry mouth [Rating 10] back acne (never had acne before starting) you have to make your self eat and drink, headaches at the end of the day, dry mouth [Rating 5] Side effects: FREEZING COLD HANDS [Rating 10] Final straw after taking 40 mg (which I'd taken before) my BP shot up to 168/103. This scared me as it did not show signs of coming down. I was so scared it would continue to increase I even drove myself to sit outside the emergency department just in case. That whole afternoon it kept spiking to a very high blood pressure. [Rating 1] It does significantly raise my blood pressure and bp, unfortunately [Rating 9] I have no heart racing, No problem with anxiety, no jitters [Rating 10] I don't get the jitters, nausea, and crashes that I did before, so don't necessarily let negative experiences with stimulants deter you [Rating 9] No stomach upset, no headaches, actually no side effects yet, other than the good ones! [Rating 10] I don't experience a crash [Rating 9]
4b. Absence of physiological side effects	7	9.0 (1.0)	

positively-valenced themes were overrepresented among higher vs. lower raters; the most prevalent were ‘reduced binge eating’ (Subtheme 1a; 81.1% vs. 36.1%; χ^2 [1, n = 89] = 18.62, $p < 0.0001$), ‘weight loss’ (Subtheme 2a; 50.9% vs. 22.2%; χ^2 [1, n = 89] = 7.41, $p = 0.0065$), and ‘improved focus and attention’ (Subtheme 5c; 52.8% vs. 19.4%; χ^2 [1, n = 89] = 10.01, $p = 0.0016$). The most prevalent negatively-valenced theme associated with higher efficacy ratings was ‘physiological side effects’; this occurred at a similar frequency compared to those who provided lower ratings (Subtheme 4a; 26.4% vs. 27.8%, $p = 0.8869$). Among the lower ratings group, there were several negatively-valenced subthemes that were overrepresented compared to the higher ratings group; the most frequent subtheme was ‘reduced efficacy with prolonged use (tolerance)’ (Subtheme 1d), with this theme being mentioned in almost half of lower rated reviews (44.4% vs. 5.7%; χ^2 [1, n = 89] = 19.21, $p < 0.0001$). Other negative themes associated with lower vs. higher efficacy ratings were ‘insomnia’ (Subtheme 3a; 22.2% vs. 5.7%; χ^2 [1, n = 89] = 5.43, $p = 0.0198$), ‘return of binge eating at night’ (Subtheme 1c; 16.7% vs. 3.8%; χ^2 [1, n = 89] = 4.36, $p = 0.0369$), ‘no change in binge eating/appetite’ (Subtheme 1b; 16.7% vs. 3.8%; χ^2 [1, n = 89] = 4.36, $p = 0.0369$), ‘weight gain associated with LDX treatment’ (Subtheme 2c; 8.3% vs. 0.0%; χ^2 [1, n = 89] = 4.57, $p = 0.0325$), and

‘loss of energy, particularly in the afternoon (crashing)’ (Subtheme 3b; 13.9% vs. 1.9%; χ^2 [1, n = 89] = 4.91, $p = 0.0267$). There was a higher representation of the ‘worsening of anxiety and depression’ (Subtheme 5a; 33.3% vs. 18.9%) and ‘desire to discontinue treatment’ (Subtheme 6a; 25.0% vs. 11.3%) subthemes among lower vs. higher raters, however these failed to reach statistical significance (p 's > 0.05).

4. Discussion

LDX is the only approved medication for the treatment of BED. Clinical trial data indicates that LDX is most effective at higher doses that may be associated with more frequent and/or severe side effects (McElroy et al., 2016a; McElroy et al., 2017; McElroy et al., 2015). To date, there have been no published studies that we are aware of that qualitatively assess subjective experiences of BED patients treated with LDX (although see discussion below on a recent qualitative assessment of LDX for the treatment of bulimia nervosa). As part of the study, we explored subjective experiences with a (self-identified) patient-centered approach using a thematic analysis of user reviews of LDX on the website [Drugs.com](https://www.drugs.com). This analysis revealed seven major themes that users highlighted as being central to their experience with LDX as a medication: (1)

Table 5
Representative quotes for the Theme 5 “Psychiatric functioning”.

Subtheme	n	Median (MAD) Efficacy Rating (0–10)	Examples of review comments
5a. Worsening of anxiety, depression	22	8.0 (2.0)	For About A Week Now I am feeling very anxious all The time [Rating 10] I took it for several days two separate times but was anxious as anything, mind racing, sleepless so I stopped. [Rating 4] I started yelling a lot & having random fits of rage I would feel extremely depressed & unhappy tired & aggravated [Rating 3] The only emotion I really feel right now is frustration because I know other people are able to feel things but now I [am] incapable of that. I am a very empathetic and warm person. But now I feel so cold and unavailable. Even my boyfriend of 2+ years just annoys me with his affection [Rating 2] I've been taking it almost 8 years now and my productivity has diminished greatly [Rating 6] This medicine is noting to mess with its very powerful and can change your entire personality while on this medicine I lost a relationship with my kids and my spouse ... I would stay awake for days have violent mood swings and worst I felt suicidal all the time ... got off the meds put my weight back on and fixed the relationships I ruined while this medicine I honestly think if I would have continue use it would be dead from either malnutrition or suicide BE AWARE VERY AWARE OF THIS MED!! [Rating 1] I became very antisocial & withdrawn very angry agitated no 1 could speak 2 me without me having an attitude [Rating 3]
5b. Improved mood and anxiety outcomes	11	10.0 (0.0)	I don't hate myself or want to die anymore [Rating 10] One again I felt great about my depression and my anxiety [Rating 2] I don't feel anxiety or depressed anymore [Rating 10]
5c. Improved focus and attention	35	10.0 (0.0)	I feel alert but not to the point where I feel like my heart is beating fast or anything like that [Rating 9] I am on the lowest dose and I also feel like I have been better focused at work [Rating 10] it also has helped me focus more in school [Rating 10] My thinking feels sharper and quicker and I'm more fluid in my conversations [Rating 10]

Table 6
Representative quotes for the Theme 6 “Intention to discontinue medication”.

Subtheme	n	Median (MAD) Efficacy Rating (0–10)	Examples of review comments
6a. Desire to discontinue treatment - concerns with craving, dependency/abuse liability	15	8.0 (2.0)	I do not plan on staying on the medication, because I don't want to be dependent. My doctor even said the prescription won't be permanent, and we'll slowly weaned off of them [Rating 10] I began craving Vyvanse about 12 h after taking it for the FIRST TIME. I didn't, because I refuse to abuse this medication with all the other medications I'm on, anyways [Rating 5] I'll probably only use the medication long enough to really change my eating habits and the get off of it [Rating 10] I should probably get off of this medication but I am terrified I will binge more again and gain more weight back [Rating 7]
6b. Cost of treatment	6	8.5 (1.5)	Very, very cost prohibitive [Rating 1] I also highly do not recommend taking Vyvanse if you have no insurance, it is very expensive [Rating 8]

Table 7
Representative quotes for the Theme 7 “LDX as an adjunct to psychotherapy”.

Subtheme	n	Median (MAD) Efficacy Rating (0–10)	Examples of review comments
7. An ongoing need for psychotherapy	6	7.5 (2.0)	I'm in therapy and hope this will be a good aid in my efforts [Rating 7] I highly recommend Vyvanse for BED, but also strongly encourage to do therapy along with it [Rating 10] My doctor recommended me take this while also weekly or bi weekly therapy sessions [Rating 9]

binge eating and general appetite; 2) body weight; 3) sleep and energy levels; 4) other physiological side effects; 5) psychiatric functioning; 6) intentions to discontinue medication; and 7) LDX as an adjunct to psychotherapy. Most of these themes encompassed several subthemes, which typically reflected a spectrum of patient experiences related to the overall theme (eg. Theme 1 included subthemes ‘Reduced bingeing/appetite,’ ‘No change in bingeing/appetite,’ ‘Exacerbation of binge eating in evening,’ and ‘Reduced efficacy with prolonged use (tolerance)’). Although many respondents indicated that LDX was effective at reducing binge eating, they also reported a range of negative side effects that impacted their daily functioning. For the majority of respondents, any negative outcomes associated with LDX appeared to not affect perceptions of its efficacy, as the average quantitative rating of LDX’s efficacy across all participants was 7.89 (out of 10), the median was 9, and the most frequent rating was 10. However, for other respondents, negative themes appeared to affect perceptions of efficacy; subthemes associated with less favorable quantitative efficacy ratings included ‘reduced efficacy with prolonged use (tolerance),’ ‘insomnia,’ ‘loss of energy in the afternoon/evening (crashing),’ ‘return of binge eating in the evening,’ and ‘weight gain.’ Together, these analyses provide unique, previously unreported, insights into individual experiences with LDX as a treatment for BED and their association with perceived efficacy, which should be further explored in more representative samples in future studies.

The majority of respondents (56/90) indicated that LDX was effective at reducing binge eating episodes and/or suppressing appetite (Subtheme 1a). This is consistent with data from randomized clinical trials that generally indicate that at high doses (50, 70 mg), LDX is effective in reducing baseline binge eating days per week and increasing 4-week binge eating cessation rates in approximately 50% of patients (McElroy et al., 2015). Some respondents indicated that LDX had limited or no efficacy in preventing binge eating in the afternoon/evening, with some reporting that their binge eating becomes exacerbated “when it [LDX] wears off.” The prescribing guidelines for LDX indicate that it should be taken in the morning, reflecting the relatively long plasma half-life of d-amphetamine (8.6–15h; Ermer et al., 2016) and its potential to interfere with sleep if taken later in the day (Shen and Shi, 2021). This represents a potentially major impediment to the efficacy of LDX, as food cravings are strongest, and binge eating episodes are more likely, in the evening (Raymond et al., 2003, 2007), and may account for variability in treatment response in clinical studies. This may also

account for the sudden loss of energy in the mid-late afternoon that many users reported, referred to by one respondent as ‘the Vyvanse crash’ (Subtheme 3b). To this end, it is notable that LDX was originally developed to improve daytime, cognitive functioning and attention in ADHD (Turgay et al., 2010), which might align more closely with the recommended dosing regimen and pharmacokinetic profile of the drug.

Notable also is that some users pointed to a trial-and-error process for finding the optimal timing and dose of LDX, perhaps indicating that some patients delay dosing to suppress binge episodes later in the day. This strategy might underlie the sleep disturbances reported by many respondents (Subtheme 3a), indicating that for some patients, achieving efficacy with LDX might mean compromising on sleep (or as one user put it, “it’s a catch 22”). Such a strategy may lead to worse outcomes, as there is some evidence indicating that poor sleep itself can exacerbate binge eating (Mehr and James, 2022; Mehr et al., 2021). Also notable is that across all randomized controlled trials (RCTs) and non-RCT studies of LDX, sleep disturbances were among the most frequent TEAEs reported, with one study reporting insomnia in 44% of LDX patients following 12w treatment (Guerdjikova et al., 2016). Similarly, insomnia was among the most common TEAEs reported in a 52w (4w dose optimization, 48w dose maintenance) safety/tolerability study of LDX (12.4% of patients) and led to discontinuation of treatment in a small number (5/588) of patients (Gasior et al., 2017). Altogether, in our study, many respondents had positive perceptions of LDX as a treatment for BED. However, the pharmacokinetic profile of LDX may diminish its efficacy against binge eating that occurs later in the day, and may lead some patients to delay their dosing, potentially interfering with sleep and thus representing a barrier to patient adherence. Further interrogation in future structured studies with more representative patient samples is warranted.

It is interesting that nearly half (44.4%) of respondents that gave lower quantitative ratings of LDX’s efficacy (i.e., a rating of 1–8 out of 10) indicated concerns with the drug becoming less effective with prolonged use. These perceptions contrast with clinical data indicating a prolonged reduction in number of binge eating days in patients that received long-term (52w) LDX treatment (Gasior et al., 2017). Moreover, in another study with patients who responded to an initial 12w LDX treatment (50, 70 mg/d), relapse rates were lower in patients maintained on LDX for an additional 26w compared to those who were discontinued (placebo controls; Hudson et al., 2017). The reasons for this apparent disconnect between patient perceptions and real-world

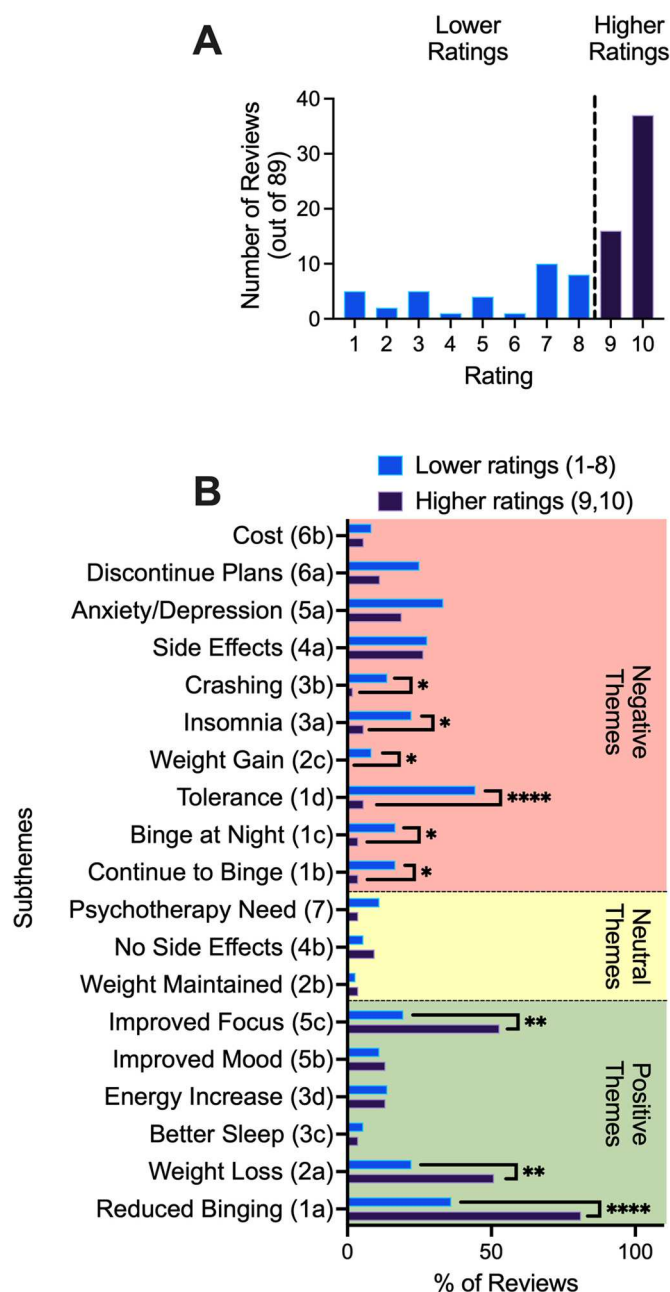


Fig. 1. A) Histogram depicting the frequency of respondents' quantitative ratings of LDX's efficacy on a 1–10 scale. Data were skewed to the left, with most frequent scores being 9 and 10. For subsequent analyses, we divided respondents into those who provided higher (scores of 9 or 10) vs lower (scores of 1–8) efficacy ratings. B) Respondents who provided higher quantitative efficacy ratings of LDX (9–10 out of 10) were more likely to highlight positive themes associated with LDX treatment, including reduced binge eating, weight loss and improved focus. Respondents who provided lower efficacy ratings (1–8 out of 10) were more likely to highlight negative themes, including developing tolerance to the medication, insomnia, return of binge eating at night, no change in bingeing/appetite, weight gain associated with LDX treatment, and loss of energy in the afternoon/evening ('crashing'). Comparisons between higher vs. lower ratings made using χ^2 analyses. * $p < 0.05$, ** $p < 0.01$, **** $p < 0.0001$. Numbers/letters in parentheses reflect the subthemes described in the Results section.

data are unclear; one possibility is that patients in our sample were reflecting on their experience of starting at lower doses (e.g. 30 mg) and having their dose gradually increased to achieve a suppression of binge eating, as is recommended clinical practice. This discrepancy might also

reflect general skepticism towards pharmacotherapy in some patients (De las Cuevas and de Leon, 2017). Notably however, these perceptions are very much consistent with an extensive animal literature indicating that repeated administration of stimulants, including d-amphetamine, can result in tolerance to its anorexic properties (Carlton and Wolgin, 1971; Wolgin and Jakubow, 2004), as well as some evidence of decreased efficacy of LDX in improving attentional outcomes with prolonged treatment in ADHD patients (Coghill et al., 2017; Findling et al., 2008, 2013; Weisler et al., 2009). Relatedly, several respondents cited concerns about the risk of becoming dependent on LDX, perhaps reflecting a perception that prolonged use of LDX might promote uncontrolled future use (i.e. 'addiction'). As a prodrug, LDX itself is biologically inactive, but is metabolized by the liver into L-lysine and d-amphetamine, the latter being a known drug of abuse. It is argued that this conversion process limits the drug's abuse liability, especially as pharmacokinetic studies point to lower maximum plasma concentrations (C_{max}) of d-amphetamine following oral LDX vs. d-amphetamine administration (Ermer et al., 2016). Consistent with this, liking scores for 50 mg LDX (delivered i.v.) did not significantly differ to those for placebo among a sample of adult stimulant abusers (Jasinski and Krishnan, 2009b). However, a more recent study reported no difference in the C_{max} of the two drugs, as well as similar concentration-time and drug effect-time curves, when a high dose of LDX (70 mg) was compared to an equivalent dose of d-amphetamine (Dolder et al., 2017). Also, LDX produces more sustained dopamine efflux in nucleus accumbens, a brain region critical for reward processing, compared to d-amphetamine (albeit at lower levels; Rowley et al., 2012). Despite these latter data, epidemiological data generally supports reduced abuse potential of LDX compared to immediate release d-amphetamine (Carton et al., 2022). It is interesting, therefore, that our data indicate that some patients are concerned about a risk of misusing LDX over long periods of time, and that this was cited as a primary contributor to patients' desire to discontinue the medication. In many cases these patients indicated that they would discontinue medication use when their binge eating was 'under control', perhaps indicating that patients are generally willing to accept this perceived risk in the short-term. It is also notable that a substantial proportion of respondents who gave higher efficacy ratings of LDX indicated that they experience medication-associated side effects (both physiological and psychological). These experiences are not surprising given that the overwhelming majority (~85%) of patients maintained on LDX for extended periods report at least one TEAE (Gasior et al., 2017), but indicates that for many respondents, these negative side effects are outweighed by the perceived therapeutic benefits (i.e. reductions in binge eating). Finally, it is interesting that the perception that LDX improved focus and attention was one of themes that was associated with higher efficacy ratings. This aligns closely with LDX being originally developed to treat ADHD, as well as evidence of elevated comorbidity between ADHD and BED (Nickel et al., 2019), and together might indicate that the utility of LDX in patients with BED and ADHD might be multifaceted.

Another theme that we identified as contributing to lower ratings of LDX was a perception that the treatment worsened anxiety and depression symptoms (Subtheme 5a). This is interesting, as others (albeit fewer) indicated in their reviews an improvement in anxiety and depression outcomes. These data broadly align with data from clinical studies that have failed to find consistent effects of LDX on mood, stress, and anxiety (Schneider et al., 2021, 2022). For example, two studies reported no effect of LDX treatment on self-reported depression and anxiety (Fleck et al., 2019; McElroy et al., 2015), whereas other studies reported treatment-associated improvements in self-reported depression (McElroy et al., 2015), anxiety or stress (Srivastava et al., 2019). Clinical data indicate that any effects of long term LDX treatment on anxiety and mood are limited; among the 588 patients maintained on LDX for 52w (described above; Gasior et al., 2017), anxiety led to discontinuation in just 4 patients (anxiety was considered related to treatment in only 2 patients). Notable, however, is that almost all clinical trials have

reported 'feeling jittery' as a common TEAE (0–36% of patients), including in trials where patients were treated with LDX for 52w (5%; Gasior et al., 2017), which might reflect the psychostimulant and anxiogenic properties of d-amphetamine (Berman et al., 2009). In any case, treatment-associated emergence of anxiety and depression symptoms did not affect overall patient perceptions of LDX efficacy in our sample, with the prevalence of this theme being statistically similar in respondents that gave higher vs. lower quantitative efficacy ratings (although there was a trend towards this subtheme being represented in a higher proportion of lower ratings). We acknowledge, however, that LDX may have differential effects on anxiety and depression outcomes that might be obfuscated by combining these into a single subtheme; future studies with larger samples should seek to examine these outcomes separately.

Although subjective experiences with LDX have not been previously explored in BED populations, a recent study exploring the feasibility of LDX as a treatment for bulimia nervosa reported qualitative outcomes related to patient perceptions (Dixon et al., 2023). Similar to our analyses, this study identified themes related to improved eating pathology and general functioning. They also identified a theme of 'renewed hope for recovery'; this was not a predominant theme in our data set and might reflect timing of the treatment course (at the end of an 8w experimental trial in the Dixon study vs. after prolonged treatment in many cases in our study) and the fact that if approved, LDX would be the first medication specifically indicated for use in BN patients. These factors may also have contributed to this study identifying only positively valenced themes whereas ours identified several negatively valenced themes.

We acknowledge several important limitations of our study. Most importantly, our data were opportunistic and thus our study sample is unlikely to be representative of all BED patients prescribed LDX. For example, online reviews for consumer products suffer from self-selection biases, including a tendency for those with extreme experiences, either positive or negative, being more likely to review a product (Bhole and Hanna, 2017); it is likely that our data are limited by a similar phenomenon. We note, however, that in exploratory research such as this, representativeness is not a requirement, as the goal is to generate hypotheses to be tested in a representative sample. Indeed, online content is a commonly utilized data source in exploratory research and has proven useful for unstructured hypothesis generation (Bremmer and Hendershot, 2024; Sakai et al., 2024; Shields et al., 2022). Future studies are therefore needed to directly explore the causal relationship between the themes identified here and overall patient perceptions of LDX's efficacy and treatment adherence. Relatedly, the source of our data meant that it was not possible to confirm BED diagnosis, duration of diagnosis, nor length of LDX treatment in respondents – these shortcomings should be considered when interpreting the current data and should be addressed in any structured future research designed to further explore the themes identified here. As is common for the field (Guest et al., 2020), thematic analysis ceased once the coders collectively agreed that thematic saturation had been reached. Although we believe it unlikely that exhaustive analysis would have yielded additional themes, we cannot rule this out entirely. If nothing else, the coding of remaining data sets would have added to the statistical power of our quantitative analyses. Finally, as noted in the Methods, qualitative outcomes are likely influenced by biases held by the coders; future studies should consider utilizing artificial intelligence approaches to help overcome these challenges (Richards and Richards, 1991).

In conclusion, we took a novel approach to determining how subjective, qualitative perceptions are related to quantitative ratings of LDX's efficacy as a medication for BED. Respondents with higher perceived efficacy ratings were more likely to highlight improved focus resulting from LDX treatment and less likely to highlight negative side effects. Lower ratings of LDX efficacy were associated with concerns relating to diminished therapeutic efficacy, insomnia, loss of energy in the afternoon/evening, and return of binge eating in the evening.

Regardless of quantitative ratings, some patients reported a difficult balancing act between taking LDX early enough in the day to avoid insomnia, but also trying to avoid a sudden loss of energy and binge eating in the afternoon/evening. At present, the wake-promoting effects of LDX have not been fully explored in BED populations, who already are prone to sleep disturbances (Brown and James, 2023; Kenny et al., 2018; Mehr and James, 2022; Mehr et al., 2021); this should be a focus of further study. Moreover, the findings of the current study should inform future studies designed to test if the themes identified here are causally related to perceptions of efficacy and treatment adherence.

CRediT authorship contribution statement

Abanoub J. Armanious: Writing – review & editing, Writing – original draft, Project administration, Investigation, Formal analysis, Data curation, Conceptualization, Methodology. **Audrey Asare:** Investigation, Formal analysis, Data curation. **Deborah Mitchison:** Writing – review & editing, Investigation, Formal analysis, Conceptualization. **Morgan H. James:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

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