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# CNS SPECTRUMS

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**CME Review Article**

**A Primer on Binge Eating Disorder Diagnosis and  
Management**

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- Implement evidence-based treatment strategies for patients with binge eating disorder
- Account for binge eating disorder when making prescribing decisions for comorbid disorders

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# A primer on binge eating disorder diagnosis and management

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Binge eating disorder (BED) is the most common eating disorder, with an estimated lifetime prevalence of 2.6% among U.S. adults, yet often goes unrecognized. In the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5), BED is defined by recurrent episodes of binge eating (eating in a discrete period of time an amount of food larger than most people would eat in a similar amount of time under similar circumstances and a sense of lack of control over eating during the episode), occurring on average at least once a week for 3 months, and associated with marked distress. It can affect both men and women, regardless if they are at normal weight, overweight, or obese, and regardless of their ethnic or racial group. Psychiatric comorbidities are very common, with 79% of adults with BED also experiencing anxiety disorders, mood disorders, impulse control disorders, or substance use disorders; almost 50% of persons with BED have  $\geq 3$  psychiatric comorbidities. Multiple neurobiological explanations have been proffered for BED, including dysregulation in reward center and impulse control circuitry, with potentially related disturbances in dopamine neurotransmission and endogenous  $\mu$ -opioid signaling. Additionally, there is interplay between genetic influences and environmental stressors. Psychological treatments such as cognitive behavioral interventions have been recommended as first line and are supported by meta-analytic reviews. Unfortunately, routine medication treatments for anxiety and depression do not necessarily ameliorate the symptoms of BED; however, at present, there is one approved agent for the treatment of moderate to severe BED—lisdexamfetamine, a stimulant that was originally approved for the treatment of attention deficit hyperactivity disorder.

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## Introduction

Binge eating disorder (BED) is the most common eating disorder, with an estimated lifetime prevalence of 2.6% among U.S. adults, more than the prevalence for bulimia nervosa and anorexia nervosa combined.<sup>1,2</sup> Although many people with BED are obese (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>), more than half have a BMI  $< 30$  kg/m<sup>2</sup>, including 19% whose weight is normal (BMI between 18.5 and 24.9 kg/m<sup>2</sup>).<sup>1</sup> In contrast to other eating disorders such as anorexia nervosa or bulimia nervosa, the gender ratio for BED is far less skewed; lifetime prevalence for BED is 2% for men and 3.5% for women.<sup>1</sup> No one ethnic or racial group is overrepresented: BED

occurs at a similar rate (lifetime prevalence) among non-Latino white (1.4%), Latino (2.1%), Asian (1.2%), and African-American (1.5%) adults in the U.S.<sup>3</sup> The onset of BED occurs at a later median age (21 years) than anorexia nervosa or bulimia nervosa (18 years), and with a much wider range.<sup>1</sup> The mean persistence of BED is about 8 years.<sup>1</sup> BED is associated with distress and problems in functioning. Functional consequences include problems adapting to social roles, poor quality of life and less life satisfaction due to health issues, increased overall medical morbidity and mortality related to weight gain and obesity, and increased use of healthcare resources.<sup>4</sup> Psychiatric comorbidities are very common, with 79% of adults with BED also experiencing anxiety disorders (65%), mood disorders (46%), impulse control disorders (43%), or substance use disorders (23%).<sup>1</sup> Almost 50% of persons with BED have  $\geq 3$  psychiatric comorbidities. The psychiatric comorbidity is linked to the severity of binge eating and not to the degree

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of obesity.<sup>4</sup> Impaired role functioning in work/school, social, and family life, as measured by the Sheehan Disability Scale, was observed in 63% of adults with BED, with 18.5% of adults with BED reporting severe functional impairment.<sup>1</sup> It must be emphasized that BED is distinct from obesity; most obese individuals do not engage in recurrent binge eating, and, compared with weight-matched obese individuals without BED, those with BED consume more calories in laboratory studies and have greater functional impairment, lower quality of life, more subjective distress, and greater psychiatric comorbidity.<sup>4</sup>

Psychological treatments, including cognitive behavioral interventions, have been recommended as first line<sup>5</sup> and are supported by meta-analytic reviews.<sup>6</sup> Unfortunately, routine medication treatments for anxiety and depression do not necessarily ameliorate the symptoms of BED; however, at present, there is one approved agent for the treatment of moderate to severe BED—lisdexamfetamine, a stimulant that was originally approved for the treatment of attention deficit hyperactivity disorder.<sup>7</sup>

### What Are the Diagnostic Criteria for Binge Eating Disorder?

BED often goes unrecognized, and thus untreated, in part because it was not included as a diagnosis in the *Diagnostic and Statistical Manual of Mental Disorders* until the Fifth Edition (DSM-5) was published in 2013.<sup>4</sup> In the DSM-5, BED is defined by recurrent episodes of binge eating (eating in a discrete period of time an amount of food larger than most people would eat in a similar amount of time under similar circumstances *and* a sense of lack of control over eating during the episode), occurring on average at least once a week for 3 months, and associated with marked distress. Binge episodes are also associated with  $\geq 3$  of the following: eating rapidly, eating until feeling uncomfortably full, eating large amounts of food when not feeling physically hungry, eating alone because of feeling embarrassed by how much one is eating, and feeling disgusted with oneself, depressed, or guilty afterwards. It is not unusual for all five of these associated features to be present. Although overvaluation of shape or weight is often seen (40%), it is not part of the DSM-5 criteria for BED.<sup>8</sup> BED is distinguished from bulimia nervosa in that BED is not associated with regular compensatory behaviors such as purging or excessive exercise, or with dietary restriction, although frequent dieting may be reported.

Since binge eating is often a secretive behavior, and commonly associated with a high degree of embarrassment or shame,<sup>9</sup> it is not ordinarily revealed unless the clinician makes a direct inquiry regarding eating patterns.

Although physical comorbidities including obesity and metabolic syndrome are common, and may prompt

a discussion of eating behaviors, not all persons with BED are obese. BED is commonly associated with other psychiatric disorders that bring them to treatment, such as anxiety, depression, impulse control disorders, and substance use. Routine assessment of eating behaviors is advisable because persons with prominent co-existing psychiatric conditions, and as yet undiagnosed BED, may not bring up eating issues on their own.

DSM-5 also provides for the specification of partial remission, where after full criteria for BED were previously met, binge eating occurs at an average frequency of less than one episode per week for a sustained period of time. For full remission, after full criteria for BED were previously met, none of the criteria have been met for a sustained period of time.

Current severity can also be specified. The minimum level of severity is based on the number of weekly binge eating episodes (mild, 1–3; moderate, 4–7; severe, 8–13; extreme,  $\geq 14$ ); however, severity level can be increased to reflect other symptoms and functional disability.

DSM-5 provides additional guidance that is helpful when assessing eating behaviors. Context is important: for example, a quantity of food that might be regarded as excessive for a typical meal might be considered normal during a celebration or holiday meal, such as Thanksgiving. The “discrete period of time” refers to a limited period, usually less than 2 hours, but a single episode of binge eating need not be restricted to one setting. DSM-5 gives the example of an individual starting a binge in a restaurant and then this continues upon returning home. However, when evaluating a patient for BED, continual snacking on small amounts of food throughout the day would not be considered an eating binge. The food consumption *must* be accompanied by a sense of lack of control to be considered an episode of binge eating. This means that the person with BED is unable to refrain from eating or to stop eating once started. It is not unusual for an individual to continue binge eating if the phone rings; however, if a roommate or spouse unexpectedly enters the room, the behavior may immediately cease, and can be followed by significant embarrassment. Patients may also describe the eating as a dissociative experience. Some patients with BED may be unable to clearly articulate an acute feeling of loss of control but instead describe a generalized pattern of uncontrolled eating. The text in DSM-5 adds that if individuals report that they have abandoned efforts to control their eating, loss of control may still be considered as present. In addition to spontaneous episodes of binge eating when opportunities present themselves, binge eating can also be planned in some instances by the hoarding of foods in secret places. The actual types of foods consumed are not necessarily sugary or salty snacks, or carbohydrates, but can also include fruit, yogurt, or foods ordinarily considered

as “healthy.” The types of food consumed during binge eating episodes vary both across individuals and for a given individual, and the binge eating episode is characterized more by an abnormality in the amount of food consumed than by a craving for a specific food.

### Is Binge Eating Disorder New?

BED is not a new entity. Variations of binge eating have been described in the literature since the 1950s. For example Walter Hamburger in 1951 described “a compulsive craving for food.... This craving is frequently uncontrollable and must be satisfied.”<sup>10</sup> Albert Stunkard in 1959 described “enormous amounts of food may be consumed in relatively short periods ... is regularly followed by severe discomfort and self-condemnation.”<sup>11</sup> In 1980, binge behavior was included as a component of the DSM-III diagnostic criteria for bulimia, and interestingly these criteria included, but did not necessarily require, engaging in inappropriate compensatory behaviors.<sup>12</sup> The 1980s subsequently ushered in a flood of additional research in binge eating, usually focused among obese persons, and, in general, observed differences between obese binge and obese non-binge eaters included greater levels of psychopathology, a greater likelihood to drop out of weight-loss treatment, and being more likely to regain lost weight more rapidly.<sup>13</sup> The concept of “purging” and “non-purging” bulimia was further refined, with persons with either disorder exhibiting lower self-esteem and higher anxiety than non-bulimic controls.<sup>14</sup> In 1987, the diagnostic entity of “Bulimia” in DSM-III was replaced by “Bulimia Nervosa” in DSM-III-R,<sup>15</sup> and criteria were made more specific, requiring both binge eating and compensatory behaviors, with a minimum average of 2 binge eating episodes a week for at least 3 months, and with persistent overconcern with body shape and weight. Unfortunately, with this significant change in the diagnosis of bulimia from the wording in DSM-III to that in DSM-III-R, binge eaters without compensatory behaviors could no longer be diagnosed using DSM-III-R. The diagnostic entity of BED was offered as a solution to this problem.<sup>16</sup> Despite field trials for BED,<sup>17,18</sup> BED was not adopted for the DSM-IV when it was released in 1994,<sup>19</sup> and the use of the diagnostic entity “Eating Disorder Not Otherwise Specified” (EDNOS) was the option provided to diagnose BED patients. Research criteria for BED were outlined in Appendix B (Criteria Sets and Axes Provided for Further Study) of the DSM-IV, and were not intended for clinical use outside research settings. This situation remained unchanged in 2000 with the release of DSM-IV-TR.<sup>20</sup> It was observed that EDNOS was frequently diagnosed, and was the most common eating disorder diagnosis made in adult outpatient settings from 2000-2004.<sup>21</sup> Overreliance on “Not Otherwise Specified” or

miscellaneous categories is not desirable in any diagnostic schema, and ultimately BED was recognized as a distinct eating disorder upon the publication of DSM-5 in 2013.

To date, there are over 1750 publications listed in the U.S. National Library of Medicine’s PubMed resource containing the text words “binge eating disorder,” together with over 250 clinical trials listed in the U.S. ClinicalTrials.gov registry.

### What Is the Neurobiology Behind Binge Eating Disorder?

Multiple neurobiological explanations have been proffered for BED, including dysregulation in reward center and impulse control circuitry,<sup>22-24</sup> with potentially related disturbances in dopamine neurotransmission<sup>25,26</sup> and endogenous  $\mu$ -opioid signaling.<sup>27,28</sup> For example, in one study, obese individuals with BED were compared to BMI-matched obese individuals and lean comparison participants using functional magnetic resonance imaging while completing the Stroop color-word interference task.<sup>23</sup> Brain activity in the BED group was differentiated by relative hypoactivity in brain areas involved in self-regulation and impulse control, specifically in the ventromedial prefrontal cortex, inferior frontal gyrus, and insula. Moreover, dietary restraint scores were negatively correlated with brain activation; the authors concluded that persons with BED have a diminished ability to recruit impulse-control-related brain regions, and that this is associated with impaired dietary restraint.

Additionally, there is interplay between genetic influences<sup>29,30</sup> and environmental stressors.<sup>31,32</sup> Functional polymorphisms of the dopamine D2 receptor gene and of the  $\mu$ -opioid gene suggest that proneness to BED may be influenced by “wanting food” (mediated by dopamine signaling) and “liking food” (mediated by  $\mu$ -opioid signaling).<sup>28</sup> Antecedents to binge eating include negative affect; interpersonal stressors; dietary restraint; negative feelings related to body weight, body shape, and food; and boredom.<sup>4</sup>

### Recognizing and Diagnosing Binge Eating Disorder

Feelings of shame and embarrassment about eating behaviors are very common among persons with BED. Symptom concealment is often encountered, with families often unaware of the extent of the binge eating behaviors. Persons with BED may not be aware that BED is an actual disorder and that there are treatments for it. In addition, it is commonly a person’s psychiatric and somatic comorbidities that are the focus of a healthcare provider’s attention, and the BED consequently goes unrecognized.

The extent of this was recently quantified in an Internet survey conducted in U.S. adults.<sup>33</sup> Among the 22,397 respondents, 344 participants (1.5%) met the DSM-5 criteria for BED in the past 12 months, but of the 344 respondents with BED, only 11 (3.2%) had ever been diagnosed with BED by a healthcare provider.

A screening instrument, the Binge Eating Disorder Screener-7 (BEDS-7), has been developed based in part on the DSM-5 diagnostic criteria.<sup>34,35</sup> The BEDS-7 is completed by the patient and is intended for screening use only. The first question is, “During the last 3 months, did you have any episodes of excessive overeating (ie, eating significantly more than what most people would eat in a similar period of time)?” If the answer is no, the remaining 6 questions do not apply. Otherwise, the remainder of the screener is completed, and, depending on the answers provided, should trigger a more thorough clinical evaluation based on the complete DSM-5 criteria for BED.

DSM-5 provides information on differential diagnosis<sup>4</sup>:

- BED vs. bulimia nervosa: Recurrent inappropriate compensatory behavior (eg, purging, excessive exercise, diuretic abuse, laxative abuse) seen in bulimia nervosa is absent in BED, and although persons with BED may report frequent attempts at dieting, they do not display marked or sustained dietary restriction.
- BED vs. obesity: Levels of overvaluation of body weight and shape, and rates of psychiatric comorbidity, are higher in obese individuals with BED than in those without BED.
- BED vs. bipolar and depressive disorders: Increases in appetite and weight gain are included in the criteria for major depressive episode and in the atypical features specifiers for depressive and bipolar disorders. However, increased eating in the context of a mood episode may or may not be associated with loss of control; if the full criteria for both disorders are met, both diagnoses can be given.
- BED vs. borderline personality disorder: binge eating is included in the impulsive behavior criterion that is part of the definition of borderline personality disorder; if the full criteria for both disorders are met, both diagnoses should be given.

## Treatments for Binge Eating Disorder

Psychological treatments such as cognitive behavioral therapy and interpersonal psychotherapy can reduce binge eating behavior.<sup>5,6,36</sup> In one 16-week study, the effectiveness of group cognitive-behavioral treatment (CBT) and group interpersonal psychotherapy (IPT) for binge eating was assessed in 56 women with “nonpurging bulimia” using a randomized design with a wait-list

control.<sup>37</sup> At study’s end, both group CBT and group IPT treatment conditions showed significant improvement in reducing binge eating, whereas the wait-list condition did not. Moreover, binge eating remained significantly below baseline levels for both treatment conditions at 6-month and 1-year follow-ups. A similar randomized study of group CBT vs. group IPT, this time larger (N = 162) but without a control condition, found that both treatments showed initial and long-term efficacy for the core and related symptoms of BED.<sup>38</sup> In a meta-analysis of randomized controlled trials, psychotherapy and structured self-help, both based on cognitive behavioral interventions, were found to have large effects on the reduction of binge eating.<sup>6</sup> Unfortunately, access to such treatments may be limited because of local availability and/or cost. Moreover, psychological treatment approaches have generally not resulted in weight loss, although successfully eliminating binge eating might protect against future weight gain.<sup>5</sup>

Pharmacotherapies for BED have been actively researched.<sup>39-42</sup> These have included antidepressants that target neurotransmitter dysregulation (such as selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and bupropion), anticonvulsants with complex mechanisms of action (for example, topiramate), anti-obesity/anorectic agents that target appetite and weight (for example, sibutramine [withdrawn from the U.S. market and elsewhere because of increased risk of cardiovascular events]), attention deficit-hyperactivity disorder medications that target impulsivity (for example, lisdexamfetamine), and medications for addictive disorders that target the reward center and opioid dysfunction (for example, naltrexone). Until the studies of lisdexamfetamine, the tested medicines fell short in terms of robustness of effect, tolerability, or both. Each alternative appeared to have a significant shortcoming. For example, although antidepressants can reduce the frequency of binge eating behavior, they are not efficacious regarding weight loss. Although topiramate has efficacy regarding reduction of both binge eating and weight, it has a negative impact on cognitive function.

As noted, lisdexamfetamine is currently the only U.S. Food and Drug Administration (FDA)-approved agent for the treatment of BED. As per the product label,<sup>43</sup> lisdexamfetamine is indicated for the treatment of moderate to severe BED and has a limitation of use in that lisdexamfetamine is not indicated for weight loss. As with all CNS stimulants, the presence of cardiac disease and risk of abuse must be assessed when prescribing. The recommended starting dose is 30 mg/day to be titrated in increments of 20 mg at approximately weekly intervals to achieve the recommended target dose of 50–70 mg/day. Lisdexamfetamine is taken once daily in the morning, with or without food; afternoon doses are to be avoided because of the potential for insomnia.

Approval of lisdexamfetamine for the treatment of BED was based on a clinical development program that included an 11-week, Phase II, proof-of-concept, placebo-controlled study that tested fixed doses of lisdexamfetamine (30, 50, and 70 mg/day)<sup>44</sup> and 2 12-week, Phase III, placebo-controlled studies examining lisdexamfetamine (50–70 mg/day).<sup>45</sup> Statistically significant reductions in binge eating days/week, the primary outcome measure, were observed for lisdexamfetamine doses of 50 and 70 mg/day, with large effect sizes.<sup>45</sup> Additionally, large effects were observed on reductions in the Yale–Brown Obsessive Compulsive Scale Modified for Binge Eating.<sup>45</sup> Number needed to treat (NNT) and number needed to harm (NNH) can be used to quantify the effect sizes for desired and undesired outcomes, respectively.<sup>46–48</sup> Optimal NNT values representing medium to large effect sizes range from 2 to 5, the lower the better, and optimal NNH values are generally  $\geq 10$ , the higher the better.<sup>48</sup> Response rates across all trials (as defined by a Clinical Global Impressions–Improvement score of “very much improved” or “much improved”) were 86% for lisdexamfetamine vs. 48% for placebo, resulting in a NNT of 3.<sup>7</sup> Remission rates (as defined by 4-week cessation of binge eating) were 40% for lisdexamfetamine vs. 15% for placebo, resulting in a NNT of 4.<sup>7</sup> Reductions in weight ranged between 5.2% and 6.25% for lisdexamfetamine 50 or 70 mg/day vs. no relevant changes observed for placebo. Discontinuation rates because of adverse events (AEs) were low (4.6% for lisdexamfetamine vs. 2.3% for placebo), yielding a NNH of 44.<sup>7</sup> The most common AEs (incidence  $\geq 5\%$  and at a rate at least twice that for placebo) in the Phase III trials as summarized in the product label<sup>43</sup> were dry mouth (36% and 7%, for lisdexamfetamine and placebo, respectively), insomnia (20% vs. 8%), decreased appetite (8% vs. 2%), increased heart rate (7% vs. 1%), constipation (6% vs. 1%), feeling jittery (6% vs. 1%), and anxiety (5% vs. 1%), with NNH values of 4, 9, 17, 17, 20, 20, and 25, respectively.<sup>7</sup> A limitation inherent to registration trials in general, and to the above trials as well, is the exclusion of patients with clinically significant comorbidities.

The results of a 39-week, long-term maintenance of efficacy study of lisdexamfetamine for BED have recently been made available in a press release.<sup>49</sup> The primary endpoint was time to relapse of binge eating symptoms in adults with moderate to severe BED. During the 26-week, double-blind, randomized-withdrawal phase of the study, lisdexamfetamine demonstrated superiority over placebo on time to relapse. Observed relapsed rates for lisdexamfetamine vs. placebo were 3.7% vs. 32.1%, resulting in a NNT of 4.

Unknown is whether or not the combination of lisdexamfetamine with cognitive behavioral therapy would be superior to either treatment alone, as has been

tested with some success with topiramate in a 21-week, double-blind, randomized, placebo-controlled trial in obese adults with BED.<sup>50</sup>

## Conclusions

BED is different from overeating and requires the presence of distinguishing features, such as loss of control and strong feelings of shame and guilt, which are not normally associated with overeating. Psychiatric and somatic comorbidities are very common, as are functional impairments; however, BED may go undiagnosed for many years because patients seeking treatment for psychiatric or somatic disorders are not always specifically asked about their eating behaviors. BED occurs in both men and women across racial and ethnic groups, and although BED is frequently associated with obesity, the majority of adults with BED are of healthy weight or overweight. The precise etiology of BED is not known; however, research suggests an underlying neurobiological basis for BED, with risk factors that include genetic and environmental influences. Effective treatment modalities include psychotherapy and pharmacologic approaches.

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## Optional CME Posttest and Certificate

*CME Credit Expires: November 30, 2018*

### CME Posttest Study Guide

**NOTE: The posttest can only be submitted online.** The below posttest questions have been provided solely as a study tool to prepare for your online submission. **Faxed/mailed copies of the posttest cannot be processed** and will be returned to the sender. If you do not have access to a computer, contact NEI customer service at 888-535-5600.

1. A 23-year-old woman presents in great distress, saying she thinks she has binge eating disorder. For the past 3 months she has had weekly episodes (a couple of times more than once per week) where she eats far beyond the point of hunger, typically at night and when she is alone. The patient feels very guilty and disgusted with herself about her eating habits and her “lack of self control”. Her body mass index (BMI) is 22.4 and she does not engage in inappropriate compensatory behavior. Does this patient meet the diagnostic criteria for binge eating disorder?
  - A. No, because her BMI is normal
  - B. No, because her episodes are not frequent enough
  - C. No, because she does not engage in inappropriate compensatory behavior
  - D. Yes
  
2. A 24-year-old woman has just been diagnosed with binge eating disorder. Her symptoms include recurrent episodes of compulsive eating late at night while alone, feeling a lack of control over eating during the episodes, feeling disgusted with herself after episodes, and overvaluation of her body shape. She has a BMI of 28.6. Which of the following are part of the diagnostic criteria for binge eating disorder?
  - A. Feeling a lack of control during episodes
  - B. Feeling disgusted with oneself after episodes
  - C. Overvaluation of one’s body shape
  - D. A and B
  - E. A, B, and C
  
3. Lisdexamfetamine is approved for:
  - A. Moderate to severe binge eating disorder
  - B. Weight loss associated with binge eating disorder
  - C. A and B
  
4. Which of the following is true regarding comorbidities in patients with binge eating disorder?
  - A. Close to 50% of persons with BED have at least 3 psychiatric comorbidities
  - B. Close to 100% of persons with BED are obese
  - C. The most common psychiatric comorbidity in BED is substance use disorder

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