

# Overview of the treatment of binge eating disorder

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We performed a qualitative review of treatment studies of binge eating disorder (BED), focusing on randomized clinical trials (RCTs). Limited effectiveness has been demonstrated for self-help strategies, and substantial effectiveness has been shown for cognitive behavioral therapy (CBT) and interpersonal therapy (IPT). CBT and IPT may each be more effective than behavior weight loss therapy (BWL) for reducing binge eating over the long term. The stimulant pro-drug lisdexamfetamine dimesylate (LDX) is the only drug approved by the FDA for the treatment of BED in adults based on 2 pivotal RCTs. Topiramate also decreases binge eating behavior, but its use is limited by its adverse event profile. Antidepressants may be modestly effective over the short term for reducing binge eating behavior and comorbid depressive symptoms, but are not associated with clinically significant weight loss. A RCT presented in abstract form suggests that intranasal naloxone may decrease time spent binge eating. There is no RCT of obesity surgery in BED, but many patients with BED seek and receive such surgery. While some studies suggest patients with BED and obesity do just as well as patients with obesity alone, other studies suggest that patients with BED have more post-operative complications, less weight loss, and more weight regain. This evidence suggests that patients with BED would benefit from receiving highly individualized treatment.

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## Introduction

Binge eating disorder (BED), now recognized as a formal mental disorder in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5), is characterized by recurrent binge eating episodes during which an unusually large amount of food is ingested for the situation, and there is a sense of loss of control over eating.<sup>1</sup> The binge eating behavior produces marked distress but is not accompanied by the inappropriate weight loss behaviors of bulimia nervosa (BN).

BED is the most common eating disorder, present as a lifetime diagnosis in 2.6% of United States (U.S.) adults, 1.3% of U.S. adolescents, and 1.9% adults worldwide.<sup>2–4</sup> It is associated with other psychiatric disorders, obesity, pain syndromes, and components of metabolic syndrome; reduced quality of life; functional impairment; increased

healthcare utilization; and increased healthcare costs.<sup>2–7</sup> The pathophysiology of BED is unknown, but is thought to involve genetic factors, increased food-related impulsivity and reward sensitivity, and central dopamine dysfunction.<sup>8–10</sup>

Despite the magnitude of BED as a public health problem, most people with BED remain untreated.<sup>2</sup> Indeed, widely accepted guidelines for the treatment of people with BED are not yet available. The past several years, however, have witnessed an increase in study of the treatment of binge eating disorder (BED). In this article, we review the literature on the treatment of BED to provide an overview of available options for managing this condition. We focus on randomized, controlled trials (RCTs) and meta-analyses, but in the absence of such data, we describe open-label findings.

## Methods

We searched PubMed for treatment studies of BED through March 24, 2015, using the term “randomized controlled trial” matched with “binge eating disorder.” We also searched the Cochrane data base using the same terms.

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Our search generated 271 references, 98 of which discussed treatment of BED (sometimes with BN). (We excluded RCTs of BN only and of obesity only, but did include studies of obesity with binge eating behavior.) Eighty-two of these were clinical trials, and 16 were meta-analyses or reviews. We summarize the findings of these studies below according to 4 broad categories of treatment: psychological treatment, physical activity, pharmacotherapy, and obesity surgery.

## Psychological Treatment

A wide range of psychological treatments have been studied in people with BED. These treatments range from self-help strategies requiring no to minimal clinician time to specialized psychotherapies where clinicians require considerable training. A number of excellent reviews have summarized these studies.<sup>11–15</sup>

### Self-help treatments

Various forms of self-help treatment of BED have been studied in RCTs, including bibliotherapy, cognitive behavior therapy-guided self-help (CBT-GSH), CD-ROM-based interventions, and Internet-based interventions.<sup>16,17</sup> Reviewing 26 RCTs in patients with BED or BN, Sysko and Walsh<sup>16</sup> concluded that self-help provided more benefit than a waiting list control group, but that studies using an active control were not as positive. For example, in the largest RCT (N = 259), therapist-led self-help and therapist-assisted self-help had higher binge eating remission rates (51.7% and 33.3%, respectively) than self-help alone (17.9%) and a waiting list (10.1%) at the end of 20 weeks of treatment.<sup>18</sup> However, no between-group differences were observed at 6 and 12 months follow-up.

RCTs comparing self-help with usual clinical care have had mixed results.<sup>19–21</sup> In one RCT, CBT-GSH was superior to treatment as usual in 123 individuals with recurrent binge eating (48% with BED): at 12-month follow-up, binge eating remission rates were 64.2% and 41.4% for CBT-GSH and usual treatment, respectively.<sup>19</sup> In a replication RCT, rates of remission were 35% for CBT-GSH and 14% for usual care.<sup>20</sup> By contrast, in a RCT of 48 obese patients with BED (N = 48), CBT-GSH was not superior to usual care after 4 months.<sup>21</sup>

Recently, Beintner *et al*<sup>17</sup> conducted a systematic review of 50 clinical trials of manualized self-help interventions for BED and BN, 34 of which were RCTs. Rates of participants achieving remission of binge eating post-intervention varied widely, from 9% to 64%. Study dropout rates, which ranged from 1% to 88%, were highest in CD-ROM interventions and lowest in Internet-based interventions. Intervention outcomes were moderated by provision of personal guidance by a

healthcare professional and number of guidance sessions, as well as participant's age, body mass index (BMI), and eating disorder psychopathology. Specifically, compared with BN patients, BED patients (who were older and had higher BMIs) were more likely to persist with treatment and to benefit from both guided and unguided self-help (while BN patients needed guidance).

Several RCTs of self-help treatment also assessed motivational interviewing, a psychotherapy that focuses on strengthening a person's internal motivation to change, with mixed results.<sup>22–25</sup> In the first, 90 patients with BED or BN attended a 1-hour motivational enhancement session before receiving a self-help manual or received the self-help manual alone.<sup>22</sup> The intervention group showed increased readiness to change, but there were no differences between the 2 groups on measures of binge eating behavior or eating attitudes at 4-month follow-up. In the second RCT, 108 women with BED received 1 individual adaptive motivational interviewing session plus a self-help handbook or the handbook alone.<sup>23</sup> At 16-week follow-up, both groups reported improved binge eating behavior and depressive symptoms, but the group receiving motivational interviewing improved significantly more.

In the third RCT, 60 participants with BED or nonpurging BN were randomly assigned to 60 minutes of motivational interviewing followed by a self-help manual or 60 minutes of psychoeducation followed by a self-help manual.<sup>24</sup> Patients were assessed with questionnaires before and after the session of motivational interviewing, and at 1 and 4 months post-session. Although motivational interviewing increased readiness to change and confidence in the ability to control binge eating while psychoeducation did not, there were no group differences in binge eating behavior or eating disorder attitudes. In the fourth study, 89 overweight or obese patients, 25.8% with BED by DSM-5 criteria, were randomized to 3 months of motivational interviewing, nutrition psychoeducation, an attention control intervention, or usual care in a primary care setting.<sup>25</sup> Patients randomized to motivational interviewing and those randomized to nutrition psychoeducation were also given information on an Internet-based program that provided nutrition and fitness tips. Nutrition psychoeducation, but not motivational interviewing, was superior to usual care for reducing body weight, triglyceride levels, and depression scores at post-treatment. Weight loss results were maintained at 3-month follow-up: 25% of both treatment groups achieved at least 5% weight loss. BED status was not associated with weight loss outcomes.

In short, self-help treatments reduce binge eating behavior in some patients with BED, but are not effective for weight loss. Clinician guidance, but not motivational interviewing, may enhance the effectiveness of self-help treatments. While BED patients may respond better than

BN patients, no clear predictors of response to self-help treatments have been found among patients with BED.

### **Mindfulness-based approaches**

Several reviews have evaluated mindfulness-based approaches for binge eating.<sup>26–28</sup> Katterman *et al*<sup>26</sup> reviewed 14 studies that evaluated mindfulness meditation as the primary intervention and binge eating, emotional eating and/or weight change as outcomes. Mindfulness meditation decreased binge eating and emotional eating, but its effects on weight loss were mixed. Reviews by O'Reilly *et al*<sup>27</sup> and by Godfrey *et al*<sup>28</sup> yielded similar conclusions.

### **Behavioral weight loss therapy**

Results of RCTs of behavioral weight loss therapy (BWLTL) for persons with BED and overweight or obesity have been mixed<sup>29–34</sup> (as have been post-hoc evaluations of the effect of binge eating on weight loss in RCTs of BWLTL for patients with obesity<sup>25,35,36</sup>). Thus, in a RCT of BWLTL and CBT in 80 overweight patients with BED, both treatments were comparably effective post-treatment and at 6-month follow-up.<sup>34</sup> In another RCT in 125 obese patients with BED, patients were randomized to 1 of 3 treatments: CBT, BWLTL, or CBT followed by BWLTL.<sup>33</sup> At 12-month follow-up, all 3 treatments were comparably effective for reducing binge eating and BMI. Similarly, a RCT of dietary therapy with CBT (N = 50) suggested that dietary therapy did not enhance binge eating remission or weight loss.<sup>32</sup> In a 16-week RCT of CBT versus BWLTL in overweight or obese patients with BED, CBT was superior to BWLTL at post-treatment for reducing binge eating behavior, general psychopathology, and BMI.<sup>30</sup> However, after 12 months, there were no significant differences between the 2 treatment groups. In a 12-week RCT comparing interpersonal therapy (IPT), CBT-GSH, and BWLTL, binge eating remission rates were similar across all 3 treatments, while BWLTL had greater weight loss.<sup>31</sup> At 2-year follow-up, however, IPT and CBT-GSH had higher greater binge eating remission rates than BWLTL, and weight loss was no longer different across treatment groups.

In sum, BWLTL may be effective for reducing weight and binge eating in some overweight or obese BED patients over the short term, but weight loss is usually not maintained. For reduction of binge eating, BWLTL is comparable to or less effective than specialized therapies. Neither adjunctive dietary therapy nor subsequent BWLTL appears to enhance the effectiveness of CBT.

### **Specialized psychotherapies**

A growing number of studies have shown that CBT and IPT are both effective for reducing binge eating in

BED,<sup>31,37–41</sup> including over the long term<sup>42–44</sup> and in adolescents.<sup>45,46</sup> CBT and IPT appear to be comparably effective to one another and may be superior to BWLTL for reducing binge eating.<sup>31</sup> CBT has also been shown superior to fluoxetine, acutely and over the long term.<sup>38,42,47</sup> Indeed, many authorities consider CBT and IPT the treatments of choice for BED. Of note, group CBT and individual CBT have been found to be similarly effective.<sup>41</sup>

In an important RCT that compared 20 sessions of group CBT and 20 sessions of group IPT in 162 patients with BED, binge eating recovery rates (defined as having no binge eating episode in the past month) were similar for the 2 groups at post-treatment (79% and 73%, respectively) and at 1-year follow-up (59% and 62%, respectively).<sup>37</sup> Patients' weight decreased slightly but significantly; the greatest reduction occurred in patients sustaining recovery from post-treatment to 1-year follow-up. In a subsequent study, the first 90 patients enrolled in this RCT at one site were contacted and assessed 4 years after treatment cessation.<sup>43</sup> Participants showed substantial long-term reduction in BED symptoms. Specifically, 64% of patients had recovery from binge eating (defined as having no binge eating episodes in the past month) at 4-year follow-up: 52% for the CBT group and 77% for the IPT group. A significant decline in recovery rates from post-treatment and 1-year follow-up to 4-year follow-up was observed for CBT but not for IPT. BMI remained stable throughout the 4-year period, suggesting that while neither IPT nor CBT cause clinically significant weight loss, they may prevent further weight gain.

In another important RCT (mentioned above) of 205 patients with BED, IPT, CBT-GSH, and BWLTL were shown to be similarly effective for inducing remission of binge eating at post-treatment, while BWLTL was better for weight loss.<sup>31</sup> At 1-year follow-up, the 3 groups were still comparable on binge eating measures, but the BWLTL group had gained more weight. At 2-year follow-up, IPT and CBT-GSH were both more effective than BWLTL in eliminating binge eating. BWLTL was no longer significantly different from the other 2 treatments for weight loss. Self-esteem and global eating disorder psychopathology scores were moderators of treatment outcome: patients with lower self-esteem and greater eating disorder psychopathology improved more with IPT than with CBT-GSH or BWLTL. Of note, patients with depression and those receiving antidepressants were included in the trial (those with psychosis, suicidality, bipolar disorder, or substance were excluded). Moreover, IPT had a significantly lower attrition rate than either CBT-GSH or BWLTL.

Regarding other types of specialized psychotherapy, preliminary data suggest that dialectical behavior therapy (DBT), including guided self-help based on

DBT, may be helpful for reducing binge eating symptoms in patients with BED.<sup>48–50</sup> In the only RCT that did not use a waiting list control, 101 men and women with BED were randomized to 20 group sessions of DBT-BED or active comparison group therapy (ACGT).<sup>48</sup> Post-treatment cessation of binge eating was obtained more quickly for DBT-BED (64%) than for ACGT (36%), but these differences did not persist over the 3-, 6-, and 12-month follow-up assessments. DBT-BED had a significantly lower dropout rate than ACGT.

In sum, CBT and IPT are effective for reducing binge eating in a substantial subset of BED patients over the short and long term. Though neither CBT nor IPT produces clinically significant weight loss, they may be helpful for preventing further weight gain. Preliminary evidence suggests that DBT may also decrease binge eating, but large RCTs comparing DBT with CBT and IPT are needed. Although clear-cut predictors of response are not available, lower self-esteem and greater eating disorder psychopathology may predict better response to IPT than to CBT-GSH.

### Other psychological treatments

Other psychological treatments receiving attention for BED include CBT with spousal involvement,<sup>51</sup> body image interventions,<sup>52</sup> integrative response therapy,<sup>53</sup> group psychodynamic interpersonal psychotherapy,<sup>54</sup> self-compassion training,<sup>55</sup> and behavioral activation therapy.<sup>56</sup> Preliminary results were favorable for body image interventions, group psychodynamic interpersonal therapy, self-compassion training, and integrative response therapy, but not for CBT with spousal involvement or behavioral activation therapy.

### Physical activity

Vancampfort *et al*<sup>57</sup> reviewed 3 RCTs that assessed physical activity interventions involving 211 female patients with BED. Aerobic and yoga exercises reduced number of eating binges and BMI of BED patients. Aerobic exercise also reduced depressive symptoms. CBT with aerobic exercise, but not CBT alone, reduced BMI. Also, CBT with aerobic exercise was more effective for reducing depressive symptoms than CBT alone.

### Pharmacotherapy

In 2011, the World Federation of Societies of Biological Psychiatry (WFSBP) reviewed the extant pharmacotherapy literature for BED (26 RCTs). It concluded there was evidence for efficacy of sertraline and topiramate in BED.<sup>58</sup> Since then, there have been new reviews, new randomized, controlled pharmacotherapy trials, and the first drug approved for treatment of BED.<sup>14,59–64</sup>

### Stimulants/drugs for attention-deficit/hyperactivity disorder

On January 30, 2015, lisdexamfetamine dimesylate (LDX) received approval from the U.S. Food and Drug Administration (FDA) for the treatment of BED; specifically, it was approved for the treatment of moderate to severe BED in adults.<sup>64</sup> LDX is a prodrug of d-amphetamine that is also approved for treatment of children and adults with attention-deficit/hyperactivity disorder (ADHD). The approval of LDX in BED was based on 2 phase III studies (N = 724).<sup>64,65</sup> One phase II study of LDX in the treatment of BED was also conducted.<sup>66</sup> All 3 studies found LDX superior to placebo for reducing binge eating days, obsessive-compulsive binge eating symptoms, and body weight, and for inducing 4-week binge eating cessation rates. The phase II study found that 50 mg/day and 70 mg/day, but not 30 mg/day, were efficacious for reducing binge eating.<sup>66</sup> The phase III studies both found that LDX, titrated to 50 mg/day or 70 mg/day, was efficacious for reducing binge eating.<sup>65</sup>

The tolerability and safety profile of LDX was consistent with previous findings in adults with ADHD. Long-term safety (NCT01657019) and maintenance (NCT02009163) studies of LDX in BED are ongoing. Importantly, LDX is not indicated for weight loss or the treatment of obesity.

Of note, all 3 studies had similar entry criteria. Patients had to display at least 3 binge days per week recorded on take home diaries during a 2-week screening period and at least moderately severe BED as determined by a Clinical Global Impression Severity score of 4 or greater. Patients were excluded if they had a serious medical condition, including hypertension, coronary artery disease, an arrhythmia, or diabetes. Patients were also excluded if they had current anorexia nervosa (AN), BN, or prominent depressive symptoms, or a lifetime history of mania, hypomania, psychosis, ADHD, or substance abuse. The results of these trials therefore cannot be generalized to BED patients with serious co-occurring medical or psychiatric illness.

Regarding other RCTs of ADHD medications in BED, one small positive study of atomoxetine has been published,<sup>67</sup> and a comparison of extended release methylphenidate with CBT is ongoing (NCT01921582). Additionally, in a small study of 25 patients with bipolar depression, lisdexamfetamine, given as an adjunct to mood stabilizers or antipsychotics, was superior to placebo in reducing severity of binge eating symptoms.<sup>68</sup>

### Antidepressants

A growing number of studies suggest that antidepressants, including tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin norepinephrine reuptake inhibitors (SNRIs),



are modestly effective for reducing binge eating in BED, but generally do not produce clinically significant weight loss.<sup>58–63</sup> Of note, these studies excluded patients with comorbid bipolar disorder and substance use disorders, but permitted entry to patients with depressive symptoms. Importantly, in some of these studies, antidepressants also reduced concomitant depressive symptoms.<sup>42,69</sup> For example, 40 patients with BED and a co-occurring depressive disorder received the SNRI duloxetine or placebo for 12 weeks.<sup>69</sup> Duloxetine (mean dose 78.7 mg/day) was superior to placebo in reducing weekly frequency of binge eating days and binge eating episodes, global severity of BED and depressive symptoms, and body weight. A limitation of these studies is their short duration; no randomized controlled maintenance study of an antidepressant in BED has yet been conducted.

In the only published RCT of bupropion in BED, 61 overweight or obese patients received bupropion 300 mg/day or placebo for 8 weeks.<sup>70</sup> Bupropion was similar to placebo in reducing binge eating frequency but produced greater weight loss. Importantly, it was well tolerated and there were no seizures. Results of RCTs of antidepressants in combination with psychological treatments are mixed. Fluoxetine did not enhance CBT for reducing binge eating or for weight loss in 2 studies.<sup>38,42,47</sup> However, in another RCT, addition of low dose imipramine to diet counseling and psychological support was superior to addition of placebo for weight loss in 31 obese binge eaters.<sup>71</sup> Of note, several antidepressant classes have not yet been evaluated in BED in RCTs, including monoamine oxidase inhibitors (eg, phenelzine and tranylcypromine), serotonin antagonist and reuptake inhibitors (eg, nefazodone and trazodone), serotonin modulator and stimulators (vilazodone and vortioxetine), and tetracyclics (eg, mirtazepine).

### Anticonvulsants

Two RCTs (N = 61, N = 404) found that topiramate monotherapy was superior to placebo for reducing binge eating behavior, obsessive-compulsive binge eating symptoms, and body weight in obese patients with BED.<sup>72,73</sup> Of note, one of these trials permitted entry to BED patients with bipolar disorder.<sup>72</sup> A third RCT (N = 73) found that topiramate (target daily dose 200 mg) plus CBT was superior to placebo plus CBT for weight loss and remission of binge eating.<sup>74</sup> No randomized controlled maintenance studies of topiramate have been conducted in BED, but open-label data suggest that the anti-binge eating and weight loss effects may last up to 1 year.<sup>75</sup> Topiramate's use in BED, however, has been limited by the drug's adverse event profile, especially cognitive impairment. By contrast, evidence that topiramate does not exacerbate mania and is efficacious for alcohol dependence suggests that it may

be useful for BED patients with co-occurring bipolar disorder or substance use disorders, respectively.<sup>76,77</sup>

Other anticonvulsants studied in RCTs in BED are lamotrigine and zonisamide. In a 16-week trial (N = 51), lamotrigine monotherapy failed to separate from placebo in reducing binge eating behavior, obsessive-compulsive binge eating symptoms, and global illness severity, but was associated with a numerically greater amount of weight loss and significant reductions in fasting levels of glucose, insulin, and triglycerides.<sup>78</sup> Zonisamide monotherapy was superior to placebo for reducing binge eating behavior, obsessive-compulsive binge eating symptoms, body weight, and BMI in a 16-week trial (N = 60), but was associated with a high premature discontinuation rate due to adverse events.<sup>79</sup>

### Anti-obesity medications

Four anti-obesity medications have been evaluated in BED in RCTs: the serotonin-releasing agent d-fenfluramine; the lipase inhibitor orlistat; the selective cannabinoid receptor subtype 1 antagonist rimonabant; and the SNRI sibutramine. In these studies, fenfluramine decreased binge eating but not body weight<sup>80</sup>; rimonabant decreased body weight and global binge eating symptoms<sup>81</sup>; and sibutramine reduced binge eating, depressive symptoms, and body weight.<sup>82–85</sup> All 3 drugs have since been removed from the market for safety concerns (cardiovascular events for d-fenfluramine and sibutramine and adverse psychiatric events for rimonabant), and will not be discussed further.

Three RCTs have assessed orlistat in obese patients with BED, with mixed results.<sup>86–88</sup> In the first study (N = 50), orlistat (120 mg TID) with CBT for 12 weeks was superior to placebo plus CBT for weight loss and remission of binge eating.<sup>86</sup> In the second study (N = 89), 24 weeks of orlistat (120 mg TID) plus a mildly reduced calorie diet was superior to placebo plus a mildly reduced calorie diet for weight loss but not binge eating behavior.<sup>87</sup> In the third study, 4 months of orlistat (120 mg TID) plus BWLT was similar to placebo plus BWLT for improvement in binge eating, eating psychopathology, BMI, and depressive symptoms in 79 obese patients, 40 with BED.<sup>88</sup> Additionally, orlistat produced significantly greater weight loss among obese patients without BED but not among those with BED.

Of note is that 4 compounds have recently been FDA approved for weight loss in people with obesity, including the selective serotonin 2C receptor agonist lorcaserin, phenentermine/topiramate combination, bupropion/naltrexone combination, and the glucagon-like peptide-1 analog liraglutide. None of these agents has yet been studied in BED in a RCT. However, bupropion/naltrexone combination significantly decreased global binge eating severity scores in an open-label trial in 25 women receiving

the compound for treatment of major depressive disorder and obesity.<sup>89</sup> Additionally, 2 cases of patients with obesity and BED responding well to phentermine/topiramate combination have been described.<sup>90</sup>

### **Anti-craving or anti-addiction medications**

Several medications or medication classes indicated or used for addictive disorders, including acamprosate, baclofen, and opioid antagonists, have been studied in RCTs in BED. A RCT of the N-methyl-D-aspartate (NMDA) receptor modulator acamprosate (N = 40) found that the drug was superior to placebo in secondary endpoint analyses for reducing binge day frequency and improving measures of obsessive-compulsiveness of binge eating, food craving, and quality of life.<sup>91</sup> However, in the primary longitudinal analysis, acamprosate was not superior to placebo in reducing binge eating frequency. Baclofen, a gamma-aminobutyric acid (GABA) derivative, has been evaluated in one small (N = 12) crossover RCT in individuals with binge eating.<sup>92</sup> Participants received baclofen (titrated to 60 mg/d) for 48 days followed by placebo for 48 days, or the reverse. Relative to placebo, baclofen produced a slight but statistically significant reduction in binge eating frequency. Global binge eating severity and food craving scores were decreased similarly during baclofen and placebo phases. By contrast, baclofen produced a small but statistically significant increase in depressive symptoms.

The few available data on the efficacy of opioid antagonists in BED are mixed.<sup>93,94</sup> In a 6-week RCT (N = 62), the novel opioid antagonist ALKS 33 (now called samidorphan) and placebo produced similar large reductions in binge eating episode frequency.<sup>93</sup> There were also no differences between drug and placebo in other measures of binge eating, eating psychopathology, or body weight. In a Phase II RCT sponsored by Lightlake Therapeutics Inc., which has been reported in abstract form but not yet published, 127 participants with BED received intranasal naloxone spray or intranasal placebo spray for 24 weeks.<sup>94</sup> Naloxone 2 mg was administered before each binge eating episode up to a maximum of 4 mg/day; 81% of participants completed the trial. Naloxone produced a significantly greater reduction than placebo in time spent binge eating. Additionally, among naloxone recipients but not placebo recipients, BMI decreased significantly from week 12 to week 24. There were no serious adverse events. On ClinicalTrials.gov, however, the primary outcome is listed as “change in frequency of binge eating” and not time spent binge eating (NCT01567670).

### **Nutrients**

Chromium is an essential nutrient that may improve mood, appetite, and glucose regulation. In one small

RCT, 24 overweight or obese patients with BED were randomized to one of 3 treatments for 6 months: high dose (1000 mcg/d) chromium, moderate dose (600 mcg/d) chromium, or placebo.<sup>95</sup> Numerically greater reductions in binge frequency, body weight, and depressive symptoms were observed in chromium recipients compared with placebo recipients, but reductions were not statistically significant. Fasting glucose was significantly reduced in both chromium groups, with larger effects noticed with high dose chromium. Chromium was well tolerated.

### **Other medications**

In a recently published RCT of the alerting agent armodanil (N = 60), drug was not superior to placebo on the primary outcome of change in binge eating days per week.<sup>96</sup> However, armodafinil was superior to placebo on several secondary outcomes, including reduction of binge eating episode frequency, obsessive compulsive symptoms of binge eating, and BMI. Medications found to be effective in BED in open-label trials include the NMDA receptor modulator memantine<sup>97</sup> and the cataplexy/narcolepsy medication sodium oxybate.<sup>98</sup>

### **Bariatric Surgery**

Although no RCT of bariatric surgery has been conducted in BED, many patients seeking and receiving such surgery have BED, and many studies have explored the effects of BED on response to bariatric surgery.<sup>99,100</sup> Some studies have found that BED patients do just as well as their non-BED counterparts in terms of weight loss and maintenance of weight loss. Other studies, by contrast, have found that BED is associated with a higher rate of post-operative complications, less weight loss, and more weight regain. Several studies have found that binge eating or loss-of-control eating after surgery is associated with less weight loss.<sup>101</sup>

### **Conclusion**

A growing number of options are available for the treatment of patients with BED (see Table 1). CBT and IPT reduce binge eating behavior over both the short term and the long term, and are considered by some authorities to be the treatments of choice for BED. Other treatments that may be helpful include self-help treatments, especially when clinical guidance is provided, BWLT, mindfulness-based approaches, DBT, and prescription of physical activity. These treatments are all effective for reduction of binge eating symptoms but, with the exception of BWLT, usually do not produce clinically meaningful weight loss. IPT and CBT may be more effective than BWLT for reduction of binge eating. Though BWLT may be more effective for

TABLE 1. Qualitative assessment of most-studied treatments in BED

| Treatment modality     | Effectiveness  |
|------------------------|--|
| Self-help treatments   | Modestly effective for decreasing BE; not effective for weight loss.   |
| Motivational treatment | No evidence of effectiveness.  |
| Mindfulness treatments | Modestly effective for decreasing BE; effects on weight loss mixed.  |
| BWLT                   | Decreases BE and weight over short term but not long term. Both CBT and IPT both more effective for decreasing BE.   |
| CBT                    | Decreases BE over short and long term. Not effective for weight loss but no further weight gain in responders. More effective than fluoxetine for decreasing BE. |
| IPT                    | Decreases BE over short and long term. Not effective for weight loss but no further weight gain.   |
| DBT                    | Decreases BE over short term but not effective for weight loss. Further research needed.   |
| Physical activity      | Aerobic and yoga exercise may reduce binge eating and weight.  |
| Lisdexamfetamine       | Superior to PBO for decreasing BE, OC-BE Sx, and weight. May have long-term effectiveness.   |
| Antidepressants        | Modestly effective in decreasing BE, but not weight, over short term. Effective for comorbid depressive Sx.  |
| Orlistat               | Mixed effects on decreasing weight and BE.   |
| Opioid antagonists     | Mixed effects on decreasing BE and weight  |
| Bariatric surgery      | May be effective for decreasing weight and binge eating but results are mixed.   |

BE, binge eating; BED, binge eating disorder; BWLT, behavioral weight loss treatment; CBT, cognitive behavioral therapy; IPT, interpersonal therapy; OC-BE Sx, obsessive-compulsive binge eating symptoms; PBO, placebo; Sx, symptoms.

weight loss, the weight loss is often not maintained. There are no clear factors that predict response to one versus another psychological intervention, except that lower self-esteem and increased eating disorder psychopathology may favor response to IPT over CBT-GSH and BWLT.

LDX has just been approved for the treatment of moderate to severe BED in adults—an approval based on 2 phase III RCTs. A phase II dose-finding study found LDX at 50 mg/d and 70 mg/d, but not 30 mg/d, was efficacious for decreasing binge eating behavior. Safety and maintenance studies of LDX in BED are ongoing. Topiramate has efficacy in BED based on 3 RCTs, but its use is limited by the lack of controlled maintenance data and adverse effects, especially cognitive impairment. Antidepressants may be moderately helpful for BED, including for associated depressive symptoms, but have not been studied in long-term RCTs. Bupropion may induce modest weight loss in BED associated with obesity without causing seizures. Regarding RCTs of combination treatment in BED, topiramate may enhance the efficacy of CBT, but results are inconsistent regarding the ability of antidepressants and orlistat to enhance BWLT or CBT.

Small RCTs suggest that baclofen and armodafinil may decrease binge eating, and that chromium may have beneficial effects on glucose metabolism in BED associated with overweight or obesity. RCTs of opioid antagonists in BED are mixed; one small study of the opioid antagonist ALKS 33 in BED was negative, while a RCT presented only in abstract form suggests intranasal naloxone may reduce time spent binge eating. Regarding other treatments studied in BED, there are preliminary positive open-label data for body image interventions, self-compassion training, integrative response therapy, memantine, and sodium oxybate.

Unfortunately, there is a paucity of comparative data to inform choice of treatment modality for individual patients with BED. For example, there are no empirically determined guidelines for choosing psychotherapy, pharmacotherapy, or bariatric surgery. Choice of treatment modality is often based on patient preference, as well as comorbid psychiatric and medical illnesses.

For patients who choose psychological treatment, reduced self-esteem and increased eating disorder psychopathology may predict better response to IPT than to CBT-GSH or BWLT. For patients who chose pharmacotherapy over psychotherapy, no comparative data are available to guide medication choice. In BED patients with obesity who want to lose weight, topiramate may be favored over LDX, as topiramate causes clinically significant and persistent weight loss, while LDX's long-term effects on weight are unknown (and it is specifically not approved by the FDA for weight loss). Other factors that would favor use of topiramate over LDX would include comorbid bipolar or substance use disorder, as topiramate does not worsen mania and is efficacious for alcohol dependence, while LDX may destabilize mood in bipolar patients and is generally contraindicated in people with addiction. Factors that might lead to consideration of LDX include comorbid ADHD, inability to tolerate topiramate, or a relative contraindication to topiramate (eg, renal stones). For BED patients who are clinically depressed, treatment with an antidepressant should be considered. Though no adjunctive or combination medication RCTs have yet been conducted in BED, preliminary data suggest some patients may do best with combination pharmacotherapy.<sup>102</sup> Finally, for patients with BED and severe obesity and complications of obesity (eg, hypertension or diabetes) that has not responded adequately to psychotherapy and/or medication, bariatric surgery should be considered.

In short, significant progress has been made in developing treatments for BED, but further research is essential. As the number of therapeutic options for BED increases, it will be increasingly important to individualize treatment for patients with BED.

## Disclosures

Dr. McElroy is a consultant to, or member of the scientific advisory boards, and/or a principal or co-investigator on research studies sponsored by Agency for Healthcare Research & Quality (AHRQ), Alkermes, Bracket, Cephalon, F. Hoffman-La Roche Ltd., Forrest Laboratories, Marriott Foundation, MedAvante, National Institutes of Mental Health, Naurex, Novo Nordisk, Orexigen Therapeutics, Shire, Sunovion, and Takeda Pharmaceutical Company. She is also inventor on United States Patent No. 6,323,236 B2, Use of Sulfamate Derivatives for Treating Impulse Control Disorders, and, along with the patient's assignee, University of Cincinnati, Cincinnati, OH, has received payment from Johnson & Johnson Pharmaceutical Research & Development, L.L.C., which has exclusive rights under the patent. Filed February 18, 2000; approved November 27, 2001. Dr. Keck is a consultant to, or member of the scientific advisory boards, and/or a principal or co-investigator on research studies sponsored by Alkermes, Forest, Cephalon, Marriott Foundation, National Institute of Mental Health (NIMH), Shire, and Sunovion. He is also inventor on United States Patent No. 6,387,956: Shapira NA, Goldsmith TD, Keck, PE Jr. (University of Cincinnati) Methods of treating obsessive-compulsive spectrum disorder comprises the step of administering an effective amount of tramadol to an individual. Filed March 25, 1999; approved Mary 14, 2002.

Anna I. Guerdjikova, Nicole Mori, and Maura Munoz declare that they have no conflict of interest.

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