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Pharmacological Treatment of Binge Eating Disorder: Update Review and Synthesis

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Abstract

Introduction—Binge-eating disorder (BED), a formal eating-disorder diagnosis in the DSM-5, is characterized by recurrent binge-eating, marked distress about binge-eating, and the absence of extreme weight compensatory behaviors. BED is more prevalent than other eating-disorders, with broader distribution across age, sex, and ethnic/racial groups, and is associated strongly with obesity and heightened risk for psychiatric/medical comorbidities.

Areas Covered—This article provides an overview of pharmacotherapy for BED with a focus on III randomized controlled trials (RCTs). The search with minimal methodological inclusion requirements yielded 22 RCTs investigating several different medication classes; most were pharmacotherapy-only trials with eight trials testing combination approaches with psychological-behavioral methods.

Expert Opinion—The evidence base regarding pharmacotherapy for BED remains limited, although this year the FDA approved the first medication (i.e., lisdexamfetamine dimesylate; LDX) specifically for moderate-to-severe BED. Data from RCTs suggests certain medications are superior to placebo for reducing binge-eating over the short-term; almost no data exist regarding longer-term effects of pharmacotherapy for BED. Except for topiramate, which significantly reduces both binge-eating and weight, tested medications yield minimal weight loss and LDX is not indicated for weight loss. Psychological-behavioral and combination approaches with certain medications yield superior outcomes to pharmacotherapy-only acutely and over longer-term follow-up.

Keywords

binge eating disorder; binge eating; pharmacotherapy; medication; placebo; obesity

1. Introduction

Binge eating disorder (BED) is a formal eating-disorder diagnosis in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* [1]. BED is defined by recurrent binge eating (i.e., eating unusually large quantities of food while experiencing subjective feelings of loss of control), marked distress about the binge eating, and the absence

of extreme weight compensatory behaviors (e.g., self-induced vomiting, laxative misuse, excessive exercise, or extreme restraint) that characterize bulimia nervosa. The diagnosis also requires that the binge eating occur at least once weekly over the past three months. BED is prevalent, with an estimated lifetime prevalence rate of roughly 2.6% in adults [2], making this diagnosis more common than bulimia nervosa and anorexia nervosa combined in both the US and world-wide [2, 3]. BED, unlike the two other formal eating disorders, is common in both sexes, across different ethnic/racial and minority groups, and is distributed across broader age groups [2, 4]. BED is associated strongly with obesity and is associated significantly with elevated rates of medical and psychiatric co-morbidity and impairment [2, 3]. BED shares certain features with, but is distinct from, the other eating disorders and obesity [5-7].

2. Body

2.1 Method/Search Strategy

An electronic search was performed for all English-language articles using MEDLINE via PubMed, the Cochrane Library, and Google Scholar using keywords *binge eating* or *binge eating disorder* paired sequentially with terms *pharmacotherapy*, *randomized controlled trial*, and *placebo-controlled* published between January 1, 1985 and March 1, 2015. A supplemental electronic search was performed specifically targeting drug classes (e.g., antiepileptics, antidepressants) and individual medications (e.g., topiramate, fluoxetine). Literature was also searched by cross-referencing and manually-searching reference lists, further utilizing links to *related articles* or *cited by* provided under search results. Registered and ongoing clinical trials for binge eating disorder were identified via the United States National Institutes of Health web-based registry of private and publicly-supported clinical studies. All Phase II and Phase III randomized controlled trials (RCTs) involving 40 subjects which investigated the effects pharmacotherapy for BED (either monotherapy alone or in combination with psychological-behavioral interventions) were considered. We summarized and reviewed RCTs published in peer-reviewed journals. Exclusion criteria were: 1) phase I trials (open-label, case series, retrospective cohort designs), 2) non-English language, 3) N < 40 subjects, 4) studies pertaining to non-purging bulimia nervosa, mixed eating disorder samples, atypical eating disorders, or the ICD 10 category *overeating associated with psychological disturbances*, and 5) studies of withdrawn medications due to safety concerns and adverse effects (i.e., d-fenfluramine, sibutramine, and rimonabant).

3. Overview of Pharmacotherapy for Binge Eating Disorder

The inclusion of BED as a research category in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* [8], stimulated treatment research [9]. Although progress has been made, the treatment literature remains limited and additional research is needed to develop improved methods for treating BED. The present review summarizes the published (in peer-reviewed journals) pharmacotherapy treatment literature for BED with a view towards providing a critical overview with implications for clinical practice and future controlled research.

Table 1 lists 22 trials determined eligible for inclusion in this review. Of these RCTs, the majority tested pharmacotherapy-only treatments for BED, although eight RCTs tested

additive/combination approaches involving pharmacotherapy and some form of psychological-behavioral intervention. Several classes of medications were tested including antidepressants (various mechanisms of action), antiepileptics, anti-obesity agents (three anti-obesity agents have been withdrawn from the market due to safety concerns since our previous meta-analysis of pharmacotherapy for BED [9], leaving orlistat as the sole anti-obesity medication option tested for BED), “anti-craving” agents, and “ADHD” stimulant-type medications. It is important to note that the classification scheme in Table 1 is used for organizational purposes; however, drugs may have several plausible mechanisms by which they affect binge eating. For example, topiramate and lamotrigine have many CNS effects and potential mechanisms of action, so that their classification as an anticonvulsant is somewhat arbitrary.

Table 2 summarizes the designs, methods, and specific findings from the 22 RCTs testing pharmacotherapy (either alone as monotherapy or in combination with psychological-behavioral methods) for BED. We summarize the RCT findings by discussing attrition and two clinical outcomes: binge eating and weight loss. Treatment completion rates are a useful overall metric for treatment acceptability or tolerability plus they provide an important context for interpreting outcome analyses and findings. Binge eating, the core feature of BED, has served as the primary outcome measure in nearly all RCTs, although studies have varied considerably in how binge eating was measured, how binge-eating outcomes were conceptualized (e.g., change or reduction in binge-eating, rate of change in binge eating, abstinence or remission from binge eating, etc), and how binge eating was analyzed. Finally, weight loss – although *not* a core criterion of BED (which is found across all weight categories) was considered for several important clinical reasons: BED is associated strongly with heightened risk for obesity and associated medical comorbidities [2], inspection of BMI characteristics of RCTs summarized in Table 1 reveals that average body mass indices (BMIs) were generally all above 35, and BED is associated with future and often rapid weight gains especially among treatment-seeking persons with BED [10]. The findings are discussed below by different medication classes.

3.1 Antidepressant Medications

Selective serotonin reuptake inhibitors (SSRIs) have been the most frequently studied medication for BED, perhaps reflecting the demonstrated efficacy of fluoxetine for bulimia nervosa (another eating disorder characterized by binge eating) [11] and the FDA approval for that indication. Five RCTs [12-16] tested monotherapy fluoxetine either against placebo [12] against monotherapy sertraline [15] against monotherapy fluvoxamine [16] and against CBT alone and CBT plus monotherapy with one of two SSRIs (fluoxetine or fluvoxamine) [13, 14, 16]. Two RCTs tested whether fluoxetine was superior to placebo for enhancing CBT [14] or BWL [13] short-term outcomes. Fluoxetine was superior on some measures of binge eating to placebo in one 6-week study [12] but not in a second 16-week study [14]; note that in the first study [12], binge-eating reduced significantly faster with fluoxetine than placebo but both end-point analyses and binge-eating abstinence rates were not significantly different between fluoxetine and placebo. Fluoxetine did not differ significantly from either sertraline [15] or from fluvoxamine [16]; one study [15] did not include a placebo or control condition thus precluding any statement about efficacy, while the second study [16] reported that both SSRI anti-depressants (fluoxetine and fluvoxamine) were significantly inferior to CBT alone.

Additional RCTs testing SSRIs [17, 18] and serotonin–norepinephrine reuptake inhibitors (SNRIs) [19] reported that most outcomes failed to differ significantly from placebo. Hudson et al. (1998) [17] reported binge eating reduced faster with fluvoxamine than placebo but there was no statistical difference in binge-eating remission, a statistically significant but clinically-meaningless rate of weight loss (2.7 lbs vs 0.3 lbs) was reported. Escitalopram did not differ significantly from placebo in either binge-eating remission or binge-eating frequency; statistically significant weight loss was reported (mean difference of 3.52 lbs) but this figure is clinically meaningless given the participants' mean BMI of roughly 40 [18].

Findings from the RCTs testing additive/combination approaches converged in suggesting that SSRIs did *not* enhance outcomes achieved by CBT [14] or behavioral treatments [13]. Only three RCTs testing SSRI antidepressants for BED reported longer-term follow-up data following medication discontinuation and they converged in reporting lack of efficacy for both monotherapy fluoxetine [20] and fluvoxamine [16] and no additive effect relative to placebo when combined when CBT [20] or with behavioral weight loss [21]. Four RCTs have tested other antidepressants, including trials testing monotherapy duloxetine [19] and bupropion [22] and a trial with an additive/combination design testing desipramine as part of an added treatment component in a sequential approach with CBT followed by behavioral weight loss [23]. Duloxetine was associated with significantly faster reduction in binge-eating than placebo but did not differ from placebo in binge-eating remission, end-point binge-eating frequency, or weight loss [19]. Bupropion did not differ from placebo on binge-eating remission or binge-eating frequency; bupropion produced statistically significantly greater weight loss than placebo but the amount was clinically insignificant (1.8% BMI loss vs 0.6% BMI loss) [22]. Adding desipramine during the last 6 months of a sequenced CBT-behavioral weight loss treatment did not enhance binge-eating outcomes or weight loss meaningfully (weight loss was statistically significant but not meaningful)[23].

3.2 Antiepileptic Medications

Five RCTs have tested anti-epileptic medications for BED [24-26]. Three RCTs have tested topiramate: two tested monotherapy topiramate versus placebo [25, 26] and one tested topiramate versus placebo for enhancing CBT [24]. Topiramate was significantly superior to placebo [25, 26] for producing faster reductions in binge eating and for achieving binge-eating remission and for resulting in greater weight loss. The binge-eating remission rates achieved in both RCTs testing topiramate for BED were robust (64% and 58%, respectively) and the significant weight losses approached clinical meaningfulness (means of 5.9 kg and 4.5 kg, respectively) making topiramate the only available medication that has resulted in substantial weight losses in patients with BED. One RCT found that the addition of topiramate versus placebo to CBT significantly enhance binge eating remission rates (based on one week end-point analysis) and resulted in significantly and meaningfully greater weight loss (-6.8 kg vs -0.9 kg) [24]. It is important to emphasize, however, that the significant clinical outcomes observed with topiramate must be considered carefully alongside the observed high rates of adverse events and dropout rates (i.e., 47% in one RCT [25] and 28% in another RCT [26]). Moreover, a longer-term open-label maintenance study of topiramate found that 68% of patients discontinued taking topiramate and this was often associated with high rates of adverse events and difficulties tolerating the medication [27]. Interestingly, dropout associated with

topiramate was much lower (ie., roughly 19% attrition) when the medication was combined with CBT in one study [24]. Two RCTs testing other anti-epileptics [28, 29] produced less robust findings than reported for topiramate. One RCT [29] found that zonisamide was significantly superior to placebo for producing more rapid reduction in binge-eating (although binge eating remission rates did not differ) and greater weight loss. A second RCT reported that lamotrigine [28] was not superior to placebo for any measure of binge eating or weight loss.

3.3 Anti-obesity Medications

There has been strikingly little research on anti-obesity medications for BED. Obesity, while not a criterion for BED, is associated strongly with BED in epidemiological studies [2, 3] and is nearly universal among participants in RCTs for BED regardless of recruitment methods and inclusion requirements (see Table 1). Tables 1 and 2 summarize three RCTs testing orlistat (a locally-acting medication that blocks fat absorption in the gut without CNS effects) for BED [30-32]. Two anti-obesity medications have been withdrawn from the market (sibutramine and rimonabant; rimonabant was never marketed in the US and investigation of this agent were halted due to safety concerns). A third drug was removed prior to that (d-fenfluramine) due to safety concerns. None of these agents are reviewed here. It is important to emphasize that, in contrast to research and treatment guidelines for obesity emphasizing longer “lifestyle” interventions, the RCTs testing anti-obesity agents for BED have been relatively short term (acute care) designs.

Three RCTs have tested orlistat [30-32]. One RCT, which tested monotherapy orlistat versus placebo prescribed with a hypocaloric diet [30], reported that orlistat significantly enhanced weight loss but did not differ from placebo for reducing binge eating. Two RCTs tested orlistat versus placebo for enhancing either CBT [31] or behavioral weight loss [32]. The addition of orlistat to CBT did not significantly enhance reductions in binge eating but did significantly enhance weight loss outcomes relative to placebo [31]. A second RCT found that the addition of orlistat to behavioral weight loss did not significantly enhance either binge eating or weight loss outcomes in patients with BED; importantly, this study which randomized obese patients with versus without BED, observed a significant moderator effect for BED (adding orlistat to behavioral weight loss enhanced weight losses relative to placebo among obese patients without BED but not among obese patients with BED)[32].

3.4 Other Medications

Two RCTs have tested different “anti-craving (“anti-addiction”) medications - acamprosate [33] and ALKS-33 [34]; neither trial observed a statistical advantage relative to placebo for any outcome measure and high dropout rates. One trial has tested a selective norepinephrine (noradrenaline) reuptake inhibitor. In a small RCT [35], atomoxetine was reported to be significantly superior to placebo for reducing binge eating, achieving binge-eating remission, and weight loss (although statistically significant, the mean weight losses were clinically meaningless: 2.7 kg for atomoxetine versus 0.0 kg for placebo).

3.5 Stimulant (“ADHD”) Medications

Table 2 summarizes findings from one RCT for a CNS stimulant (“ADHD”) medication for BED [36]. This RCT tested lisdexamfetamine dimesylate (SPD489; LDX) [36] as part of an integrated series of studies with BED funded by the manufacturer of this medication that previously had FDA-approval for the treatment of attention deficit hyperactivity disorder (ADHD). LDX received approval for the treatment of moderate-to-severe BED January 30th, 2015 based primarily on findings from one phase II RCT (NCT01291173), and two essentially identically-designed phase III RCTs testing BED in adults aged 18 to 55 (ClinicalTrials.gov, NCT10718483, NCT01718509). To date, only the Phase II RCT has been published in a peer-reviewed journal [36] and is therefore reviewed here. The reader is referred to Citrome (2015) [37] who provides a systematic review of the efficacy and safety data for LDX compiled from all available sources include LDX product labeling, scientific conferences [38] and ClinicalTrials.gov entries.

McElroy et al (2015) [36] tested the efficacy and safety of LDX for BED in a large sample of patients with “moderate-to-severe” BED (protocol defined as a minimum of 3 or more days with binge-eating per week). LDX (at 50-mg and 70-mg dosing) was significantly superior to placebo on the study’s primary outcome measure – reduction in binge-eating days per week. LDX (at 50-mg and 70-mg dosing) was also superior to placebo on the study’s secondary outcome of binge eating cessation (42.2% and 50.0%, respectively, versus 21.3%). Table 2 also summarizes weight loss outcomes achieved with LDX versus placebo; however, we emphasize here (and in Table 2), that weight loss was examined as a safety measure rather than a clinical outcome measure in this study. LDX was associated with significantly greater weight loss than placebo [36]. With regard to this finding, we note here that the FDA-approval and manufacturer product labeling included a “Limitation of Use” highlighting that LDX is *not* indicated or recommended for weight loss. This is because other sympathomimetic medications for weight loss have been associated with severe cardiovascular problems and the safety and efficacy of LDX for obesity has not been demonstrated.

4. Conclusion

The empirical base regarding pharmacotherapy for BED is still in its early stages and remains limited. The inclusion of BED as a research category in the DSM-IV [8] and the anticipated (and eventual) inclusion of BED as a formal diagnosis in the DSM-5 [1] stimulated additional research. One especially major advance occurred earlier this year (January 2015) when the FDA approved LDX as the first medication with a specific indication for moderate-to-severe BED. On the other hand, two anti-obesity medications (sibutramine, rimonabant) tested for BED have recently been withdrawn from the market or had research stopped due to safety concerns and the majority of pharmacotherapy treatment research continues to consist of relatively small scale RCTs characterized by mixed results ranging from little to modest clinical benefits. The limited number of RCTs performed and published for BED is at odds with the substantial prevalence and public health impact characteristic of BED. BED is more prevalent than the two other formal eating disorders combined and is associated strongly with obesity, with heightened risk for psychiatric and medical comorbidities, and with functional impairment in the US [2] and worldwide [3].

Prior to offering expert opinion regarding the implications of our review findings for clinical practice, we provide a brief overview of major methodological limitations as context. The majority of pharmacotherapy treatment research for BED has been performed by a relatively limited number of investigators and nearly all RCTs were performed in the United States and were funded by industry (i.e., specific drug manufacturers). Nearly all RCTs used media recruitment methods for participants were performed in research specialty clinics. Several studies had a limited sample size, and therefore susceptible to failure to detect a clinically meaningful effect due to inadequate power. Published RCTs were typically of very short duration, ranging 6 to 24 weeks, testing only acute-treatment effects of the medications on BED and very few follow-up data have been reported. The lack of follow-up precludes any guidance regarding optimal length of treatment, durability of the observed acute outcomes, and risk of relapse after medication discontinuation. In addition, typical study eligibility criteria exclude many potential patients with BED (e.g., several pharmacotherapy RCTs – including but not limited to the recent major LDX trial [36] - excluded participants with commonly occurring psychiatric comorbidities) and most RCTs have limited gender and racial/ethnic diversity that diverge from epidemiologic rates. For example, of the N = 2001 participants enrolled in the 22 RCTs reviewed in this paper, 85.2% (N = 1705) were female, and of the 18 RCTs (N = 1682) reporting race data, approximately 79% (N = 1331) of participants were white. Finally, even in the pharmacotherapy-only studies with the best outcomes, a substantial proportion (typically the majority) of patients do not achieve abstinence from binge-eating and most report little weight loss even over the short term.

5. Expert Opinion

Within the context of the methodological limitations noted above, we offer the following expert opinion. Currently, there is only one FDA-approved medication for BED – LDX is indicated for the treatment of moderate-to-severe BED. The product labeling for LDX, however, includes a “Limitation of Use” that LDX not indicated for weight loss, its effects on obesity are unknown, and similar medication classes have been associated with cardiovascular adverse events in the past. LDX is also a DEA-controlled substance and the product labeling including a “Warning” that CNS stimulants have high potential for abuse and dependence and this indicates the need for careful assessment and on-going monitoring for signs of misuse. Alternatively, the effect sizes for binge eating reductions were large in the McElroy et al (2015) [36] RCT and Citrome [37] recently calculated a favorable likelihood to be helped versus to be harmed using LDX based on all sources of data including the two phase III RCTs that have yet to be published [38].

Available empirical evidence from RCTs for additional medications suggests that certain medications are superior to placebo for helping patients to stop binge eating and for achieving faster reductions in binge eating. Certain medications are also superior to placebo, albeit to limited degrees, for achieving weight loss over the short-term; topiramate is the sole medication that appears to reliably produce substantial weight loss over the short term in BED (LDX does result in weight loss but product labeling includes a “Limitation of Use”). Almost nothing is known regarding the longer-term effects of medication for BED and the few available data indicate that relapse occurs following discontinuation. Certain psychological interventions (e.g., CBT) and the combination of medication with CBT/behavioral interventions produce

binge-eating outcomes that are superior to pharmacotherapy-only over both short-term and longer-term follow-ups. Combining medications with CBT/behavioral interventions does not significantly enhance binge-eating outcomes, but the addition of specific medications (e.g., topiramate and orlistat) may enhance weight losses, albeit modestly.

In closing, we offer implications for future research. Larger and longer studies with comprehensive assessment protocols for assessing changes in both binge eating and associated eating-disorder psychopathology is clearly indicated along with added consideration of metabolic functioning which has received essentially no attention to date. In addition to standard efficacy trials, there is a pressing need to perform treatment studies of medications with more diverse patient groups performed in diverse clinical settings in order to increase generalizability (e.g., [32, 39]. Larger studies with greater patient demographic diversity and clinical variability may also allow for the integration of analyses testing predictors and moderators of outcome [40] similar to those performed for CBT approaches [41] and combination treatments [39]. Such research could eventually inform a more rational approach to selecting and prescribing specific medications. Future treatment research should include planned analyses of processes and treatment response. For example, early rapid response has been with positive outcomes with different medications for BED [42, 43]. A pressing need is for longer-term studies which are needed to address clinical questions about optimal treatment length, whether to discontinue medication and/or when to do so and in whom. The BED field needs to consider more fully treatment models for obesity, a frequently co-occurring problem in BED, and view weight control as a chronic or on-going treatment need. Finally, further research is needed using additive or combined approaches in order to enhance outcomes, particularly to enhance weight loss outcomes. For example, four new anti-obesity medications (phentermine/topiramate, lorcaserin, naltrexone/bupropion, and liraglutide) have been recently approved by the FDA for the treatment of obesity but none has been tested for BED.

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Highlights

- Binge-eating disorder (BED), characterized by recurrent binge-eating and the absence of weight compensatory behaviors, is prevalent and associated strongly with obesity and heightened risk for psychiatric/medical comorbidities.
- Review of randomized controlled trials (RCTs) of pharmacotherapy for BED focused on phase III trials.
- The evidence base regarding pharmacotherapy for BED remains limited, with relatively few RCTs and almost no data regarding longer-term effects.
- Certain medications are superior to placebo for reducing binge-eating over the short-term.
- Currently, there is only one FDA-approved medication (lisdexamfetamine dimesylate) specifically for moderate-to-severe BED, but it is not indicated for weight loss or treating obesity (a frequent co-morbid problem).
- Psychological-behavioral and combination approaches with certain medications yield superior outcomes to pharmacotherapy-only acutely and over longer-term follow-up.

Table 1

Characteristics of Phase II and Phase III RCTS (N = 40) investigating pharmacotherapy for binge eating disorder by drug class.

Class	Drug	RCT	N	% Female	% White	Trial length (weeks)	FUP (mo)	Age (yrs)		BMI (kg/m ²)	
								Drug	Placebo	Drug	Placebo
SSRI	Fluoxetine	Arnold et al. (2002) [12]	60	93	88.3	6	None	41.9	40.8	39.6	36.7
		Devlin et al. (2005, 2007) [21]	116	78	77	20	24	43.0 ^a	-	40.9 ^a	-
		Grilo et al. (2005, 2012) [14, 20]	108	78	89	16	6, 12	44.0 ^a	-	36.3 ^a	-
		Ricca et al. (2001) [16] ^b	108	59	NA	24	12	25.9 ^a	-	32.3 ^a	-
		Leombruni et al. (2008) [15] ^b	42	100	NA	24	None	39.6 ^a	-	39.3 ^a	-
	Fluvoxamine	Hudson et al. (1998) [17]	85	90.5	96.4	9	None	41.2	43.0	34.2	36.8
		Ricca et al. (2001) [16] ^b	-	-	-	-	-	-	-	-	-
	Sertraline	Leombruni et al. (2008) [15] ^b	-	-	-	-	-	-	-	-	-
	Escitalopram	Guerdjikova et al. (2008) [18]	44	97.7	75	12	None	36.9	41.0	40.1	40.3
SNRI	Duloxetine	Guerdjikova et al. (2012) [19]	40	88	83	12	None	44.4	35.7	38.7	42.8
Tricyclic	Desipramine	Agras et al. (1994) [23]	108	100	NA	40	3	45.0 ^a		38.6 ^a	
Aminoketone	Bupropion	White & Grilo (2013) [22]	61	100	84	8	None	45.2	43.1	36.2	35.4
Anti-epileptic	Topiramate	Claudino et al. (2007) [24]	73	96	57.5	21	None	41.1	35.4	37.4	37.4
		McElroy et al. (2003) [25]	61	87	NA	14	None	40.9	40.7	44.2	NA
		McElroy et al. (2007) [26]	404 ^c	78.4	84.2	16	None	44.0	45.0	38.0	39.0
	Zonisamide Lamotrigine	McElroy et al. (2006) [29]	60	88.3	71.6	16	None	44.8	43.0	42.7	40.6
		Guerdjikova et al. (2009) [28]	51	76.4	80.3	16	None	46.1	42.9	38.7	41.5
Anti-obesity	Orlistat	Golay et al. (2005) [30]	89	91	97	24	None	41.2	40.6	35.7	37.3

Class	Drug	RCT	N	% Female	% White	Trial length (weeks)	FUP (mo)	Age (yrs)		BMI (kg/m ²)	
								Drug	Placebo	Drug	Placebo
Anti-craving	Acamprosate ALKS-33	Grilo et al. (2005)[31]	50	88	88	12	3	45.2	47.0	36.2	36.8
		Grilo & White(2013)[32]	40 ^d	77.5	0 ^e	12	6	45.9	45.6	39.0	37.2
Norepinephrine reuptake inhibitor	Atomoxetine	McElroy et al. (2011)[33]	40	85	87.5	10	None	46.2	45.8	39.8	39.2
		McElroy et al. (2013)[34]	62	90	81	6	None	40.6	48.6	38.6	39.2
ADHD	LDX ^f	McElroy et al. (2007)[35]	40	83	85	10	None	43.1	39.2	37.3	41.4
		McElroy et al. (2015)[36]	259 ^g	81.5	78	11	None	38.9 ^h	38.0	35.1 ^h	34.3

Note: BED = binge eating disorder; FUP = follow-up; RCT = randomized controlled trial; LDX = lisdexamfetamine dimesylate.

^aTotal sample mean;

^bStudies by Leombruni et al. (2008) and Ricca et al. (2001) included arms to investigate two drugs, thus appearing twice in the table. Please refer to the initial entry for demographic data.

^cDemographic data shown is based on the safety sample (N = 404);

^dAn additional n = 39 obese patients without BED were also randomized to the treatments but they were not considered in the present review. The reader is referred to the publication for findings which notably included BED status as a significant predictor and modifier of outcome;

^eSample included Spanish-speaking-only Latino/as.

^fTwo additional RCTs (NCT01718483 and NCT01718509) of LDX has been presented at a conference [38] and study characteristics are available at <http://www.ClinicalTrials.gov>.

^gIntention-to-treat analyses included 255 adults and safety sample included 259 adults.

^hData shown represents combined total of all 3 dosage groups.

Table 2
Summary of design, methods and outcome for RCTs investigating the pharmacological treatment of BED (1985 – 2015)

Study	Intervention	Recruitment/Assessment	Findings
Agras et al. (1994)[23]	Design: Additive Randomized allocation to one of three treatments: BWL-only for 9 months; CBT for 3 months followed by BWL for 6 months (CBT/WL); or CBT for 3 months followed by BWL for 6 months plus desipramine (CBT/WL-D). Flexible dosing: 25 mg/day up to maximum of 300 mg/day. Mean dose of desipramine was 285 mg/day.	Country: USA Single-site trial Recruitment via media DSM-IV research criteria for BED, including OBE twice weekly for 6months	Attrition (n.s.) WL only: 27% (10/37) CBT/WL: 17% (6/36) CBT/WL-D: 23% (8/36) Abstinence at 36 weeks (n.s.): WL only: 19% CBT/WL: 37% CBT/WL-D: 41% Binge Eating at 36 weeks (n.s.) WL only: 4.5 (1.6) to 1.5 (0.2) CBT/WL: 4.4 (1.4) to 1.2 (1.3) CBT/WL-D: 5.1 (1.4) to 0.9 (0.9) Weight Loss at 36 weeks (n.s.) WL only: 102.9 (15.8) to 99.2 (16.9) CBT/WL: 102.1 (15.7) to 100.5 (17.6) CBT/WL-D: 111.9 (17.4) to 105.9 (20.5)
Hudson et al. (1998) [17]	Placebo-controlled, double-blind, flexible-dose RCT of fluvoxamine Start dosage = 50 mg/day Increased to 300 mg/day, as tolerated End dosage mean = 260 mg/day	Country: USA Multi-site trial Recruitment via media SCID for DSM-III-R; DSM-IV criteria applied	Attrition (p = .04) Drug:31% (13/42) Placebo: 12% (5/43) Abstinence: (ITT, n.s.) Drug: 38% Placebo:26% Binge Eating (p < .01) <i>Note:</i> A treatment-by-time interaction was significant, showing a greater rate of reduction in OBE frequency (mean log) for drug. Weight Loss (p = .04) Drug: 2.7 lbs estimated weight loss Placebo: 0.3 lbs estimated weight loss
Ricca et al. (2001)[16]	Design: Controlled, parallel-series Controlled parallel-series open-label study compared five treatment conditions: CBT; CBT+ fluoxetine ; CBT+ fluvoxamine ; fluoxetine-only ; fluvoxamine-only . Fluoxetine: 30 mg/day Fluvoxamine: 300 mg/day	Country: Italy Two-site study Recruitment via two outpatient clinics DSM-IV criteria assessed by face-to-face interview;EDE (v. 12.0) defined binge frequency (OBE/28 days) administered SCID for DSM-III-R assessed comorbid Axis I disorders.	Attrition (n.s.) CBT: 15% (3/20) CBT + fluoxetine: 27% (6/22) CBT+ fluvoxamine: 22% (5/23) Fluoxetine-only: 24% (5/21) Fluvoxamine-only:27% (6/22). Binge Eating at 6 and 12-months (p < .001) CBT: 18 (2.3) to 8.0 (3.9) to 8.0 (5.1) CBT + fluoxetine: 17 (3.1) to 6.0 (4.6) to 7.0 (3.4) CBT+ fluvoxamine: 18.0 (3.5) to 8.0 (3.2) to 8.0 (2.4)

Study	Intervention	Recruitment/Assessment	Findings
			<p>Findings</p> <p>Fluoxetine-only: 20.0 (4.3) to 19.0 (3.5) to 21.0 (3.1)</p> <p>Fluvoxamine-only: 20.0 (5.8) to 18.0 (2.4) to 18.0 (1.7)</p> <p><u>Weight Loss ($p < .01$)</u></p> <p><i>Note:</i> BMI and OBE were significantly reduced at T1 and T2 for CBT, CBT + fluoxetine, and CBT + fluvoxamine, but not for the drug-only groups.</p>
Arnold et al. (2002)[12]	<p>Placebo-controlled, double-blind, forced titration, flexible-dose RCT of fluoxetine</p> <p>Start dosage = 20 mg/day</p> <p>Increased to 80 mg/day, as tolerated</p> <p>End dosage mean = 71.3 mg/day</p>	<p>Country: USA</p> <p>Single-site</p> <p>Recruitment via media</p> <p>SCID-I/P interview to assess DSM-IV criteria and patients also had 3 OBE weekly for 6 months.</p>	<p><u>Attrition ($p = .02$)</u></p> <p>Drug: 23% (7/30)</p> <p>Placebo: 57% (17/30)</p> <p><u>Abstinence (n.s.)</u></p> <p>Drug: 45%</p> <p>Placebo: 23.8%</p> <p><u>Binge Eating ($p = .03$)</u></p> <p>Drug: 6.0 to 1.8</p> <p>Placebo: 6.1 to 2.7</p> <p><i>Note:</i> A faster rate of reduction for fluoxetine ($p = .03$). Endpoint analyses showed no group difference ($p = .22$)</p> <p><u>Weight Loss ($p = .05$)</u></p> <p>Drug: 3.3 kg loss</p> <p>Placebo: 0.7 kg weight gain</p>
McElroy et al. (2003) [25]	<p>Placebo-controlled, double-blind, flexible-dose RCT of topiramate.</p> <p>Start dosage = 25 mg/day</p> <p>Increased to 600 mg/day, as tolerated</p> <p>End dosage median = 212 mg/day 14 weeks.</p>	<p>Country: USA</p> <p>Single-site trial</p> <p>Recruitment via media</p> <p>DSM-IV-TR established by SCID for DSM-IV</p>	<p><u>Attrition (n.s.)</u></p> <p>Drug: 47% (14/30)</p> <p>Placebo: 39% (12/31)</p> <p><u>Abstinence ($p < .05$)</u></p> <p>Drug: 64%</p> <p>Placebo: 30%</p> <p><u>Binge Eating ($p < .001$)</u></p> <p>Drug: 5.3 (2.8) to < 1.0 OBE/week</p> <p>Placebo: 6.3 (2.8) to approx. 4 OBE/week</p> <p><u>Weight Loss ($p < .001$)</u></p> <p>Drug: 5.9 kg</p> <p>Placebo: 1.2 kg</p>
Devlin et al. (2005, 2007)[13, 21]	<p>Design: Additive</p> <p>Placebo-controlled, double-blind RCT (2 by 2 balanced factorial design) comparing fluoxetine vs. placebo versus CBT + fluoxetine vs. CBT + placebo, all given in addition to behavioral weight loss (BWL).</p> <p>Start dose: 20 mg/day with increase to 60 mg/day after 4-5 weeks; flexible dosing below 60mg/day if needed to manage side-effects.</p>	<p>Country: USA</p> <p>Single-site trial</p> <p>Recruitment via media</p> <p>BED diagnosis established with the EDE-interview (12.0) and additional items from DSM-IV Appendix B.</p> <p>SCID interview assessed comorbid Axis I disorders</p>	<p><u>Attrition (n.s.)</u></p> <p>Fluoxetine-only: 9%</p> <p>Placebo: 13%</p> <p>CBT + fluoxetine: 6%</p> <p>CBT + placebo: 9%</p> <p><u>Binge Eating ($p < .001$)</u></p> <p>At post-treatment and 2-year FUP, the addition of CBT to BWL significantly enhanced reduction in binge eating frequency ($p < .001$)</p>

Study	Intervention	Recruitment/Assessment	Findings
Golay et al. (2005)[30]	Design: Additive Placebo-controlled, double-blind RCT comparing orlistat versus placebo in combination with mildly hypo-caloric diet. Fixed dosage of 120 mg three times daily.	Country: Switzerland Two-site trial Recruitment via clinics DSM-IV criteria for BED. Semi-structured interview by trained clinician.	Findings and binge remission rates (62% vs 33%; $p < .001$) relative to BWL without CBT. <u>Weight Loss (n.s.)</u> At post-treatment and 2-year FUP, no significant main effects for either CBT assignment or medication assignment on weight loss. <u>Attrition</u> Drug: 11% (5/44) Placebo: 29% (13/45) % still meeting DSM-IV BED criteria at end of trial (n.s.) Drug: 23% (9/29) Placebo: 29% (10/34) <u>Binge Eating Frequency (n.s.)</u> Drug: 5.4 to 1.0 Placebo: 6.2 to 1.7 <u>Weight Loss ($p < .001$)</u> Drug: 7.4% weight loss Placebo: 2.3% weight loss
Grilo et al. (2005)[31]	Design: Additive Placebo-controlled, double-blind RCT comparing orlistat versus placebo in combination with cognitive behavioral therapy delivered using guided self-help (CBTgsh). Fixed dosage of 120 mg three times daily.	Country: USA Single-site trial Recruitment via media DSM-IV research criteria for BED established by SCID-I/P for DSM-IV Axis I disorders and confirmed by EDE-interview	<u>Attrition (n.s.)</u> Drug + CBTgsh: 24% (6/25) Placebo + CBTgsh: 20% (5/25) Abstinence ($p < .05$ at post-tx; n.s. at FUP) Drug + CBTgsh: 64% at post-treatment, 52% at 3-month FUP Placebo + CBTgsh: 36% at post-treatment, 52% at 3-month FUP <u>Binge Eating (n.s.)</u> Drug + CBTgsh: 16.4 (8.0) to 3.2 (5.5) to 3.4 (6.5) Placebo + CBTgsh: 13.5 (6.6) to 3.6 (5.2) to 2.8 (5.3) <u>Weight Loss of 5% IBW ($p = .02$; $p = .03$)</u> Drug + CBTgsh: 36% at post-tx and 8% at 3-mo FUP Placebo + CBTgsh: 32% at post-tx and 8% at 3-month FUP
Grilo et al. (2005, 2012) a[14, 20]	Design: Additive Placebo-controlled, double-blind RCT comparing fluoxetine-only , CBT-only , and CBT + fluoxetine Fixed dosage of 60 mg/day. CBT delivered in 16 one-hour individual weekly sessions following manualized protocol.	Country: USA Single-site Recruitment via media SCID for DSM-IV-TR BED	<u>Completion rates for 12-mo FUP</u> Fluoxetine-only: 62.9% (17/27) CBT + fluoxetine: 73% (19/26) CBT + placebo: 78.5% (22/28) <u>Binge abstinence at 12-mo FUP</u> Fluoxetine-only: 3.7% (1/27) CBT + fluoxetine: 26.9% (7/26)

Study	Intervention	Recruitment/Assessment	Findings
McElroy et al. (2006) [29]	Placebo-controlled, double-blind, flexible-dose RCT of zonisamide Start dosage = 100mg/day Increased to 600 mg, as tolerated End dosage mean= 436 mg/day	Country: USA Single-site trial Recruitment via media DSM-IV-TR criteria for BED established by SCID-I/P for Axis I disorders	Findings CBT + placebo: 35.7% (10/28) <i>Note:</i> Fisher's Exact tests showed CBT + fluoxetine and CBT + placebo did not differ from each other, but both differed from fluoxetine-only ($p = .01$). Weight loss in lbs at 12-mo FUP (<i>n.s.</i>) Fluoxetine-only: -1.48 CBT + fluoxetine: -4.13 CBT + placebo: -9.84
			Attrition Drug: 60% (18/30) Placebo: 40% (12/30) Abstinence (<i>n.s.</i>): Drug: 54% Placebo: 45% Binge Eating ($p = .02$) Drug: 4.7 (1.4) to below 2 OBEs/week Placebo: 4.4 (2.0) to below 2 OBEs/week <i>Note:</i> Rate of reduction in OBE frequency was significantly greater in the zonisamide group ($p = .02$). Endpoint analyses for binge frequency were not significant. Weight Loss ($p < .001$) Drug: 4.8 kg loss Placebo: 1.0 kg loss
Claudio et al. (2007) [24]	Design: Additive Placebo-controlled, double-blind RCT comparing topiramate versus placebo in combination with CBT Start dose: 25 mg/day for 14 days, increased to 200 mg/day.	Country: Brazil Multi-site trial Recruitment via media DSM-IV criteria > 17 BES cut-off score binge eating were prescribed additional increments of 25 mg weekly up to maximum dose of 300 mg/day	Attrition Drug: 19% (7/37) Placebo: 28% (10/36) Abstinence ($p = .03$) Drug: 84% Placebo: 61% Binge Eating (<i>n.s.</i>) Drug: 4.2 (3.4) to 0.0 (0.2) Placebo: 3.4 (1.3) to 0.3 (0.6) Weight Loss, ($p < .001$) Drug: 6.8 kg Placebo: 0.9 kg
McElroy et al. (2007) [26]	Placebo-controlled, double-blind, flexible-dose RCT of topiramate Start dosage = 25mg/day Increased to 400 mg over 8-week period, or as tolerated End dosage mean= 300 mg/day	Country: USA Multi-site trial (19 sites) Recruitment via media and clinical referrals DSM-IV criteria est. by SCID I/P and EDE-interview; moderate –to-severe BED defined as 3 binge days/wk in the 2 wks prior to randomization	Attrition (<i>n.s.</i>) Drug: 28% (55/195) Placebo: 30% (5/199) Abstinence ($p < .001$) Drug: 58% Placebo: 29% Binge Eating ($p < .001$)

Study	Intervention	Recruitment/Assessment	Findings
McElroy et al. (2007) [35]	Placebo-controlled, double-blind, flexible-dose RCT of atomoxetine Start dosage = 40 mg/day Increased to 80 mg in 2nd week, increased to 120 mg/day in 3rd week, or as tolerated End dosage mean = 106 mg/day	Country: USA Single-site trial Recruitment via media SCID for DSM-IV-TR	Findings Drug: 4.6 to 0.9 Placebo: 4.6 to 2.2 <u>Weight Loss ($p < .001$)</u> Drug: 4.5 kg weight loss Placebo: 0.2 kg weight gain Attrition (n.s.) Drug: 30% (6 of 20) Placebo: 45% (9 of 20) <u>Abstinence ($p < .05$)</u> Drug: 70% Placebo: 32% Binge Eating ($p < .05$) Drug: 4.2 (1.4) to <2.0 Placebo: 4.9 (2.5) to <2.0 <u>Weight Loss ($p < .01$)</u> Drug: 2.7 (3.7) kg loss Placebo: 0.0 (3.2) kg
Guerdjikova et al. (2008) [18]	Placebo-controlled, double-blind, flexible-dose RCT of escitalopram Start dosage = 10 mg/day Increased to 30 mg/day, as tolerated End dosage mean = 26.5 mg/day	Country: USA Single-site Recruitment via media SCID for DSM-IV	Findings Attrition (n.s.) Drug: 25% (5/20) Placebo: 17.3% (4/23) <u>Abstinence (n.s.)</u> Drug: 50% Placebo: 26% Binge Eating ($p = .04$) Drug: 4.9 (2.6) to 0.9 (1.4) Placebo: 5.1 (2.3) to 1.7 (1.5) <i>Note:</i> No significant group differences were found in rate of improvement, but endpoint analyses indicated some advantage to escitalopram for binge frequency ($p = .04$) <u>Weight Loss ($p < .001$)</u> Drug: 1.0 (2.6) kg weight loss Placebo: 0.6 (2.4) kg weight gain
Leombruni et al. (2008) [15]	Double-blind RCT comparing fluoxetine vs. sertraline Fluoxetine (mg/day) : Start dosage: 10 End dosage: 64.5 (9.9) Sertraline (mg/day) : Start dosage = 25 End dosage = 165.9 (32.3)	Country: USA Single-site trial Recruitment via media SCID-IP to establish DSM-IV BED, EDE-interview	Findings Attrition (n.s.) Fluoxetine: 25% (5/20) Sertraline: 25% (6/20) <u>Binge abstinence (n.s.)</u> Fluoxetine: 53% Sertraline: 60% <u>Weight loss (n.s.)</u> Fluoxetine: 40.2 to 38.5 Sertraline: 38.6 to 36.6

Study	Intervention	Recruitment/Assessment	Findings
Guerdjikova et al. (2009) [28]	Placebo-controlled, double blind RCT of lamotrigine . Start dosage (mg/day): 25 End dosage (mg/day): 236	Country: USA Single-site Recruitment via media SCID for DSM-IV BED	Attrition Drug: 44% (11/26) Placebo: 29% (7/25) Binge abstinence ($p < .001$) Drug: 52% Placebo: 75% Binge day frequency (n.s.) Drug: 3.92 (1.47) to 1.65 (2.35) Placebo: 3.28 (1.31) to 0.76 (1.71) Weight loss (n.s.) Drug: 38.72 (5.38) to 38.24 (5.70) Placebo: 41.52 (7.24) to 41.50 (7.42)
McElroy et al (2011) [33]	Placebo-controlled, double-blind RCT of acamprosate Start dosage (mg/day): 1998 Increased to a maximum dosage of 2997 mg/day.	Country: USA Single-site Recruitment via media SCID for DSM-IV-TR BED	Attrition Drug: 25% (5/20) Placebo: 55% (11/20) Binge abstinence (n.s.) Drug: 32% Placebo: 20% Binge day frequency (n.s.) Drug: 4.5 (2.1) to 1.9 (2.4) Placebo: 4.5 (2.2) to 2.8 (2.5) Mean BMI loss (n.s.) Drug: 39.7 (7.7) to 39.7 (7.4) Placebo: 39.2 (8.4) to 39.7 (8.9)
Guerdjikova et al. (2012)[19]	Placebo-controlled, double-blind RCT of duloxetine Start dosage (mg/day): 30 End dosage (mg/day): 78.7	Country: USA Single-site trial Recruitment via media Patients met DSM-IV criteria (SCID-I/P) for both BED and a current depressive disorder	Attrition (n.s.) Drug: 35% (7/20) Placebo: 30% (6/20) Binge abstinence (n.s.) Drug: 56% Placebo: 30% Binge day frequency ($p = .04$) Drug: 4.0 (1.8) to 1.0 (1.7) Placebo: 3.5 (1.5) to 1.3 (1.2) <i>Note: Significantly greater rate of binge reduction for drug in longitudinal analysis ($p = .04$), but not LOCF endpoint analyses</i> Mean weight loss ($p = .04$), Drug: 38.7 (6.8) to 37.7 (7.5) Placebo: 42.8 (7.6) to 42.9 (7.3)

Study	Intervention	Recruitment/Assessment	Findings
Grilo & White (2013) [32]	Design: Additive Placebo-controlled, double-blind RCT comparing orlistat + BWL versus placebo + BWL Fixed dosage of 120 mg three times daily.	Country: USA Single-site trial Recruitment via community mental health center DSM-5 criteria est. by SCID-I/P and EDE interview following LEAD standard	Attrition Orlistat + BWL: 30% (6/29) Placebo + BWL: 25% (5/20) <i>Note:</i> 90% of both groups completed 6-mo FUP. Binge abstinence at post-tx (n.s.) Orlistat + BWL: 60% (12/20) Placebo + BWL: 70% (14/20) <i>Note:</i> 50% of both groups were in remission at 6-mo FUP. Mean BMI loss (n.s.) Orlistat + BWL: 39.0 (7.0) to 37.9 (6.9) to 37.6 (5.7) Placebo + BWL: 37.2 (5.3) to 36.0 (5.0) to 36.7 (5.3)
McElroy et al. (2013) [34]	Placebo-controlled, double-blind RCT of ALKS-33 Fixed-dose of 10 mg/day, but 1 dose decrease to 5 mg/day permitted in event of poor tolerability	Country: USA Multi-site 2 academic ED programs and 4 private research centers SCID-P for DSM-IV-TR BED	Attrition Drug: 50% (16/32) Placebo: 11% (4/37) Binge abstinence (n.s.) Drug: 35% (9/26) Placebo: 53% (19/36) Binge frequency reduction/wk (n.s.) Drug: -3.3 (2.4) Placebo: -3.2 (1.8) Weight loss (n.s.) Drug: -0.03 (2.02) Placebo: -0.23 (3.16)
White & Grilo (2013) [22]	Placebo-controlled, double-blind RCT of bupropion Fixed dose of 300 mg/day	Country: USA Single-site Recruitment via media advertisements for overweight women seeking weight loss and binge eating treatment SCID-I/P for DSM-IV BED, EDE-interview	Attrition Drug: 13% (4/31) Placebo: 10% (3/30) Binge abstinence (n.s.) Drug: 42% Placebo: 27% Binge frequency/wk decrease (n.s.) Drug: 3.3 (3.3) to 0.8 (1.2) Placebo: 3.0 (2.6) to 1.0 (1.5) Weight loss Drug: 1.8% BMI loss or 1.68 (2.59) kg Placebo: 0.6% BMI loss or 0.43 (2.12) kg <i>Note:</i> Bupropion was associated with significantly greater rate of weight loss in the mixed models.

Study	Intervention	Recruitment/Assessment	Findings
McElroy et al. (2015) [36]	Randomized, double-blind, parallel-group, forced dose titration, placebo-controlled trial of lisdexamfetamine dimesylate (LDX) at 30, 50, or 70 mg/day^a . Start dose = 30 mg/day. 3-week forced-dose titration period was followed by an 8-wk dose-maintenance period. Patients assigned to 50 or 70 mg/day were titrated weekly by 20 mg/d until reaching their target. Capsules were taken orally 1 × per day for 11 weeks.	Country: USA Multi-site trial Recruitment via media DSM-IV-TR criteria est. by SCID-I/P and EDE interview Inclusion required protocol-defined moderate-to-severe BED operationalized as ≥ 3 binge days per week	<p>Attrition Placebo: 26.9% (17/63) LDX 30: 22.7% (15/66) LDX 50: 20% (13/65) LDX 70: 20% (13/65)</p> <p>Binge cessation (no binge episodes during last 4 weeks of trial)* Placebo: 21.3% LDX 30: 34.9% LDX 50: 42.2% LDX 70: 50.0%</p> <p><i>Note:</i> LDX 50 and 70-mg/d groups differed significantly from placebo at $p < .01$ and $p < .001$, respectively (Cochran-Mantel-Haenszel).</p> <p>Binge day frequency (mean pre- and post; non- and log-transformed least squares [LS] mean (SE) change from baseline to 11 weeks) Placebo: 4.3 to 1.1; -3.3 (2.04); -1.23 (0.069) LDX 30: 4.5 to 1.0; -3.5 (1.95); -1.24 (0.067) LDX 50: 4.5 to 0.4; -4.1 (1.52); -1.49 (0.066) LDX 70: 4.6 to 0.5; -4.1 (1.57); -1.57 (0.067)</p> <p><i>Note:</i> Differences for LS mean change of log-transformed binge days per week were significant for 50 mg/d and 70 mg LDX vs placebo but not 30 mg LDX in mixed models analysis.</p> <p>Weight loss (kg)^b Placebo: -0.1 (3.09) LDX 30: -3.1 (3.64) LDX 50: -4.9 (4.43) LDX 70: -4.9 (3.93)</p> <p><i>Note:</i> Weight was assessed as a safety variable not an efficacy measure. Post-hoc analyses indicated a significantly greater reduction in percentage body weight for all treatment groups at week 11.</p>

Note: BED = binge eating disorder; RCT = randomized, placebo-controlled trial; n.s. = non-significant findings; ITT = intent-to-treat analysis; OBE = objective binge episode; BWL = behavioral weight loss, CBT = cognitive-behavior therapy; ADHD: attention-deficit hyperactivity disorder. *Note:* BED = binge eating disorder; RCT = randomized, placebo-controlled trial; n.s. = non-significant findings; ITT = intent-to-treat analysis; OBE = objective binge episode; BWL = behavioral weight loss, CBT = cognitive-behavior therapy;

^aTwo additional RCTs (NCT01718483 and NCT01718509) of LDX have been presented at a conference [38] and the results and trial characteristics of those phase III trials are available at <http://www.ClinicalTrials.gov>. The results of the RCTs testing LDX that were used to seek and obtain FDA approval for its use for "moderate-to-severe BED" were compiled from [ClinicalTrials.gov](http://www.ClinicalTrials.gov) (NCT01718483 and NCT01718509) and conference presentations [38] and summarized by Citrome [37]. The reader is referred to Citrome [37] for those results which are consistent with the first RCT findings shown here in Table 2. We do not review those findings in the present review as they are still not published in a peer-reviewed outlet. We have added this information and referencing in light of the recent FDA-approval.

^bThe LDX manufacturer emphasizes and the product label includes a "Limitation of Use" that LDX is not indicated or recommended for weight loss, that other sympathomimetic medications for weight loss have been associated with severe cardiovascular problems, and that neither the safety nor efficacy of LDX for treating obesity have been shown. The LDX product label also includes a "Warning" that CNS stimulants have potential for abuse and dependence and indicating the need for careful assessment and on-going monitoring for signs of misuse.