

Psychological, pharmacological, and combined treatments for binge eating disorder: A systematic review and meta-analysis (#24297)

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I commend the authors for their extensive data set, compiled over many years of detailed fieldwork. In addition, the manuscript is clearly written in professional, unambiguous language. If there is a weakness, it is in the statistical analysis (as I have noted above) which should be improved upon before Acceptance.

Psychological, pharmacological, and combined treatments for binge eating disorder: A systematic review and meta-analysis

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Objective: To systematically review the efficacy of psychological, pharmacological and combined treatments for binge eating disorder (BED). **Method:** Systematic search and meta-analysis. **Results:** We found 45 unique studies with low/medium risk of bias, and moderate support for the efficacy of Cognitive Behavior Therapy (CBT) and CBT guided self-help (with moderate quality of evidence), and modest support for Interpersonal Psychotherapy (IPT), Selective Serotonin Reuptake Inhibitors (SSRI) and lisdexamfetamine (with low quality of evidence) in the treatment of adults with BED in terms of cessation of or reduction in the frequency of binge eating. The results on weight loss were disappointing. Only lisdexamfetamine showed a very modest effect on weight loss (low quality of evidence). While there is limited support for the long-term effect of psychological treatments, we have currently no data to ascertain the long-term effect of drug treatments. Some undesired side effects are more common in drug treatment compared to placebo, while the side effects of psychological treatments are unknown. Direct comparisons between pharmaceutical and psychological treatments are lacking as well as data to generalize these results to adolescents. **Conclusions:** We found moderate support for the efficacy of CBT and guided self-help for the treatment of BED. However, IPT, SSRI and lisdexamfetamine received only modest support in terms of cessation of or reduction in the frequency of binge eating. The lack of long-term follow-ups is alarming, especially with regard to medication. Long-term follow-ups, standardized assessments including measures of quality of life, and the study of underrepresented populations should be a priority for future research.

**Psychological, pharmacological, and combined treatments for binge eating disorder: A
systematic review and meta-analysis**

Running title:

Systematic review of treatment of BED

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Abstract

Objective: To systematically review the efficacy of psychological, pharmacological and combined treatments for binge eating disorder (BED). **Method:** Systematic search and meta-analysis. **Results:** We found 45 unique studies with low/medium risk of bias, and moderate support for the efficacy of Cognitive Behavior Therapy (CBT) and CBT guided self-help (with moderate quality of evidence), and modest support for Interpersonal Psychotherapy (IPT), Selective Serotonin Reuptake Inhibitors (SSRI) and lisdexamfetamine (with low quality of evidence) in the treatment of adults with BED in terms of cessation of or reduction in the frequency of binge eating. The results on weight loss were disappointing. Only lisdexamfetamine showed a very modest effect on weight loss (low quality of evidence). While there is limited support for the long-term effect of psychological treatments, we have currently no data to ascertain the long-term effect of drug treatments. Some undesired side effects are more common in drug treatment compared to placebo, while the side effects of psychological treatments are unknown. Direct comparisons between pharmaceutical and psychological treatments are lacking as well as data to generalize these results to adolescents. **Conclusions:** We found moderate support for the efficacy of CBT and guided self-help for the treatment of BED. However, IPT, SSRI and lisdexamfetamine received only modest support in terms of cessation of or reduction in the frequency of binge eating. The lack of long-term follow-ups is alarming, especially with regard to medication. Long-term follow-ups, standardized assessments including measures of quality of life, and the study of underrepresented populations should be a priority for future research.

Introduction

Binge eating disorder (BED) became an official diagnosis within the Eating and Feeding disorders in the fifth edition of the Diagnostic and statistical Manual for Mental Disorders (DSM-5: American Psychiatric Association 2013). BED is characterized of episodes of eating an amount of food that is definitely larger than most people would eat during similar circumstances and a similar period of time while experiencing a lack of control over eating.

Epidemiological studies suggest that 1-4% in the population suffer from BED (Hoek 2006; Kessler et al. 2013). The onset is usually in the late adolescent or early adult years (Nicholls et al. 2011) with an increasing incidence in the late adolescence and early adulthood in both sexes (Hudson et al. 2007; Stice et al. 2013). Recent studies suggest that the lifetime prevalence of BED (1.4%) is higher than that of bulimia nervosa (0.8%)(Kessler et al. 2013).

Patients with BED often present with comorbid psychiatric and somatic diagnoses, lower quality of life, more suicide ideation and attempts, and lower social functioning compared to the general population (Agh et al. 2015; Favaro & Santonastaso 1997; Grilo et al. 2009; Hudson et al. 2007; Kessler et al. 2013; Ulfvebrand et al. 2015; Wilfley et al. 2003). In studies using semi-structured interviews, the lifetime prevalence of obesity in BED-patients is 42-49% (Hudson et al. 2007; Kessler et al. 2013), which translates into an increased risk of conditions as diabetes and metabolic syndrome (Citrome 2017), with increased health care consumption and health care costs (Agh et al. 2015).

In terms of treatment interventions, Cognitive Behavior Therapy (CBT), CBT guided self-help (CBT-gsh), Interpersonal Psychotherapy (IPT), behavior weight loss (BWL), dialectical behavior therapy (DBT), pharmaceutical treatments and different combinations of medical and psychological treatments have been studied (e.g., Grilo 2017; McElroy 2017). CBT and CBT-gsh are the most well studied treatments, with a large number of studies. BWL programs have been evaluated in individual (Wilson 2011), group (Munsch et al. 2007), and self-help program formats (Grilo & Masheb 2005). Since a majority of BED patients also suffer from overweight or obesity many treatments have not only addressed the binge-eating behavior, but also aimed at weight loss (e.g., Agras et al. 1994). Some studies have also

investigated the effect of bariatric surgery on binge eating behaviors, in addition to its weight loss effects (Colles et al. 2008; de Man Lapidoth et al. 2011; de Zwaan et al. 2010; McElroy et al. 2011a; McElroy et al. 2011b).

In terms of pharmacological treatments, the efficacy of a broad spectrum of pharmacotherapeutic agents have been investigated (McElroy 2017). Given the short-term efficacy of anti-depressants, specifically fluoxetine, for bulimia nervosa, anti-depressants for BED has been studied in several randomized controlled trials (RCT). Due to high comorbidity of overweight and obesity in BED (de Man Lapidoth et al. 2006; de Zwaan 2001; Decaluwe & Braet 2003; Vamado et al. 1997), the efficacy of anti-obesity agents such as fenfluramine, orlistat and sibutramine have also been investigated. On the basis of the hypothesized biological underpinnings of BED or similarity with some other conditions such as addiction disorders (McElroy 2017), other drugs such as antiepileptics (e.g., topiramate, and lamotrigine) as well as drugs that are usually prescribed for attention deficit and hyperactivity disorders (e.g., lisdexamfetamine), or anti-addiction drugs (e.g., naloxone) have also been tested. Most of the pharmacological trials are short-term interventions (6-16 weeks) with effects investigated at post-treatment, but almost no long-term follow-ups exist.

There have been some previous reviews and meta-analyses of the treatment of BED that have focused on RCTs (e.g., Amianto et al. 2015; Brownley et al. 2016; Brownley et al. 2015; Grilo 2017; Iacovino et al. 2012; McElroy 2017; McElroy et al. 2015b; Reas & Grilo 2014; Reas & Grilo 2015; Vocks et al. 2010). Brownley and colleagues (2016) found nine RCTs that investigated psychological treatments versus waitlist controls and 25 RCTs investigating the effect of drugs. Significantly more participants achieved abstinence from binge eating with CBT versus waitlist. Other forms of psychological treatments such as dialectic behavior therapy and behavioral weight loss also reduced binge-eating and related psychopathology. CBT (whether delivered in therapist-led, partially therapist-led, or CBT-gsh) did not significantly reduce weight or symptoms of depression. Interestingly, the authors defined many forms of therapy such as psychodynamic psychotherapy as a BED-focused CBT. Further, the review reported that second-generation antidepressants (SGA) such as citalopram, fluoxetine, and

sertraline decreased binge eating and reduced symptoms of depression. Similar outcomes were found for topiramate as well. Lisdexamfetamine reduced binge-eating and binge-eating-related obsessions and compulsions. Interestingly only lisdexamfetamine and topiramate reduced weight. However, the authors note the inconsistencies of outcome measures across trials and the paucity of assessments beyond the end of treatment (Brownley et al. 2015). A review evaluating controlled studies of pharmacotherapy for BED found 22 RCTs (Reas & Grilo 2015) of which 14 were pharmacotherapy-only trials and 8 trials investigating combinations with CBT and/or BWL. All but two studies had been reported in an earlier report by the authors (Reas & Grilo 2014). Reviews of RCTs suggest that the outcome of psychological treatments and their combination with drugs are superior to drugs only, while the combined treatments of BED (Grilo 2017; Reas & Grilo 2014) failed to show superiority compared to CBT only. Nevertheless, adding some drugs to psychological treatments might enhance the level of weight loss, compared to CBT or BWL treatment only, although the effects are modest (Reas & Grilo 2014). Summing up, reviews of treatment research of BED showed that CBT, individually or in groups, was most researched and produced the best results in terms of proportion of patients reaching remission compared to waiting list. The evidence-base for pharmacotherapy was limited. In the short term SGAs seem to reduce the number of binge episodes but there are almost no RCTs on longer-term effects.

The outcome of reviews and meta-analyses is highly dependent on the inclusion and exclusion criteria, and transparency in the procedure is crucial for solid and reliable interpretation of outcomes. It has been suggested that systematic reviews often do not report key information adequately, which limits their potential usefulness and the reliability of the conclusions (e.g., Hemels et al. 2004; Moher et al. 2007). The PRISMA statement (Moher et al. 2009) provides a clear frame for high transparency in all the steps of systematic reviews and meta-analysis.

Aims of the study

Given the importance of independent replications, the aim of the present study was to evaluate the efficacy and quality of evidence, as well as side-effects of controlled psychological, pharmacological, and combined treatment interventions for BED. Eligible outcomes were remission, episodes of binge

136 eating, weight loss, measures of specific psychopathology of eating disorders, depressive symptoms,
137 quality of life, and side effects. **To produce a high quality review** included only studies characterized
138 by low or moderate risk of bias.

140 **Methods**

141 The systematic review was conducted in accordance with the PRISMA statement (Moher et al. 2009).
142 The inclusion criteria were as follows: randomized controlled trials (RCT) and prospective controlled
143 clinical trials (CCT), participants with full or threshold BED according to DSM-IV (American Psychiatric
144 Association 2000) research criteria, or BED according to DSM-5 (American Psychiatric Association
145 2013) regardless of age or weight status, and all types of interventions except for outdated treatment
146 (e.g., studies investigating drugs that have been withdrawn from the market due to serious side effects).
147 **Eligible** outcomes were remission, episodes of binge eating, weight loss, measures of specific
148 psychopathology of eating disorders, depressive symptoms, quality of life, and **side effects**. We did not
149 decide upon imposing any a priori specific inclusion or exclusion criteria regarding the duration of
150 treatment, length of follow-up(s) or number of participants.

151 **Search strategy**

152 The databases PubMed (NLM), Embase (Elsevier), Cochrane Library (Wiley), Scopus and HTA
153 databases from Centre for reviews and disseminations (CRD) were searched until November 2015. The
154 search was updated again in November 2016. Reference lists and books were also used to identify further
155 studies. Search strategies are listed in Appendix A. Two reviewers screened the titles and abstracts
156 independently. Full text articles were retrieved if one or both reviewers considered a study potentially
157 eligible. Both reviewers read the full texts, and consensus was reached regarding eligibility. The
158 excluded articles are provided in Appendix B.

159 Two pairs of reviewers assessed eligible studies for risk of bias independently. Studies were
160 scored as having either high or acceptable (i.e., low or medium) risk of bias. Assessment of the risk of
161 bias of each study was based on the quality of the randomization procedure and equality of the conditions

before the treatment, allocation concealment, blinding (participants, assessors, treatment providers), drop-out (<30% of total sample and <10% difference between the conditions), potential conflict of interest, and analysis of confounders. Studies were excluded if they were not controlled, or if the drop-out rate was lag¹ than those reported above. In addition to independent ratings by at least two experts for each paper, whenever any minor issues related to randomization, allocation, blinding etc. were unclear, they were thoroughly discussed by the entire group to reach consensus on the level of risk of bias. Only studies with acceptable risk of bias were included in this review.

Data management

For all studies, we extracted country, type of setting, method of recruitment, type of treatment, treatment length, number of sessions, treatment format, age, Body Mass Index (BMI) and gender. Extraction from drug treatments also included dosage during the trial. Study characteristics are reported in Appendix C. Outcomes included remission defined as complete cessation of binge eating, BE frequency (i.e. number of binges/week), BMI (weight reduction), specific psychopathology of eating disorder² depressive symptoms, and quality of life, and side effects.

Statistical analysis

For dichotomous outcomes, we estimated the risk difference (RD) or risk ratio (RR) and for continuous outcomes we estimated the mean difference (MD) or standard mean difference (SMD). All outcomes were reported with 95% confidence intervals (CI). Dichotomous effects were weighted using the Mantel Haenszel method and continuous effects were weighted using Inverse Variance.

In one case we contacted the authors and received supplementary data from one study (Schlup et al. 2009), which enabled inclusion in the meta-analysis. Data synthesis was carried out using Rev Man (5.3) (Review Manager (RevMan) 2014), employing the random effects model due to clinical heterogeneity.

The certainty of evidence was assessed with Grading of Recommendations Assessment, Development and Evaluation (GRADE: strong, moderate, low or insufficient) (Guyatt et al. 2008). In brief, preliminary certainty of the evidence was classified as high (labeled ⊕⊕⊕⊕) if the results were based on data from

RCT, otherwise the preliminary certainty of evidence starts with low (labeled $\oplus\oplus\text{OO}$). Thereafter, we analyzed to what extent the results from the meta-analysis might be affected by the five risk domains in GRADE. These are: overall risk of bias across studies, degree of heterogeneity between studies (inconsistency), size of the confidence intervals for the summary measures (imprecision), risk for publication bias and risk that the results are not generalizable to the actual context (indirectness). The final certainty of the evidence depended on whether there were severe deficiencies in any of the five risk domains. Thus, the resulting certainty of evidence could be high ($\oplus\oplus\oplus\oplus$), moderate ($\oplus\oplus\oplus\text{O}$), low ($\oplus\oplus\text{□□}$) or insufficient/very low ($\oplus\oplus\text{OO}$). One special rule was applied; if an intervention was evaluated in only one small study (size<100) the certainty of the evidence was assessed as very low/insufficient ($\oplus\text{OOO}$).


Results

The search of the databases resulted in 3595 publications and the abstracts of these were screened (See Figure 1). Of these, 296 were obtained in full text and screened. A total of 99 were then classified as relevant according to the inclusion and exclusion criteria. At this stage we classified the trials according to drug, psychotherapy, or a combination of drug and psychotherapy (1:st classification). Among the selected 99 publications we found 45 unique studies (54 publications) with low/medium (i.e., acceptable) bias risk. A total of 45 publications were assessed as high bias risk and were not included in the analysis. See Appendix B for excluded publications.

Please insert Figure 1 here

Taken together, the most common reasons for exclusion due to high risk of bias were unclear randomization, allocation, whether assessors were blinded and high drop out.


Study characteristics

All of the included studies were RCT's. The studies included 4611 participants (range 18-773) and they were conducted in North America and Europe with the exception of one study from South America. Participants were 18 years and older, recruited mainly from out-patient settings and through a  and the majority were women. Standardized diagnostic interviews were used to establish BED diagnosis. The majority of studies had a lower inclusion criteria regarding BMI in the overweight to obese weight spectrum. However, the outcome of the treatment of BED was not presented separately for participants with or without concurrent obesity in any of the studies. Please see Appendix C for detailed characteristics of included studies.

Interventions

The trials included a variety of interventions and various combinations of them (drugs, psychotherapy, behavioral weight loss (BWL), and low-energy-density diet counseling) in different formats (individual or group, as well as self-help with or without support) and different control conditions (wait list or placebo). We first classified the trials according to drug, psychotherapy, or a combination of drug and psychotherapy (1:st classification). In the second step, we identified and matched those with similar treatment and control condition. This resulted in the following potential meta-analyses: Drugs vs. placebo (SSRI, lisdexamfetamine, mood stabilizer, anorexiant), combination of drug and CBT/CBT-gsh vs. placebo, CBT vs. wait list, CBT-gsh vs. wait list, IPT vs. CBT/CBT-gsh, and BWL vs. CBT/CBT-gsh.

Included studies not in the meta-analyses per 1:st classification

Drug vs. placebo: For some of the remaining studies with acceptable risk of bias, only one study per drug was identified. There was insufficient scientific evidence to assess the effect  the following drugs (n<100): bupropion (Norepinephrine–dopamine reuptake inhibitor, NDRI) (White & Grilo 2013), duloxetine (Serotonin–norepinephrine reuptake inhibitor; SNRI)(Guerdjikova et al. 2012), baclofen (muscle relaxant)(Corwin et al. 2012), imipramine (tricyclic antidepressant) (Laederach-Hofmann et al. 1999) and armodafinil (sympathomimetic) (McElroy et al. 2015a). One study investigated fluoxetine vs. sertraline (Leombruni et al. 2008). Thus, a total of 14 studies were included in the meta-analyses for drugs vs. placebo for BED.

Combination of drug and psychological treatment: The remaining five studies with acceptable risk of bias investigated unique combinations of drug and psychological treatment. All studies were too small ($n < 100$) and thus there was insufficient scientific evidence to assess the following combinations; desipramine (tricyclic anti-depressive) + CBT (Agras et al. 1994), topiramate (anticonvulsive) combined with CBT (Claudino et al. 2007), orlistat (anorexiant) combined with CBT-gsh (Grilo et al. 2005a), orlistat (anorexiant) combined with BWL (Grilo & White 2013), and fluoxetine (SSRI) combined with CBT (Grilo et al. 2005b).

Psychological treatment: Of the remaining 24 studies (i.e., 31 publications) with acceptable risk of bias, 13 were not included in any meta-analysis. Alfonsson (2015) investigated behavioral activation vs. wait list, and Shapiro (2007) investigated CBT for healthy eating and weight control in group format as one of three arms (the wait list vs. CBT-gsh comparison were included in the CBT-gsh vs. wait list meta-analyses). These two interventions were assessed as providing a too general CBT approach not including the specific eating disorder interventions as the included publications in the meta-analysis for CBT vs. wait list. The mindfulness based eating awareness training condition and psychoeducation with elements of CBT condition vs. wait list (Kristeller et al. 2014) were excluded due to too low similarity with the included interventions in the meta-analysis for CBT vs. wait list. In addition, in some studies only one study per intervention was identified; brief strategic therapy vs. CBT (Castelnuovo et al. 2011), adapted motivational interviewing combined with self-help vs. self-help (Cassin et al. 2008), self-help combined with Treatment as Usual (TAU) vs. TAU (Grilo et al. 2013), shape exposure CBT vs. cognitive restructuring CBT (Hilbert & Tuschen-Caffier 2004), CBT combined with low calorie diet (Masheb et al. 2011), CBT vs. CBT in group format (Ricca et al. 2010) and finally a study with three conditions; CBT vs. schema therapy vs. Appetite focused CBT (McIntosh et al. 2016).

In Carter (1998), only the CBT-gsh vs. wait list was included (the third condition, self-help, was not included in any meta-analysis) (Carter & Fairburn 1998). The CBT vs. BWL comparison from the Grilo (2011) study was included while the third arm (CBT+BWL) was not included in any meta-analysis.

In Kelly et al (2014) the self-help meal planning combined with self-compassion therapy arm was not included. However, we included the CBT-gsh vs. wait list comparisons (Kelly & Carter 2014).

Overall evidence quality

The GRADE method was used and the majority of studies were downgraded 2 levels. The two most common reasons for downgrading were precision and study quality. Only four meta-analyses received moderate rating (the highest level of quality in this review assigned to any single study) and the majority received limited evidence of quality. Please see Table 1 for details.

Meta-analyses

In the following, we present the summary of the meta-analyses (please see Table 1 for detailed information on each meta-analysis). The results from the RD analyses should be interpreted as per this example; $RD = 0.15 [0.02; 0.27]$ means that for every set of 1000 participants receiving treatment, there was 150 [95% CI: 20-270] more remitted persons among those who received the treatment compared to those in the control condition. Regarding side effects, only significantly reported differences between groups are reported in this summary.

Please insert Table 1 here

SSRI vs. placebo

SSRI vs. placebo was investigated in six studies (Grilo et al. 2012; Grilo et al. 2005b; Guerdjikova et al. 2008; Hudson et al. 1998; McElroy et al. 2000; McElroy et al. 2003; Pearlstein et al. 2003). Participants' age were 18-60 years, mostly women (>70%) with weight >85% of ideal body weight. Treatments ranged between 6-16 weeks and only one study reported 6 and 12 months follow ups (Grilo et al. 2012; Grilo et al. 2005b). Flexible dosage and titration was used in all studies but one (Grilo et al. 2005b).

Remission was reported in all six studies ($n = 264$). The $RD=0.15$ was in favor of SSRI treatment compared with placebo at the end of the treatment. *Binge eating frequency* was reported in all six studies ($n = 257$), and comparisons resulted in $SMD = -0.45$ in favor of SSRI treatment compared with placebo at the end of the treatment. *Eating disorder psychopathology* was only reported in one study comparing SSRI vs. placebo (Grilo et al. 2005b). *BMI* was reported in five studies ($n = 237$) (Grilo et al. 2005b; Guerdjikova et al. 2008; Hudson et al. 1998; McElroy et al. 2000; McElroy et al. 2003). There was no significant difference for SSRI vs. placebo. *Symptoms of depression* were reported in four studies ($n = 148$) (Grilo et al. 2005b; Guerdjikova et al. 2008; McElroy et al. 2003; Pearlstein et al. 2003) showing no significant difference between SSRI and placebo.

Side effects. Hudson et al reported significantly more insomnia, nausea, and abnormal dreams in the fluoxetine condition compared with placebo (Hudson et al. 1998). McElroy et al (2003) reported significantly more fatigue and perspiration in the citalopram group compared with the placebo group (McElroy et al. 2003). There were significantly more participants in the sertraline group who reported insomnia (McElroy et al. 2000). One study reported 1.3 to 4 times more sedation, nausea, dry mouth and decreased libido (Pearlstein et al. 2003).

Lisdexamfetamine vs. placebo

One research group had two publications ($n = 850$) (McElroy et al. 2015c; McElroy et al. 2015d) including a multicenter study with participants from Holland, Spain and Sweden (McElroy et al. 2015c). Hence, the results from three samples are combined for this meta-analysis. Participants were 18-55 years, mostly women >81% with a BMI range of 18-45. Treatment length was 11 or 12 weeks. One study (McElroy et al. 2015d) investigated the effect of flexible dosages (30-70 mg/day), while the other one (Guerdjikova et al. 2016) administered a standardized dosage (70 mg/day). The outcomes are based on those who received 70 mg/day. The studies did not report any follow up data.

Remission was reported in three studies ($n = 850$). The $RD = 0.25$ was in favor of lisdexamfetamine compared to those receiving placebo at the end of treatment. *Binge eating frequency* was reported in all three studies ($n = 849$). There was a significant difference in favor for lisdexamfetamine compared with

placebo (Table 1). *Eating disorder psychopathology* was not reported. *BMI*: Three studies reported weight difference from baseline ($n = 852$), and the result ($SMD = -5.23$) favored the lisdexamfetamine condition compared with placebo. *Symptoms of depression* were reported from one study only (McElroy et al. 2015c).

Side effects. In both publications, a majority of participants in the lisdexamfetamine group (>80%) and the placebo group (>50%) reported side effects. In the placebo group, 0-3% discontinued due to side effects compared with 3-6% in the lisdexamfetamine group. One participant died due to methamphetamine and amphetamine toxicity (McElroy et al. 2015d).

Anti-convulsive vs. placebo

Two studies investigated the effect of anti-convulsive medication for their mood stabilization characteristics vs. placebo ($n = 443$) (Guerdjikova et al. 2009; McElroy et al. 2007). Participants were between 18-65 years with $BMI > 30$ (mean $BMI > 38.5$) and the majority were women (> 80%). The treatment in both studies was 16 weeks with no follow-ups. Both studies used flexible dosage of lamotrigine (Guerdjikova et al. 2009) and topiramate (Guerdjikova et al. 2009; McElroy et al. 2007).

Remission: The outcome in terms of remission was inconsistent between the two studies ($n = 443$), resulting in a non-significant outcome. *Binge eating frequency* was inconsistent ($n = 445$) between the two studies, resulting in a non-significant outcome (Table 1). *Eating disorder psychopathology* was only reported in one study (Guerdjikova et al. 2009). *BMI*: only one study reported data in a proper format for inclusion in a meta-analysis (McElroy et al. 2007). *Symptoms of depression* were investigated in both studies but only one study reported the mean and thus, no meta-analysis was performed.

Side effects. In the topiramate study (McElroy et al. 2007), significantly more participants in the intervention condition compared to placebo reported the following adverse events: paresthesia, upper respiratory tract infection, taste perversion, difficulty with concentration/attention, and difficulty with memory not otherwise specified (McElroy et al. 2007).

Anorexiant vs. placebo

Two studies ($n = 103$) were identified. They investigated chromium picolinate with two dosages (800-1000 $\mu\text{g/day}$) (Brownley et al. 2013) and Orlistat (120 mg/day) (Golay et al. 2005). Participants were 18-65 years (mean ages were 37 and 41) and they were mostly women (>83%) with a mean BMI of 37 and 43 respectively. One study included overweight and obese (Brownley et al. 2013) while the other included only obese participants. The duration of the treatments were six months in both studies with no follow-ups.

The outcome measures were presented in different formats between the two studies such that no meta-analysis was performed. *Remission*: Only one study reported results on remission (Golay et al. 2005). There was no significant difference between the treatment and the placebo group. *Binge eating frequency* was reported in both studies but with no significant differences between treatment and placebo in both studies. *Eating disorder psychopathology* was reported in one study (Brownley et al. 2013) with no significant differences between treatment groups and placebo. *BMI*: weight reduction was significantly larger for the orlistat group compared with placebo (Golay et al. 2005). *Symptoms of depression*: there were no significant effects in either study. *Quality of life* was presented in one study with no significant effect (Golay et al. 2005).

Side effects. No significant differences between groups were reported in the chromium picolinate study (Brownley et al. 2013) and no side effects were reported in the orlistat study (Golay et al. 2005).

Drug & psychological treatment combined

The five studies could not be combined for a meta-analysis (Agras et al. 1994; Claudino et al. 2007; Grilo et al. 2005a; Grilo et al. 2005b; Grilo & White 2013). The following combinations were investigated: A combination of desipramine, weight loss, and CBT vs. CBT combined with weight loss program (Agras et al. 1994); topiramate combined with CBT versus CBT (Claudino et al. 2007); combination of orlistat, dietary advice, and CBT vs. placebo, dietary advice, and CBT (Grilo et al. 2005a); a combination of fluoxetine and CBT vs. placebo and CBT (Grilo et al. 2005b); and a

combination of orlistat and BWL vs. placebo and BWL (Grilo & White 2013). Participants were 18-65 years old, >78% were women, with BMI ≥ 27 . Treatments were 12 to 36 weeks and followed up at three months (Agras et al. 1994; Grilo et al. 2005a), 6 months (Grilo & White 2013), and at 12 months (Grilo et al. 2012).

Side effects. Two studies did not report on side effects (Agras et al. 1994; Grilo et al. 2005b).

Those who received topiramate reported significantly more paresthesia, taste perversion, dysuria, and leg pain compared with the placebo group. However, the placebo group reported significantly more insomnia (Claudino et al. 2007). Those who received orlistat reported more gastrointestinal events that resolved (Grilo et al. 2005a; Grilo & White 2013). However, two participants dropped out due to these side effects (Grilo et al. 2005a).

CBT vs. wait list

CBT vs. wait list was investigated in four studies (Dingemans et al. 2007; Grilo et al. 2005b; Peterson et al. 2009; Schlup et al. 2009). Participants were mostly women (>70%), 18-65 years old, with a mean age of 43.5 years and a mean BMI of 36.6. Treatments ranged between 8 (Schlup et al. 2009), 16 (Grilo et al. 2005b), and 20 weeks (Dingemans et al. 2007; Peterson et al. 2009), and the number of sessions ranged between 8 and 16. No follow up data were presented. The effects were investigated in individual format in one study (Grilo et al. 2005b), while the other three studies used group format (Dingemans et al. 2007; Peterson et al. 2009; Schlup et al. 2009). The content of the interventions was assessed as fairly equal despite different formats, number of sessions and the duration of treatment.

Remission: Four studies reported remission ($n = 272$) in favor of CBT compared with wait list, $RD=0.40$. *Binge eating frequency* was reported in all four studies ($n = 272$), however due to different frequency assessments (BE episodes (Grilo et al. 2005b; Schlup et al. 2009), and BE days during the last 28 days (Dingemans et al. 2007; Peterson et al. 2009)) the results in the meta-analysis are presented as SMD. The results were in favor of CBT compared with wait list, $SMD = -0.83$. *Eating disorder psychopathology* was investigated with the EDE-Q and presented in four studies ($n = 269$) (Dingemans et

al. 2007; Grilo et al. 2005b; Peterson et al. 2009; Schlup et al. 2009). The results favor the CBT intervention compared with the wait list, $SMD = -0.50$. *BMI*: Three of the four studies reported data for inclusion in the meta-analysis ($n = 220$) on BMI change (Grilo et al. 2005b; Peterson et al. 2009; Schlup et al. 2009). No significant effect was found (Table 1). The fourth study did not show any significant results either (Dingemans et al. 2007). *Symptoms of depression* were reported in four studies ($n = 267$) (Dingemans et al. 2007; Grilo et al. 2005b; Peterson et al. 2009; Schlup et al. 2009). Different outcome scales were used in the studies but were synthesized for this meta-analysis showing a result in favor of the CBT compared with the wait list condition, $SMD = -0.42$.

Side effects were not reported in any of the studies.

CBT self-help vs. wait list

There were eight studies investigating CBT-gsh vs. wait list (Carrard et al. 2011; Carter & Fairburn 1998; Grilo & Masheb 2005; Grilo et al. 2014; Kelly & Carter 2014; Masson et al. 2013; Shapiro et al. 2007; ter Huurne et al. 2015). Participants were 18 years and older and 87% were women. Two studies included only overweight / obese participants ($BMI \geq 27$) (Grilo & Masheb 2005; Shapiro et al. 2007) and one study included only obese participants (Grilo et al. 2014). The remaining studies had no BMI inclusion criteria. The number of treatment weeks varied between 3 (Kelly & Carter 2014), 10–13 (Carter & Fairburn 1998; Grilo & Masheb 2005; Masson et al. 2013; Shapiro et al. 2007), 15–18 (ter Huurne et al. 2015), 16 (Grilo et al. 2014), and 24 (Carrard et al. 2011). There were five studies (Carrard et al. 2011; Carter & Fairburn 1998; Grilo & Masheb 2005; Grilo et al. 2014; ter Huurne et al. 2015) that investigated eating disorder specific CBT, one study investigated DBT (Masson et al. 2013) and one study investigated a treatment with focus on healthy eating and weight control with CBT (Shapiro et al. 2007). The degree of support varied between the studies: it ranged between no support (Carter & Fairburn 1998; Grilo et al. 2014), only one session before the program started (Kelly & Carter 2014), one phone call (Shapiro et al. 2007), 20 minutes telephone support biweekly (Masson et al. 2013), mail correspondence twice a week (ter Huurne et al. 2015), and weekly mail contact + automated feedback

from the program (Carrard et al. 2011) and six brief biweekly meetings (Grilo & Masheb 2005). First we present the results on all eight studies, followed by the results on the four studies that provided adequate and reasonable dose of support (Carrard et al. 2011; Grilo & Masheb 2005; Masson et al. 2013; ter Huurne et al. 2015).

Remission was presented in six studies ($n = 333$) (Carrard et al. 2011; Carter & Fairburn 1998; Grilo & Masheb 2005; Grilo et al. 2014; Masson et al. 2013; Shapiro et al. 2007) and the result was in favor of self-help compared with wait list, $RD = 0.25$. *Binge eating frequency* was reported in seven studies ($n = 358$) (Carrard et al. 2011; Carter & Fairburn 1998; Grilo & Masheb 2005; Grilo et al. 2014; Kelly & Carter 2014; Masson et al. 2013; Shapiro et al. 2007) and the result was in favor of self-help vs. wait list at end of treatment, $SMD = -0.51$. *Eating disorder psychopathology* was reported with the EDE-Q in six studies ($n = 348$) (Carrard et al. 2011; Carter & Fairburn 1998; Grilo et al. 2014; Kelly & Carter 2014; Masson et al. 2013) and the result was in favor of self-help, $MD = -0.58$. *BMI* was reported in seven studies ($n = 384$) (Carrard et al. 2011; Carter & Fairburn 1998; Grilo & Masheb 2005; Grilo et al. 2014; Kelly & Carter 2014; Shapiro et al. 2007; ter Huurne et al. 2015) and the result showed no significant difference between self-help vs. wait list. *Symptoms of depression* was reported in five studies ($n = 282$) (Carrard et al. 2011; Grilo & Masheb 2005; Grilo et al. 2014; Kelly & Carter 2014; ter Huurne et al. 2015) and the result was in favor of the self-help compared with wait list (Table 1), $SMD = -0.31$, albeit a small and clinically not a meaningful effect.

The results for the four studies with reasonable dose of support

Remission and *binge eating frequency* was presented in three studies ($n = 192$) (Carrard et al. 2011; Grilo & Masheb 2005; Masson et al. 2013) and the result was in favor of self-help compared with wait list, $RD = 0.32$ [95% CI:0.20; 0.43] and $SMD = -0.56$ [95% CI:-0.86; -0.26] respectively. *Eating disorder psychopathology* was reported with the EDE-Q in three studies ($n = 219$) (Carrard et al. 2011; Masson et al. 2013; ter Huurne et al. 2015) and the result was in favor of self-help, $MD = -0.56$ [95% CI:-0.85;-0.28]. *BMI* was reported in three studies ($n = 220$) (Carrard et al. 2011; Grilo & Masheb 2005; ter

Huurne et al. 2015) and the result showed no significant difference between self-help vs. wait list, MD= -0.73 [95% CI:-3.93;2.48]. *Symptoms of depression* was reported in three studies ($n = 211$) (Carrard et al. 2011; Grilo & Masheb 2005; ter Huurne et al. 2015) and the result was in favor of the CBT-gsh compared with wait list, SMD= -0.35 [95% CI:-0.63; -0.07], albeit a small and clinically not a meaningful effect.

Two studies reported follow-ups, one at two months (Shapiro et al. 2007), and at one year (Grilo et al. 2014). There is insufficient evidence for long-term evaluation.

Side effects were not reported in any of the studies.

IPT vs. CBT

Two studies investigated IPT vs. CBT or CBT-gsh (Wilfley et al. 2002; Wilson et al. 2010) with long term follow ups (Hilbert et al. 2012; Hilbert et al. 2015). Participants were 18 years and older, mean ages were 45 and 49 years, the majority were women (79% and 83%), and with a BMI range of 27 to 48 (Wilfley et al. 2002) and up to 45 (Wilson et al. 2010), with a mean BMI of 36 and 37, respectively. Treatments were 20 weekly group sessions plus 3 individual sessions for IPT and CBT (Wilfley et al. 2002) and the other study had 19 individual sessions of IPT vs. CBT-gsh with ten 25-minute sessions over 24 weeks (Wilson et al. 2010). Both studies reported 12 month follow up data that was included in meta analyses while longer term follow up showed too high rate of drop out in one study (>50%) (Wilfley et al. 2002).

Remission was reported in both studies at end of treatment ($n = 265$), and at 12 months follow-up ($n = 265$). The treatments were equivalent at end of treatment, and at 12 months follow up (Table 1). *Binge eating frequency* was reported in both studies at end of treatment ($n = 299$) and at 12 months follow up ($n = 279$). Both treatments were equal at both occasions. *Eating disorder psychopathology* was only reported in one study (Wilson et al. 2010), hence no meta-analyses was performed. *BMI* was reported in both studies at end of treatment ($n = 299$) and at 12 months follow up ($n = 279$). IPT and CBT were equal at both occasions. *Symptoms of depression* were only reported in one study (Wilfley et al. 2002) and thus there was insufficient evidence for a meta-analysis.

Side effects were not reported in any of the studies.

BWL vs. CBT

Four studies ($n = 375$) investigated the effect of BWL vs. CBT (Grilo & Masheb 2005; Grilo et al. 2011; Munsch et al. 2007; Wilson et al. 2010). Participants were 18 years and older, the majority were women (63-89%) with a BMI ≥ 27 . One study included participants with a BMI between 30 and 55 (Grilo et al. 2011) [19]. Two studies compared the effect of BWL and CBT, both in group format, over 16 sessions during 16 weeks (Munsch et al. 2007) and 24 weeks (Grilo et al. 2011). One study investigated 24 weeks of BWL (20 sessions) with CBT-gsh including 10 sessions of 25 minutes long support (Wilson et al. 2010). One study compared CBT-gsh vs. BWL-gsh with biweekly 20-minute sessions during 12 weeks (Grilo & Masheb 2005). Three studies investigated long-term follow-ups (Grilo et al. 2011; Munsch et al. 2007; Wilson et al. 2010)

Remission was reported in all four studies at end of treatment ($n = 375$) and by three studies at 1-year follow up ($n = 300$) (Grilo et al. 2011; Munsch et al. 2007; Wilson et al. 2010). At end of treatment there was no significant difference between BWL and CBT (group/CBT-gsh), but at 1 year follow up there was a significant difference in favor of CBT (group/CBT-gsh) compared with BWL, RD= -0.13. *Binge eating frequency* was reported in all four studies at end of treatment ($n = 375$) and reported in three studies at 1 year follow up ($n = 300$) (Grilo et al. 2011; Munsch et al. 2007; Wilson et al. 2010)]. At end of treatment and at 1 year follow up there were significant difference in favor of the CBT conditions, SMD = 0.27, and SMD = 0.24 respectively. *Eating disorder psychopathology* was only reported in one study (Wilson et al. 2010). *BMI* was reported in all four studies at end of treatment ($n = 376$) and in three studies at the 1-year follow up ($n = 300$) (Grilo et al. 2011; Munsch et al. 2007; Wilson et al. 2010). We found no significant difference between BWL and CBT at any of the time points. *Symptoms of depression* were reported in three studies at end of treatment ($n = 222$) (Grilo & Masheb 2005; Grilo et al. 2011; Munsch et al. 2007), and in two studies at 1 year follow up ($n = 133$) (Grilo et al. 2011; Munsch et al.

2007). We did not find any significant differences between BWL and CBT at end of treatment or at the 1 year follow up.

Side effects were not reported in any of the studies.

Discussion

The aim of this systematic review was to evaluate the efficacy and the quality of evidence of psychological, pharmaceutical and combined treatments for BED, and potential side effects. We found moderate-quality evidence for remission (i.e., discontinuation of binge eating) for the comparisons CBT versus wait list and CBT-gsh/self help (sh) vs. wait list. CBT was associated with 400 more per 1000 in remission and CBT-gsh/sh 250 more per 1000 compared with wait list. Moderate-quality evidence was also found for reduction of eating disorder specific psychopathology for CBT-gsh/sh vs. wait list. The results above had the moderate degree of confidence in this systematic review. The IPT and CBT comparisons had low-quality evidence for remission, BE frequency, and weight loss. However, they were equally efficacious at end of treatment and at one-year follow-up for these outcomes.

With regard to pharmaceutical treatments, SSRIs and lisdexamfetamine resulted in remission and decreased frequency of binge eating episodes at the end of treatment with low quality evidence. However, the long-term effect of pharmacotherapy is largely unknown. Interestingly, the effect of SSRIs on depressed mood in BED was not significant despite SSRIs being anti-depressant medications.

Lisdexamfetamine was the only intervention showing some positive effect on BMI, a finding that is expected and encouraging, as partial loss of appetite is a known side effect of this category of drugs.

The remission rate at post-treatment was thus highest for CBT, followed by CBT-gsh, Central Nervous System (CNS) stimulants, and SSRI. The effects of IPT were similar to those of CBT, although the quality of the evidence in that regard was low. However, it should be noted that psychological treatments in most studies have been compared to a wait list control group while pharmaceutical treatments are generally compared to a placebo condition. Given the difference in the nature of the control

group in psychological versus pharmaceutical studies, and lack of head-to-head studies, any indirect comparisons should be interpreted with caution.

Available recent systematic reviews of treatment of DSM-IV/DSM-5 BED published in the last decade were scrutinized with focus on RCTs (please see the Introduction). In the case of several reviews from the same group of authors, we sometimes only used the most recent publication from that group. Some reviews of RCTs have used meta-analytic techniques to measure BED treatment effectiveness. Overall, the general findings were similar across reviews (e.g., Amianto et al. 2015; Brownley et al. 2016; Grilo et al. 2016; Iacovino et al. 2012; McElroy et al. 2015b; Reas & Grilo 2014; Reas & Grilo 2015; Vocks et al. 2010). The available systematic reviews of drug treatment of BED suggest that second-generation antidepressants are modestly efficacious in cessation or reduction of binge eating frequency and depressive symptomatology, but have no effect on weight. Lisdexamfetamine and topiramate, on the other hand, seem to exert favorable modest effects on both binge eating, and weight loss according to previous reviews, although the level of weight loss is clinically not meaningful. Combination of drugs and psychological treatments is not more efficacious than psychological treatments per se, although some drugs might enhance weight loss when combined with cognitive and behavioral treatments. There is currently no data to allow evaluation of longer-term effects of pharmacotherapy-only treatment for BED. Currently available reviews also confirm the efficacy of CBT (both therapist-led and CBT-gsh) and IPT for treatment of BED. In terms of limitations, the majority of reviews mention the inconsistencies of outcomes measures across trials, the lack of long-term follow-ups, especially in trials on drug treatment of BED, and methodological shortcomings that lead to exclusion of a significant number of trials from systematic reviews and meta-analyses.

The present review and meta-analyses confirms most of the conclusions from previous reviews. The majority of studies did not report long-term follow-up. Lack of information in pharmaceutical studies about the outcome and use or discontinued use of drugs after post-treatment was striking. For CBT, CBT-gsh, IPT, and BWL, follow-ups were available up to one year after the end of the treatment in a few studies with low risk of bias. However, even fewer studies reported longer outcome than one year post

treatment, and usually with low quality and focusing on very few variables. Importantly, we observed lack of data on the specific psychopathology of BED and quality of life, even though patients with BED are known to have reduced quality of life. Only two studies included a measure of quality of life (Golay et al. 2005; Ricca et al. 2010). This is an important area for future research, together with health economic studies, which are also lacking.

Despite a fair total number of studies investigating the efficacy of treatments for BED in general, not many studies met the fairly generous inclusion criteria and survived the check upon the few exclusion criteria to be included in the current systematic review. In addition, this review clearly shows that a mentionable number of studies have relatively small samples, thus imposing limitation to reach at robust pooled data to investigate some of the specific research questions of interest. As an example, we found too few studies investigating the efficacy of several drugs such as NDRI and SNRI, and psychological treatments such as schema therapy to run meta-analyses. In some cases, such as for studies on anorexians, we found only two studies that could not be merged due to lack of adequate data. Attempts to retrieve necessary data for our analyses from the authors was met with no response.

The overall quality of the included studies was high, and limitations such as small sample size were weighted by withdrawing points from the overall rating of these studies. Lack of clarity in some aspects of the procedure (e.g., details of randomization) in several studies resulted in adjustment of the quality rating of such studies. As an example, in some studies the allocation of participants was not described adequately (i.e., to provide transparency) or, in some studies, not at all. In other studies, it was unclear to what extent the assessors were blinded to the allocation of the participants at post-treatment or at follow-up, which resulted in adjustment of the quality rating. Another indication of good quality of the included studies is use of structured or semi-structured interviews for establishing the diagnosis of BED. The exclusion criteria in the studies that were included into the current meta-analyses were logical and reflective of everyday clinical praxis (e.g., excluding those with psychosis or acute suicidality to make sure they receive adequate treatment), and thus not contributing to create limitation, or bias in terms of generalizability of the outcome of the current meta-analysis.

The majority of the participants were adult females with BED and with concurrent overweight or obesity, recruited via ads, or in some studies through referrals from different clinics. It is noteworthy that we found no studies that included adolescents. The extent to which the conclusions of the current review can be generalized to other populations (men, adolescents, or minority groups) is limited. However, the severity of the symptoms, and the comorbid psychopathology of the included participants indicate that the included total sample in the current review is not markedly different from those seeking treatment from specialist psychiatry and other relevant caregivers. In all the included studies, participants suffer from full or sub-threshold BED based on the DSM-IV (American Psychiatric Association 1994), DSM-IV-TR (American Psychiatric Association 2000), or other equivalent diagnostic systems. The majority of those with a sub-threshold BED diagnosis according the above mentioned diagnostic manuals would meet the full BED diagnosis according to the most recent version of the DSM (i.e., DSM-5: American Psychiatric Association 2013) given the changes made in DSM-5 with regard to duration and frequency of binge eating episodes.

The length of treatments varied substantially within both pharmaceutical and psychological treatments, but in the majority of the included studies, a clinically adequate dose of intervention was delivered. Titration and optimization of pharmaceutical treatments seem to become more common in newer studies, making them ecologically more valid. The length of most of the psychological treatments varied between 10 and 24 weeks, but a few studies had considerably shorter duration (e.g., a self-help treatment that was only three weeks long). The treatment content among the included psychological treatment studies varied substantially as well. As several essential components of CBT for ED were missing in some treatment packages in several trials, they could not be combined with standard CBT treatment in other studies in a meaningful way, and were thus not entered into any meta-analysis. This led to inclusion of only four comparisons between CBT and wait list.

Compliance is an important factor in the interpretation of outcome of treatment trials. For pharmaceutical trials, compliance was fairly high, but in some of the important multicenter studies, the compliance was not higher than 50% due to side effects of medication, early drop-out, divergence from

the trial protocol, lack of effects, or other reasons. Improved procedures in pharmaceutical studies such as titration and regular checks increase the safety of the participants, transparency, and fidelity. Lack of compliance was easier to detect in newer well-controlled studies, compared to earlier studies. For psychological treatments, compliance was reported in some of the studies by defining good compliance in terms of attending a specific number of sessions in face-to-face treatments, or completing a specific number of modules in self-help treatments, while other studies did not report a clear picture of compliance. In studies where compliance was reported, it ranged between 60-93 percent, and although no specific and statistically robust and reliable pattern emerged, compliance seemed to be higher in face-to-face treatments compared to guided self-help treatments.

The drop-out rate in the studies included in this meta-analysis was acceptable as a direct consequence of the inclusion and exclusion criteria of the current study. Treatment studies with high rate of drop-out (i.e., >30%) were deemed too biased to be included in the meta-analysis. We also noted a tendency toward using more advanced and adequate statistical analysis (e.g., multilevel modeling) in more recent studies that more efficiently handle the drop-out and provide intention to treat analysis per default. Half of the studies investigating psychological treatments reported and investigated the drop-out in light of demographic factors and outcome variables. Lower socio-economic status and higher severity of symptoms seemed to be related to higher drop-out, but it was not systematically investigated in the current study.

Two other interesting observations were made during the analyses. The first one was lack of an a priori power analysis in a marked number of included studies, especially the older studies. The second one was vague and general statements regarding conflict of interest in some of the pharmaceutical studies with regard to the relationship between those that conducted the study and the pharmaceutical companies supplying the drugs.

With respect to pharmacological treatments, the adverse effects associated with SSRI and lisdexamfetamine when described for other disorders (Frampton 2016; Kostev et al. 2014) were also present for participants with BED. The risk for adverse events from psychological treatments is largely

unknown; the included studies did not report any adverse events but it is unclear whether this was systematically investigated. In future studies, systematic screening and report of adverse effects should be part of psychological treatment trials as well.

Several limitations of the current meta-analysis and review should be mentioned to provide a framework for adequate interpretations. In the planning phase of the present study, we discussed running separate analysis for treatment of BED with, and without obesity. It turned out that the majority of participants in the studies had significant overweight or obesity. The number of studies meeting the criteria for the present meta-analysis was too limited to allow separate analysis with regard to weight status. Access to raw data from several studies and data aggregation might provide a very valuable source for investigating the outcome of different treatments for BED in relation to weight status of the participants. Choice of inclusion and exclusion variables and how they are defined on a scale from conservative to liberal does affect the outcome of any review and meta-analysis. Although our criteria might be considered to belong to the more conservative side, we believe that clear-cut and fairly conservative criteria are necessary to identify studies with sound methodology to make valid inferences. This is, however, a pre-analytic assumption, and the choice and definition of criteria for inclusion and exclusion can always be discussed. This may per se justify the need for replication of not only original studies, but also reviews and meta-analyses.

In conclusion, we found moderate support for the efficacy of CBT and CBT-gsh (with moderate quality of evidence), and modest support for IPT, SSRI and lisdexamfetamine (with low quality of evidence) in the treatment of adults with BED in terms of cessation of or reduction in the frequency of binge eating. It should be noted that males and adolescents were underrepresented in the included studies. Lisdexamfetamine was the only treatment that showed a clinically non-significant and very modest effect on weight loss (with low quality of evidence). While there is limited support for the long-term effect of psychological treatments, we have currently no data to ascertain the long-term effect of drug treatments. Pharmaceutical treatments were coupled with some undesired side effects compared to placebo, but the side effects of psychological treatments are unknown. Direct comparisons between pharmaceutical and

psychological treatments are needed as well as data to investigate the generalizability of these results to adolescents. Long-term follow-ups, standardized assessments including measures of quality of life, and the study of underrepresented populations should be a priority for future research.

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References

- Agh T, Kovacs G, Pawaskar M, Supina D, Inotai A, and Voko Z. 2015. Epidemiology, health-related quality of life and economic burden of binge eating disorder: a systematic literature review. *Eat Weight Disord* 20:1-12.
- Agras WS, Telch CF, Arnow B, Eldredge K, Wilfley DE, Raeburn SD, Henderson J, and Marnell M. 1994. Weight loss, cognitive-behavioral, and desipramine treatments in binge eating disorder: An additive design. *Behav Ther* 25:225-238.
- American Psychiatric Association. 1994. *Diagnostic and statistical manual of mental disorders*. Washington, D. C.: American Psychiatric Press, Inc.
- American Psychiatric Association. 2000. *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, D.C.: Author.
- American Psychiatric Association. 2013. *Diagnostic and statistical manual of mental disorders* Washington, DC: Authors.
- Amianto F, Ottone L, Abbate Daga G, and Fassino S. 2015. Binge-eating disorder diagnosis and treatment: a recap in front of DSM-5. *BMC Psychiatry* 15:70. 10.1186/s12888-015-0445-6
- Brownley KA, Berkman ND, Peat CM, Lohr KN, Cullen KE, Bann CM, and Bulik CM. 2016. Binge-Eating Disorder in Adults: A Systematic Review and Meta-analysis. *Ann Intern Med* 165:409-420. 10.7326/M15-2455
- Brownley KA, Peat CM, La Via M, and Bulik CM. 2015. Pharmacological approaches to the management of binge eating disorder. *Drugs* 75:9-32. 10.1007/s40265-014-0327-0
- Brownley KA, Von Holle A, Hamer RM, La Via M, and Bulik CM. 2013. A double-blind, randomized pilot trial of chromium picolinate for binge eating disorder: results of the Binge Eating and Chromium (BEACh) study. *J Psychosom Res* 75:36-42.
- Carrard I, Crépin C, Rouget P, Lam T, Golay A, and Linden M. 2011. Randomised controlled trial of a guided self-help treatment on the Internet for binge eating disorder. *Behaviour research and therapy* 49:482-491.

- Carter JC, and Fairburn CG. 1998. Cognitive-behavioral self-help for binge eating disorder: a controlled effectiveness study. *Journal of consulting and clinical psychology* 66:616-623.
- Cassin SE, von Ranson KM, Heng K, Brar J, and Wojtowicz AE. 2008. Adapted motivational interviewing for women with binge eating disorder: a randomized controlled trial. *Psychol Addict Behav* 22:417-425.
- Castelnuovo G, Manzoni GM, Villa V, Cesa GL, and Molinari E. 2011. Brief Strategic Therapy vs Cognitive Behavioral Therapy for the Inpatient and Telephone-Based Outpatient Treatment of Binge Eating Disorder: The STRATOB Randomized Controlled Clinical Trial. *Clin Pract Epidemiol Ment Health* 7:29-37.
- Citrome L. 2017. Binge-Eating Disorder and Comorbid Conditions: Differential Diagnosis and Implications for Treatment. *J Clin Psychiatry* 78 Suppl 1:9-13. 10.4088/JCP.sh16003su1c.02
- Claudino AM, de Oliveira IR, Appolinario JC, Cordas TA, Duchesne M, Sichieri R, and Bacaltchuk J. 2007. Double-blind, randomized, placebo-controlled trial of topiramate plus cognitive-behavior therapy in binge-eating disorder. *J Clin Psychiatry* 68:1324-1332.
- Colles SL, Dixon JB, and O'Brien PE. 2008. Grazing and loss of control related to eating: two high-risk factors following bariatric surgery. *Obesity (Silver Spring)* 16:615-622. 10.1038/oby.2007.101
- Corwin RL, Boan J, Peters KF, and Ulbrecht JS. 2012. Baclofen reduces binge eating in a double-blind, placebo-controlled, crossover study. *Behav Pharmacol* 23:616-625.
- de Man Lapidoth J, Ghaderi A, and Norring C. 2006. Eating disorders and disordered eating among patients seeking non-surgical weight-loss treatment in Sweden. *Eat Behav* 7:15-26. 10.1016/j.eatbeh.2005.05.006
- de Man Lapidoth J, Ghaderi A, and Norring C. 2011. Binge eating in surgical weight-loss treatments. Long-term associations with weight loss, health related quality of life (HRQL), and psychopathology. *Eat Weight Disord* 16:e263-269.
- de Zwaan M. 2001. Binge eating disorder and obesity. *Int J Obes Relat Metab Disord* 25 Suppl 1:S51-55. 10.1038/sj.ijo.0801699
- de Zwaan M, Hilbert A, Swan-Kremeier L, Simonich H, Lancaster K, Howell LM, Monson T, Crosby RD, and Mitchell JE. 2010. Comprehensive interview assessment of eating behavior 18-35 months after gastric bypass surgery for morbid obesity. *Surg Obes Relat Dis* 6:79-85. 10.1016/j.soard.2009.08.011
- Decaluwe V, and Braet C. 2003. Prevalence of binge-eating disorder in obese children and adolescents seeking weight-loss treatment. *Int J Obes Relat Metab Disord* 27:404-409. 10.1038/sj.ijo.0802233
- Dingemans AE, Spinhoven P, and van Furth EF. 2007. Predictors and mediators of treatment outcome in patients with binge eating disorder. *Behav Res Ther* 45:2551-2562.
- Favaro A, and Santonastaso P. 1997. Suicidality in eating disorders: clinical and psychological correlates. *Acta Psychiatr Scand* 95:508-514.
- Frampton JE. 2016. Lisdexamfetamine: A Review in ADHD in Adults. *CNS Drugs* 30:343-354. 10.1007/s40263-016-0327-6
- Golay A, Laurent-Jaccard A, Habicht F, Gachoud JP, Chabloz M, Kammer A, and Schutz Y. 2005. Effect of orlistat in obese patients with binge eating disorder. *Obes Res* 13:1701-1708.

- Grilo CM. 2017. Psychological and Behavioral Treatments for Binge-Eating Disorder. *J Clin Psychiatry* 78 Suppl 1:20-24. 10.4088/JCP.sh16003su1c.04
- Grilo CM, Crosby RD, Wilson GT, and Masheb RM. 2012. 12-month follow-up of fluoxetine and cognitive behavioral therapy for binge eating disorder. *Journal of consulting and clinical psychology* 80:1108-1113.
- Grilo CM, and Masheb RM. 2005. A randomized controlled comparison of guided self-help cognitive behavioral therapy and behavioral weight loss for binge eating disorder. *Behav Res Ther* 43:1509-1525.
- Grilo CM, Masheb RM, and Salant SL. 2005a. Cognitive behavioral therapy guided self-help and orlistat for the treatment of binge eating disorder: a randomized, double-blind, placebo-controlled trial. *Biol Psychiatry* 57:1193-1201.
- Grilo CM, Masheb RM, White MA, Gueorguieva R, Barnes RD, Walsh BT, McKenzie KC, Genao I, and Garcia R. 2014. Treatment of binge eating disorder in racially and ethnically diverse obese patients in primary care: randomized placebo-controlled clinical trial of self-help and medication. *Behav Res Ther* 58:1-9.
- Grilo CM, Masheb RM, and Wilson GT. 2005b. Efficacy of cognitive behavioral therapy and fluoxetine for the treatment of binge eating disorder: a randomized double-blind placebo-controlled comparison. *Biol Psychiatry* 57:301-309.
- Grilo CM, Masheb RM, Wilson GT, Gueorguieva R, and White MA. 2011. Cognitive-behavioral therapy, behavioral weight loss, and sequential treatment for obese patients with binge-eating disorder: a randomized controlled trial. *Journal of consulting and clinical psychology* 79:675-685.
- Grilo CM, Reas DL, and Mitchell JE. 2016. Combining Pharmacological and Psychological Treatments for Binge Eating Disorder: Current Status, Limitations, and Future Directions. *Curr Psychiatry Rep* 18:55. 10.1007/s11920-016-0696-z
- Grilo CM, and White MA. 2013. Orlistat with behavioral weight loss for obesity with versus without binge eating disorder: randomized placebo-controlled trial at a community mental health center serving educationally and economically disadvantaged Latino/as. *Behav Res Ther* 51:167-175.
- Grilo CM, White MA, Gueorguieva R, Barnes RD, and Masheb RM. 2013. Self-help for binge eating disorder in primary care: a randomized controlled trial with ethnically and racially diverse obese patients. *Behav Res Ther* 51:855-861.
- Grilo CM, White MA, and Masheb RM. 2009. DSM-IV psychiatric disorder comorbidity and its correlates in binge eating disorder. *Int J Eat Disord* 42:228-234. 10.1002/eat.20599
- Guerdjikova AI, McElroy SL, Kotwal R, Welge JA, Nelson E, Lake K, Alessio DD, Keck PE, Jr., and Hudson JI. 2008. High-dose escitalopram in the treatment of binge-eating disorder with obesity: a placebo-controlled monotherapy trial. *Hum Psychopharmacol* 23:1-11.
- Guerdjikova AI, McElroy SL, Welge JA, Nelson E, Keck PE, and Hudson JI. 2009. Lamotrigine in the treatment of binge-eating disorder with obesity: a randomized, placebo-controlled monotherapy trial. *Int Clin Psychopharmacol* 24:150-158.
- Guerdjikova AI, McElroy SL, Winstanley EL, Nelson EB, Mori N, McCoy J, Keck PE, Jr., and Hudson JI. 2012. Duloxetine in the treatment of binge eating disorder with depressive disorders: a placebo-controlled trial. *Int J Eat Disord* 45:281-289.

- Guerdjikova AI, Mori N, Blom TJ, Keck PE, Jr., Williams SL, Welge JA, and McElroy SL. 2016. Lisdexamfetamine dimesylate in binge eating disorder: a placebo controlled trial. *Hum Psychopharmacol* 31:382-391.
- Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schunemann HJ, and Group GW. 2008. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 336:924-926. 10.1136/bmj.39489.470347.AD
- Hemels ME, Vicente C, Sadri H, Masson MJ, and Einarson TR. 2004. Quality assessment of meta-analyses of RCTs of pharmacotherapy in major depressive disorder. *Curr Med Res Opin* 20:477-484. 10.1185/030079904125003197
- Hilbert A, Bishop ME, Stein RI, Tanofsky-Kraff M, Swenson AK, Welch RR, and Wilfley DE. 2012. Long-term efficacy of psychological treatments for binge eating disorder. *Br J Psychiatry* 200:232-237.
- Hilbert A, Hildebrandt T, Agras WS, Wilfley DE, and Wilson GT. 2015. Rapid response in psychological treatments for binge eating disorder. *Journal of consulting and clinical psychology* 83:649-654.
- Hilbert A, and Tuschen-Caffier B. 2004. Body image interventions in cognitive-behavioural therapy of binge-eating disorder: a component analysis. *Behav Res Ther* 42:1325-1339.
- Hoek HW. 2006. Incidence, prevalence and mortality of anorexia nervosa and other eating disorders. *Curr Opin Psychiatry* 19:389-394. 10.1097/01.yco.0000228759.95237.78
- Hudson JI, Hiripi E, Pope HG, Jr., and Kessler RC. 2007. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry* 61:348-358. 10.1016/j.biopsych.2006.03.040
- Hudson JI, McElroy SL, Raymond NC, Crow S, Keck PE, Jr., Carter WP, Mitchell JE, Strakowski SM, Pope HG, Jr., Coleman BS, and Jonas JM. 1998. Fluvoxamine in the treatment of binge-eating disorder: a multicenter placebo-controlled, double-blind trial. *Am J Psychiatry* 155:1756-1762.
- Iacovino JM, Gredysa DM, Altman M, and Wilfley DE. 2012. Psychological treatments for binge eating disorder. *Curr Psychiatry Rep* 14:432-446. 10.1007/s11920-012-0277-8
- Kelly AC, and Carter JC. 2014. Self-compassion training for binge eating disorder: A pilot randomized controlled trial. *Psychol Psychother* 0.
- Kessler RC, Berglund PA, Chiu WT, Deitz AC, Hudson JI, Shahly V, Aguilar-Gaxiola S, Alonso J, Angermeyer MC, Benjet C, Bruffaerts R, de Girolamo G, de Graaf R, Maria Haro J, Kovess-Masfety V, O'Neill S, Posada-Villa J, Sasu C, Scott K, Viana MC, and Xavier M. 2013. The prevalence and correlates of binge eating disorder in the World Health Organization World Mental Health Surveys. *Biol Psychiatry* 73:904-914. 10.1016/j.biopsych.2012.11.020
- Kostev K, Rex J, Eith T, and Heilmaier C. 2014. Which adverse effects influence the dropout rate in selective serotonin reuptake inhibitor (SSRI) treatment? Results for 50,824 patients. *Ger Med Sci* 12:Doc15. 10.3205/000200
- Kristeller J, Wolever RQ, and Sheets V. 2014. Mindfulness-Based Eating Awareness Training (MB-EAT) for binge eating: A randomized clinical trial. *Mindfulness* 5:282-297.
- Laederach-Hofmann K, Graf C, Horber F, Lippuner K, Lederer S, Michel R, and Schneider M. 1999. Imipramine and diet counseling with psychological support in the treatment of obese binge eaters: a randomized, placebo-controlled double-blind study. *International Journal of Eating Disorders* 26:231-244.

- Leombruni P, Piero A, Lavagnino L, Brustolin A, Campisi S, and Fassino S. 2008. A randomized, double-blind trial comparing sertraline and fluoxetine 6-month treatment in obese patients with Binge Eating Disorder. *Prog Neuropsychopharmacol Biol Psychiatry* 32:1599-1605.
- Masheb RM, Grilo CM, and Rolls BJ. 2011. A randomized controlled trial for obesity and binge eating disorder: low-energy-density dietary counseling and cognitive-behavioral therapy. *Behav Res Ther* 49:821-829.
- Masson PC, von Ranson KM, Wallace LM, and Safer DL. 2013. A randomized wait-list controlled pilot study of dialectical behaviour therapy guided self-help for binge eating disorder. *Behav Res Ther* 51:723-728.
- McElroy SL. 2017. Pharmacologic Treatments for Binge-Eating Disorder. *J Clin Psychiatry* 78 Suppl 1:14-19. 10.4088/JCP.sh16003sup1c.03
- McElroy SL, Casuto LS, Nelson EB, Lake KA, Soutullo CA, Keck PE, Jr., and Hudson JI. 2000. Placebo-controlled trial of sertraline in the treatment of binge eating disorder. *Am J Psychiatry* 157:1004-1006.
- McElroy SL, Guerdjikova AI, Mori N, Blom TJ, Williams S, Casuto LS, and Keck PE, Jr. 2015a. Armodafinil in binge eating disorder: a randomized, placebo-controlled trial. *Int Clin Psychopharmacol* 30:209-215.
- McElroy SL, Guerdjikova AI, Mori N, Munoz MR, and Keck PE. 2015b. Overview of the treatment of binge eating disorder. *CNS Spectr* 20:546-556. 10.1017/S1092852915000759
- McElroy SL, Guerdjikova AI, Winstanley EL, O'Melia AM, Mori N, Keck Jr PE, and Hudson JI. 2011a. Sodium oxybate in the treatment of binge eating disorder: An open-label, prospective study. *International Journal of Eating Disorders* 44:262-268.
- McElroy SL, Guerdjikova AI, Winstanley EL, O'Melia AM, Mori N, McCoy J, Keck PE, Jr., and Hudson JI. 2011b. Acamprosate in the treatment of binge eating disorder: a placebo-controlled trial. *Int J Eat Disord* 44:81-90.
- McElroy SL, Hudson J, Ferreira-Cornwell MC, Radewonuk J, Whitaker T, and Gasior M. 2015c. Lisdexamfetamine Dimesylate for Adults with Moderate to Severe Binge Eating Disorder: Results of Two Pivotal Phase 3 Randomized Controlled Trials. *Neuropsychopharmacology* 0.
- McElroy SL, Hudson JI, Capece JA, Beyers K, Fisher AC, and Rosenthal NR. 2007. Topiramate for the treatment of binge eating disorder associated with obesity: a placebo-controlled study. *Biol Psychiatry* 61:1039-1048.
- McElroy SL, Hudson JI, Malhotra S, Welge JA, Nelson EB, and Keck PE, Jr. 2003. Citalopram in the treatment of binge-eating disorder: a placebo-controlled trial. *J Clin Psychiatry* 64:807-813.
- McElroy SL, Hudson JI, Mitchell JE, Wilfley D, Ferreira-Cornwell MC, Gao J, Wang J, Whitaker T, Jonas J, and Gasior M. 2015d. Efficacy and safety of lisdexamfetamine for treatment of adults with moderate to severe binge-eating disorder: a randomized clinical trial. *JAMA Psychiatry* 72:235-246.
- McIntosh VVW, Jordan J, Carter JD, Frampton CMA, McKenzie JM, Latner JD, Joyce PR, Author A, Department of Psychological Medicine U, of Otago CNZ, Canterbury, District Health Board CNZ, Department of Psychology UoC, Christchurch NZ, Psychology Department UoHaMH, United S, Correspondence A, and V.V.W. McIntosh DoPMUoO. 2016. Psychotherapy for transdiagnostic binge eating: A randomized controlled trial of

cognitive-behavioural therapy, appetite-focused cognitive-behavioural therapy, and schema therapy. *Psychiatry Res* 240:412-420.

Moher D, Liberati A, Tetzlaff J, Altman DG, and Group P. 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. *Open Med* 3:e123-130.

Moher D, Tetzlaff J, Tricco AC, Sampson M, and Altman DG. 2007. Epidemiology and reporting characteristics of systematic reviews. *PLoS Med* 4:e78. 10.1371/journal.pmed.0040078

Munsch S, Biedert E, Meyer A, Michael T, Schlup B, Tuch A, and Margraf J. 2007. A randomized comparison of cognitive behavioral therapy and behavioral weight loss treatment for overweight individuals with binge eating disorder. *Int J Eat Disord* 40:102-113.

Nicholls DE, Lynn R, and Viner RM. 2011. Childhood eating disorder: British national surveillance study. *British Journal of Psychiatry* 198:295-301.

Pearlstein T, Spurrell E, Hohlstein LA, Gurney V, Read J, Fuchs C, and Keller MB. 2003. A double-blind, placebo-controlled trial of fluvoxamine in binge eating disorder: a high placebo response. *Arch Womens Ment Health* 6:147-151.

Peterson CB, Mitchell JE, Crow SJ, Crosby RD, and Wonderlich SA. 2009. The efficacy of self-help group treatment and therapist-led group treatment for binge eating disorder. *Am J Psychiatry* 166:1347-1354.

Reas DL, and Grilo CM. 2014. Current and emerging drug treatments for binge eating disorder. *Expert Opin Emerg Drugs* 19:99-142.

Reas DL, and Grilo CM. 2015. Pharmacological treatment of binge eating disorder: update review and synthesis. *Expert Opin Pharmacother* 16:1463-1478.

Review Manager (RevMan). 2014. The Nordic Cochrane Centre: The Cochrane Collaboration.

Ricca V, Castellini G, Mannucci E, Lo Sauro C, Ravaldi C, Rotella CM, and Faravelli C. 2010. Comparison of individual and group cognitive behavioral therapy for binge eating disorder. A randomized, three-year follow-up study. *Appetite* 55:656-665.

Schlup B, Munsch S, Meyer AH, Margraf J, and Wilhelm FH. 2009. The efficacy of a short version of a cognitive-behavioral treatment followed by booster sessions for binge eating disorder. *Behav Res Ther* 47:628-635.

Shapiro JR, Reba-Harrelson L, Dymek-Valentine M, Woolson SL, Hamer RM, and Bulik CM. 2007. Feasibility and acceptability of CD-ROM-based cognitive-behavioural treatment for binge-eating disorder. *Eur Eat Disord Rev* 15:175-184.

Stice E, Marti CN, and Rohde P. 2013. Prevalence, incidence, impairment, and course of the proposed DSM-5 eating disorder diagnoses in an 8-year prospective community study of young women. *J Abnorm Psychol* 122:445-457. 10.1037/a0030679

ter Huurne ED, de Haan HA, Postel MG, van der Palen J, VanDerNagel JE, and DeJong CA. 2015. Web-Based Cognitive Behavioral Therapy for Female Patients With Eating Disorders: Randomized Controlled Trial. *J Med Internet Res* 17:e152.

Ulfvebrand S, Birgegård A, Norring C, Hogdahl L, and von Hausswolff-Juhlin Y. 2015. Psychiatric comorbidity in women and men with eating disorders results from a large clinical database. *Psychiatry Res* 230:294-299. 10.1016/j.psychres.2015.09.008

Vamado PJ, Williamson DA, Bentz BG, Ryan DH, Rhodes SK, O'Neil PM, Sebastian SB, and Barker SE. 1997. Prevalence of binge eating disorder in obese adults seeking weight loss treatment. *Eat Weight Disord* 2:117-124.

- Vocks S, Tuschen-Caffier B, Pietrowsky R, Rustenbach SJ, Kersting A, and Herpertz S. 2010. Meta-analysis of the effectiveness of psychological and pharmacological treatments for binge eating disorder. *Int J Eat Disord* 43:205-217.
- White MA, and Grilo CM. 2013. Bupropion for overweight women with binge-eating disorder: a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 74:400-406.
- Wilfley DE, Welch RR, Stein RI, Spurrell EB, Cohen LR, Saelens BE, Douchis JZ, Frank MA, Wiseman CV, and Matt GE. 2002. A randomized comparison of group cognitive-behavioral therapy and group interpersonal psychotherapy for the treatment of overweight individuals with binge-eating disorder. *Arch Gen Psychiatry* 59:713-721.
- Wilfley DE, Wilson GT, and Agras WS. 2003. The clinical significance of binge eating disorder. *Int J Eat Disord* 34 Suppl:S96-106. 10.1002/eat.10209
- Wilson GT. 2011. Treatment of binge eating disorder. *Psychiatr Clin North Am* 34:773-783.
- Wilson GT, Wilfley DE, Agras WS, and Bryson SW. 2010. Psychological treatments of binge eating disorder. *Arch Gen Psychiatry* 67:94-101. 10.1001/archgenpsychiatry.2009.170

Table 1(on next page)

Flowchart, illustrating the exclusion, and inclusion of relevant studies for the review

n=3236
after duplicates removed

Publications excluded based
on title or abstract due to
not meeting inclusion criteria
n=2940

Screened full text
n=296

Relevant full text
n=99 publications
n=83 unique studies

(n=89 RCT's)
n=7 controlled studies

Excluded: High bias risk
n=45 publications
n=38 unique studies

Drug vs. placebo; n=8 studies

Drug + psychological treatment;
n=6 studies (8 publications)

Psychological treatment;
n=19 studies (22 publications)

Other treatments; n=5 studies

Low/medium bias risk
n=54 publications
n=45 unique studies (RCTs)

Drug
vs. placebo

Low/medium bias risk
n=17 publications
n=17 studies

Drug + Psychological Tx
vs. placebo

Low/medium bias risk
n=7 publications
n=5 studies

Psychological Tx
vs. wait-list or other Tx

Low/medium bias risk
n=30 publications
n=23 studies

Table 2(on next page)

Effect size and quality grade of included studies along with the reason for reduction of quality grade

1 Table 1.
2 Effect size and quality grade of included studies along with the reason for reduction of quality grade
3

Outcome/intervention	<i>k</i> studies <i>n</i> participants <i>k, n</i>	Effect size (95% CI)	Overall Effect <i>Z(p)</i>	Intervention length: Weeks	Quality GRADE	Reason for reduction in quality grade
SSRI vs. Placebo	6, 285			6-16		
Remission	6, 264	RD=0.15(0.02:0.27)	2.34(.02) ^{SSRI*}		⊕⊕OO	-1 Bias -1 Imprecision
BE frequency	6, 257	SMD=-0.45(-0.82:-0.09)	2.43(.02) ^{SSRI}		⊕⊕OO	-1 Bias -1 Imprecision
ED psychopathology	1, 54	n.a.			⊕OOO	One small study***
BMI	5, 237	SMD=0.01(-0.39:0.41)	0.04(.97)		⊕OOO	-1 Bias, inconsistency -2 Precision
Depressive Symptoms	4, 148	SMD=-0.16(-0.49:0.16)	0.98(.33)		⊕OOO	-2 Imprecision -1 Bias
Lisdexamphetamine (LDX) vs. placebo	3 ^a , 850			11 and 12		
Remission	3, 850	RD=0.25(0.19:0.31)	8.60(<.001) ^{LDX}		⊕⊕OO	-1 Bias -1 Indirectness
OBE frequency	3, 849	SMD=-0.76(-0.99:-0.53)	6.43(<.001) ^{LDX}		⊕⊕OO	-2 Bias, indirectness, imprecision
BMI	3, 852	SMD=-5.23(-6.52:-3.94)	7.93(<.001) ^{LDX}		⊕⊕OO	-1 Bias -1 Indirectness
Depressive Symptoms	1, 120	Data could not be extracted			⊕OOO	One small study***
Anti-convulsive vs. placebo	2, 445			16		
Remission	2, 443	RD=0.05(-0.47:0.56)	n.a		⊕OOO	-1 Inconsistency. -2 Imprecision
BE frequency	2, 445	SMD=-0.28(-2.34:1.77)	n.a		⊕OOO	-1 Inconsistency -2 imprecision
ED psychopathology	1, 51	n.a.			⊕OOO	One small study***
BMI	2, 445	Combining outcome measures was not possible			⊕OOO	-2 Imprecision -1 Indirectness
Depressive Symptoms	2, 445	Combining outcome measures was not possible			⊕OOO	-2 Imprecision -1 Indirectness

Anorexiant vs. placebo	2, 103	Combining outcome measures was not possible		6 months	⊕○○○	one small study***
Drugs & psychol. treatment combined	5, -	Only one study per combination of drug and psychological treatment			⊕○○○	one small study***
CBT vs. waitlist				8-20		
Remission	4, 272	RD=0.40 (0.30:0.50)	7.83(<.001) ^{CBT}		⊕⊕⊕○	-1 Imprecision
BE frequency	4, 272	SMD=-0.83(-1.11:-0.55)	5.76(<.001) ^{CBT}		⊕⊕○○	-1 Imprecision -1 Indirectness
ED psychopathology	4, 269	MD=-0.50(-0.88;-0.12)	2.56(.01) ^{CBT}		⊕⊕○○	-1 Bias -1 Imprecision
BMI	3, 220	SMD=-0.09(-0.55:0.37)	0.40(.69)		⊕○○○	-1 Inconsistency -2 Imprecision
Depressive Symptoms	4, 267	SMD -0.42 (-0.67:-0.18)	3.40(<.001) ^{CBT}		⊕⊕⊕○	-1 Imprecision
CBT-gsh vs. waitlist	8, ca. 400			3-24		
Remission	6, 333	RD=0.25(0.12:0.38)	3.67(<.001) ^{CBT-gsh}		⊕⊕⊕○	-1 Imprecision, bias
BE frequency	7, 358	SMD=-0.51(-0.84:-0.17)	2.98(.003) ^{CBT-gsh}		⊕⊕○○	-1 Imprecision -1 Inconsistency, bias
ED psychopathology	6, 348	SMD=-0.58(-0.98:-0.17)	2.81(.005) ^{CBT-gsh}		⊕⊕⊕○	-1 Imprecision
BMI	7, 384	SMD=-0.52 (-2.44:1.40)	0.53(.60)		⊕○○○	-1 Imprecision -2 Inconsistency
Depressive Symptoms	5, 282	SMD=-0.35(-0.63:-0.07)	2.48(.01) ^{CBT-gsh}		⊕⊕○○	-1 imprecision -1 Bias, inconsistency
IPT vs. CBT/ CBT-gsh	2, 303			20-24		
Remission	2, 265	RD=-0.02(-0.13:0.09)	0.43(.67)		⊕⊕○○	-1 Imprecision -1 Indirectness
Remission 12 months	2, 265	RD =-0.00(-0.12:0.12)	0.07(.95)		⊕⊕○○	-1 Imprecision -1 Indirectness
BE frequency	2, 299	SMD=0.08(-0.15:0.31)	0.69(.49)		⊕⊕○○	-2 Imprecision
BE frequency 12 months	2, 279	SMD=-0.04(-0.27:0.20)	0.31(.76)		⊕⊕○○	-2 Imprecision
ED psychopathology	1, 141	n.a.			⊕○○○	One small study***
BMI	2, 299	MD=-0.25(-1.39:0.90)	0.43(.67)		⊕⊕○○	-2 Imprecision

BMI 12 months	2, 279	MD=-0.33(-1.55:0.89)	0.54(.59)		⊕⊕OO	-2 Imprecision
Depressive Symptoms	1, 158	n.a.			⊕OOO	One small study***
BWL vs. CBT **	4, 375			12-20		
Remission	4, 375	RD=-0.06(-0.22:0.11)	0.64(.52)		⊕OOO	-1 Inconsistency -2 Imprecision
Remission 12 months	3, 300	RD=-0.13(-0.25:-0.02)	2.35(.02) ^{CBT}		⊕⊕OO	-2 Imprecision
BE frequency	4, 375	SMD=0.27 (0.05:0.48)	2.40(.02) ^{CBT}		⊕⊕OO	-2 Imprecision
BE frequency 12 months	3, 300	SMD=0.24 (0.01:0.46)	2.03(.04) ^{CBT}		⊕⊕OO	-2 Imprecision
ED psychopathology	1, 139	n.a.			⊕OOO	
BMI	4, 376	SMD=-1.07(-2.40:0.25)	1.59(.11)		⊕OOO	-2 Inconsistency -1 Imprecision
BMI 12 months	3, 300	SMD= -0.23(-1.46: 0.99)	0.37(.71)		⊕⊕OO	-1 Inconsistency -1 imprecision
Depressive Symptoms	3, 222	MD=1.03(-1.20:3.25)	0.91(.37)		⊕⊕OO	-2 imprecision
Depressive Symptoms 12 months	2, 133	MD=0.25(-2.53:3.03)	0.18(.86)		⊕OOO	-2 imprecision -1 indirectness

4

5 Degree of evidence; ⊕⊕⊕⊕ = High, ⊕⊕⊕O = Moderate, ⊕⊕OO = Low, and ⊕OOO = Insufficient (Very low).

6 a = one publication involved a multicenter study

7 * superscript indicate the favored treatment

8 ** see manuscript for the different formats involved

9 *** The confidence in the estimate/evidence is very low (⊕OOO) when the evidence is based on only one small study (i.e., -2 points
10 for imprecision and -1 point for indirectness)

11