Comparative Effectiveness Review
Number 160

Effective Health Care Program

Management and Outcomes of Binge-Eating Disorder

Executive Summary

Background

Definition of Binge-Eating Disorder and Loss-of-Control Eating

Binge-eating disorder (BED) is characterized by recurrent episodes of binge eating—i.e., eating episodes that occur in a discrete period of time (≤2 hours) and involve the consumption of an amount of food that is definitely larger than most people would consume under similar circumstances. Other core features of BED are a sense of lack of control over eating during binge episodes, significant psychological distress (e.g., shame, guilt) about binge eating, and the absence of regular use of inappropriate compensatory behaviors, such as purging, fasting, and excessive exercise.

In May 2013, the American Psychiatric Association (APA) recognized BED as a distinct eating disorder in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5).[1] Previously (in the DSM-IV), BED had been designated as a provisional diagnosis.

Table A presents the DSM-IV and DSM-5 diagnostic criteria for BED. In the shift from provisional to formal diagnosis for BED, APA experts changed the criterion for frequency of BED from twice per week to once per week and the duration criterion from 6 months to 3 months, in line with those for bulimia nervosa.

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at **www.effectivehealthcare.ahrq.gov/reports/final.cfm**.

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Table A. DSM-IV and DSM-5 diagnostic criteria for binge-eating disorder

Criteria Set and Severity Grading	Specific Definitions for Each Criterion
Criterion 1	Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following: a. Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances b. The sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating)
Criterion 2	Binge-eating episodes are associated with 3 or more of the following: a. Eating much more rapidly than normal b. Eating until feeling uncomfortably full c. Eating large amounts of food when not feeling physically hungry d. Eating alone because of being embarrassed by how much one is eating e. Feeling disgusted with oneself, depressed, or very guilty after overeating
Criterion 3	Marked distress regarding binge eating is present.
Criterion 4	The binge eating occurs, on average— a. At least 2 days a week for 6 months (DSM-IV frequency and duration criteria) b. At least 1 day a week for 3 months (DSM-5 frequency and duration criteria)
Criterion 5	The binge eating is not associated with the regular use of inappropriate compensatory behavior (e.g., purging, fasting, excessive exercise) and does not occur exclusively during the course of anorexia nervosa or bulimia nervosa.
Severity Grading	DSM-IV does not include a BED severity grading scale. Applicable to DSM-5 only, BED severity is graded as follows: Mild: 1 to 3 episodes per week Moderate: 4 to 7 episodes per week Severe: 8 to 13 episodes per week Extreme: 14 or more episodes per week

BED = binge-eating disorder; DSM = Diagnostic and Statistical Manual of Mental Disorders.

A sense of loss of control (LOC) during binge episodes is a core feature of BED. The term "LOC eating" is used to describe these episodes, but it is also used more broadly throughout the literature to describe binge-like eating behavior accompanied by a sense of LOC that occurs across a wide spectrum of individuals. That spectrum includes, among others, individuals who exhibit some features of BED but do not meet full diagnostic criteria for the disorder (i.e., subthreshold BED) and individuals with other eating disorders (bulimia nervosa, anorexia nervosa binge-eating/purge subtype).

The spectrum of those described as exhibiting LOC eating also includes individuals for whom diagnosis of threshold BED is challenging for unique reasons, such as postbariatric surgery patients and children. Bariatric surgery significantly reduces the stomach size and capacity, effectively rendering it physically impossible for a patient to meet BED criterion 1a (Table A; i.e., to consume a definitely large amount of food). In the bariatric surgery literature, LOC eating is used not only to describe binge-like behavior that falls short of meeting criterion 1a, but also to describe eating behavior that is contraindicated based on meal size and meal content. Children, especially young children, may not meet BED criterion 1a because

their parents or others limit the quantity of food they consume or because they are unable to provide accurate quantification of the amount they eat. For the purposes of our review, LOC eating treatment and outcomes are limited to postbariatric surgery patients and children, and do not include individuals in other groups who may meet subclinical diagnosis of BED.

Prevalence of Binge-Eating Disorder and Loss-of-Control Eating

Prevalence estimates (and citations) are covered in more detail in the full report. In the United States, the prevalence of BED among adults is about 3.5 percent in women and about 2 percent in men based on DSM-IV criteria and slightly higher based on DSM-5 criteria.[2,3] BED is more common among obese individuals[4,5] and slightly lower among Latino- and Asian-Americans (1.9% and 2.0%, respectively) than among the general population.6,7 BED is typically first diagnosed in young adulthood (early to mid-20s);[8,9] symptoms often persist well beyond midlife.[10-12]

The prevalence of LOC eating is unknown. In postbariatric surgery patients, it may be as high as 25 percent.[13,14] In children at risk for adult obesity because of either their own overweight or that of their parents, prevalence may be as high as 32 percent.[15]

Current Challenges and Controversies in Diagnosing These Disorders

In diagnosing BED, assessing whether a patient is eating an atypically large amount of food is not wholly quantitative; it requires the clinician's evaluation of the patient's self-report. Assessment by a structured clinical interview is considered the gold standard. We included only studies in which participants were identified as meeting DSM-IV or DSM-5 criteria for BED as determined through a structured interview.

Assessing BED and LOC in children poses unique challenges, in part because neither the DSM-IV nor the DSM-5 established a minimum age for a BED diagnosis. As a result, when diagnosing adolescents, some clinicians consider BED criteria and others consider LOC eating criteria. We included studies of LOC eating in children ages 6–17 years.

In the postbariatric surgery circumstance, defining LOC eating is not straightforward; assessment methods are not standardized. Patients may report their disordered eating behaviors as a general subjective sense of lack of control over their eating rather than in terms of specific overconsumption based on the amount of food. Also, LOC eating may manifest in the consumption of food types and patterns of intake that are contraindicated after surgery.

Current Challenges and Controversies in Treating These Disorders

Treating patients with BED targets the core behavioral features (binge eating) and psychological features (i.e., eating, weight, and shape concerns, and distress) of this condition. Other important targets of treatment include metabolic health (in patients who are obese, have diabetes, or both) and mood regulation (e.g., in patients with coexisting depression or anxiety). Table B describes commonly used approaches. Treatments for LOC eating for postbariatric surgery patients and children reflect BED treatment options; treatment of children may include a role for parents.

Table B. Treatments commonly used for binge-eating disorder

Intervention Type	Treatment	Description
Psychological and behavioral	Cognitive behavioral therapy	Psychotherapy that focuses on identifying relations among thoughts, feelings, and behaviors, aiming to change negative thoughts about oneself and the world and, by doing so, reduce negative emotions and undesirable behavior patterns. Cognitive behavioral therapy is delivered is various ways—e.g., therapist-led individual and group sessions, self-help, and guided self-help.
Psychological and behavioral	Dialectical behavioral therapy	Behavioral therapy that focuses on increasing mindfulness and developing skills to improve emotion regulation, distress tolerance, and interpersonal relationships.
Psychological and behavioral	Interpersonal psychotherapy	Psychotherapy that focuses on the role of interpersonal functioning in negative mood, psychological distress, and unhealthy behaviors.
Psychological and behavioral	Behavioral weight loss	Treatment that incorporates various behavioral strategies to promote weight loss, such as caloric restriction and increased physical activity.
Pharmacological	Second-generation and tricyclic antidepressants	Treatment with a class of medications that works by selectively inhibiting reuptake of neurotransmitters involved in the regulation of mood and appetite (i.e., dopamine, norepinephrine, and serotonin). Common examples include bupropion, citalopram, desipramine, duloxetine, fluoxetine, and sertraline, commonly indicated for patients with depression.
Pharmacological	Anticonvulsants	Treatment with a class of medications used to treat epilepsy, bipolar disorder, major depression, and migraines; most commonly, topiramate.
Pharmacological	Antiobesity	Treatment with medications used to treat obesity. One example is orlistat, which inhibits pancreatic lipase, thereby decreasing fat absorption in the gut.
Pharmacological	Central nervous system stimulants	Treatment with a class of medications generally used to enhance or accelerate mental and physical processes, and specifically for treating patients with attention-deficit hyperactivity disorder and certain sleep problems. The only medication approved by the U.S. Food and Drug Administration for binge-eating disorder (lisdexamfetamine) belongs to this class.

Scope and Key Questions

This review addresses the efficacy and effectiveness of interventions for individuals meeting DSM-IV or DSM-5 criteria for BED, for postbariatric surgery patients with LOC eating, and for children with LOC eating. (Hereafter, the term "effectiveness" refers to both efficacy and effectiveness, including comparative effectiveness.) We also attempted to examine whether treatment effectiveness differed in subgroups based on sex, race, ethnicity, sexual orientation, body mass index (BMI), duration of illness, or coexisting conditions.

Broadly, we included pharmacological, psychological, behavioral, and combination interventions. We considered physical and psychological health outcomes in four major categories: (1) binge behavior (binge eating or LOC eating); (2) binge-eating–related psychopathology (e.g., weight and shape concerns, dietary restraint); (3) physical health functioning (i.e., weight and other indexes of metabolic health—e.g., diabetes); and (4) general psychopathology (e.g., depression, anxiety). Additional outcomes of interest included social and occupational functioning and harms of treatment.

We also examined the course of illness of BED and of LOC eating, particularly given their relatively high comorbidity with other medical and psychiatric conditions. In addition, clinical interest in understanding whether LOC eating reliably predicts poorer weight outcomes and new-onset BED over time is considerable. Little is known about the temporal stability of BED in the community generally, and of LOC in postbariatric surgery patients and children specifically.

Ultimately, the information produced in this review is intended to contribute to improved care for patients, better decisionmaking capacity for clinicians, and more sophisticated policies from those responsible for establishing treatment guidelines or making various insurance and related decisions.

Key Questions

We addressed 15 Key Questions (KQs). Nine are about effectiveness of treatment (benefits and harms overall and benefits for various patient subgroups)—three for BED, three for LOC eating among bariatric surgery patients, and three for LOC eating among children. The other six KQs deal with course of illness, overall and for various subgroups, for BED or LOC eating.

KQ 1. What is the evidence for the effectiveness of treatments or combinations of treatments for binge-eating disorder?

KQ 2. What is the evidence for harms associated with treatments for binge-eating disorder?

KQ 3. Does the effectiveness of treatments for binge-eating disorder differ by age, sex, race, ethnicity, initial body mass index, duration of illness, or coexisting conditions?

KQ 4. What is the course of illness of binge-eating disorder?

KQ 5. Does the course of illness of binge-eating disorder differ by age, sex, race, ethnicity, sexual orientation, body mass index, duration of illness, or coexisting conditions?

KQ 6. What is the evidence for the effectiveness of treatments or combinations of treatments for loss-of-control eating among bariatric surgery patients?

KQ 7. What is the evidence for harms associated with treatments for loss-of-control eating among bariatric surgery patients?

KQ 8. Does the effectiveness of treatments for loss-of-control eating among bariatric surgery patients differ by age, sex, race, ethnicity, initial body mass index, duration of illness, or coexisting conditions?

KQ 9. What is the course of illness of loss-of-control eating among bariatric surgery patients?

KQ 10. Does the course of illness of loss-of-control eating among bariatric surgery patients differ by age, sex, race, ethnicity, sexual orientation, initial body mass index, duration of illness, or coexisting conditions?

KQ 11. What is the evidence for the effectiveness of treatments or combinations of treatments for loss-of-control eating among children?

KQ 12. What is the evidence for harms associated with treatments for loss-of-control eating among children?

KQ 13. Does the effectiveness of treatments for loss-of-control eating among children differ by age, sex, race, ethnicity, initial body mass index, duration of illness, or coexisting conditions?

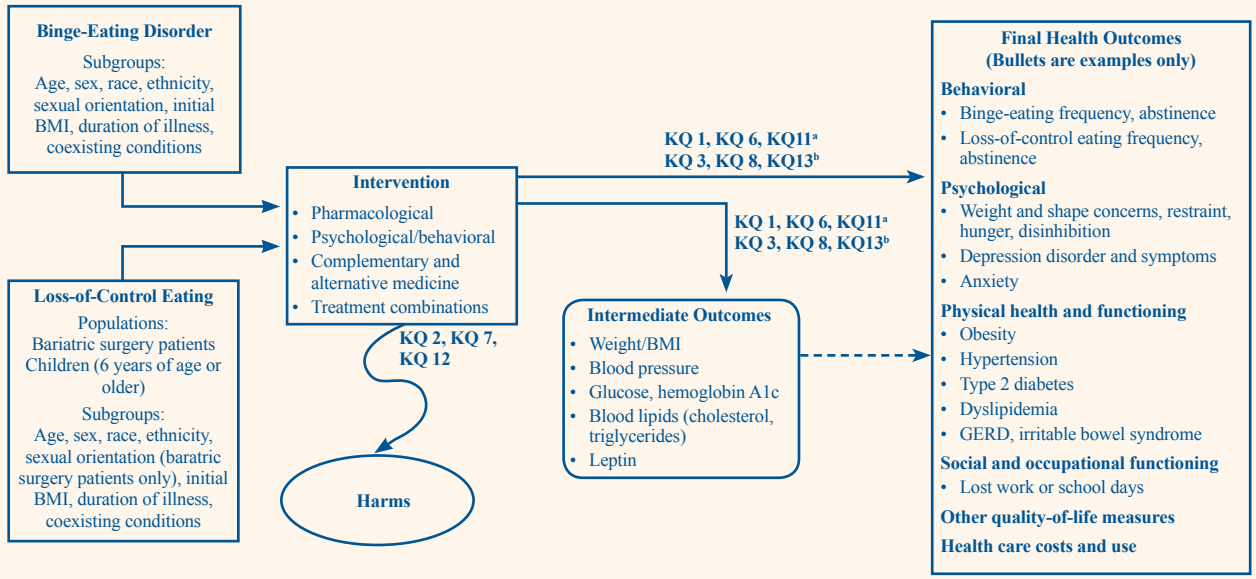
KQ 14. What is the course of illness of loss-of-control eating among children?

KQ 15. Does the course of illness of loss-of-control eating among children differ by age, sex, race, ethnicity, initial body mass index, duration of illness, or coexisting conditions?

Analytic Frameworks

The relationships among the patient populations, interventions, comparators, and outcomes are depicted for each treatment KQ in Figure A and for each course-of-illness KQ in Figure B.

Figure A. Analytic framework for binge-eating disorder and loss-of-control eating: effectiveness and harms of interventions

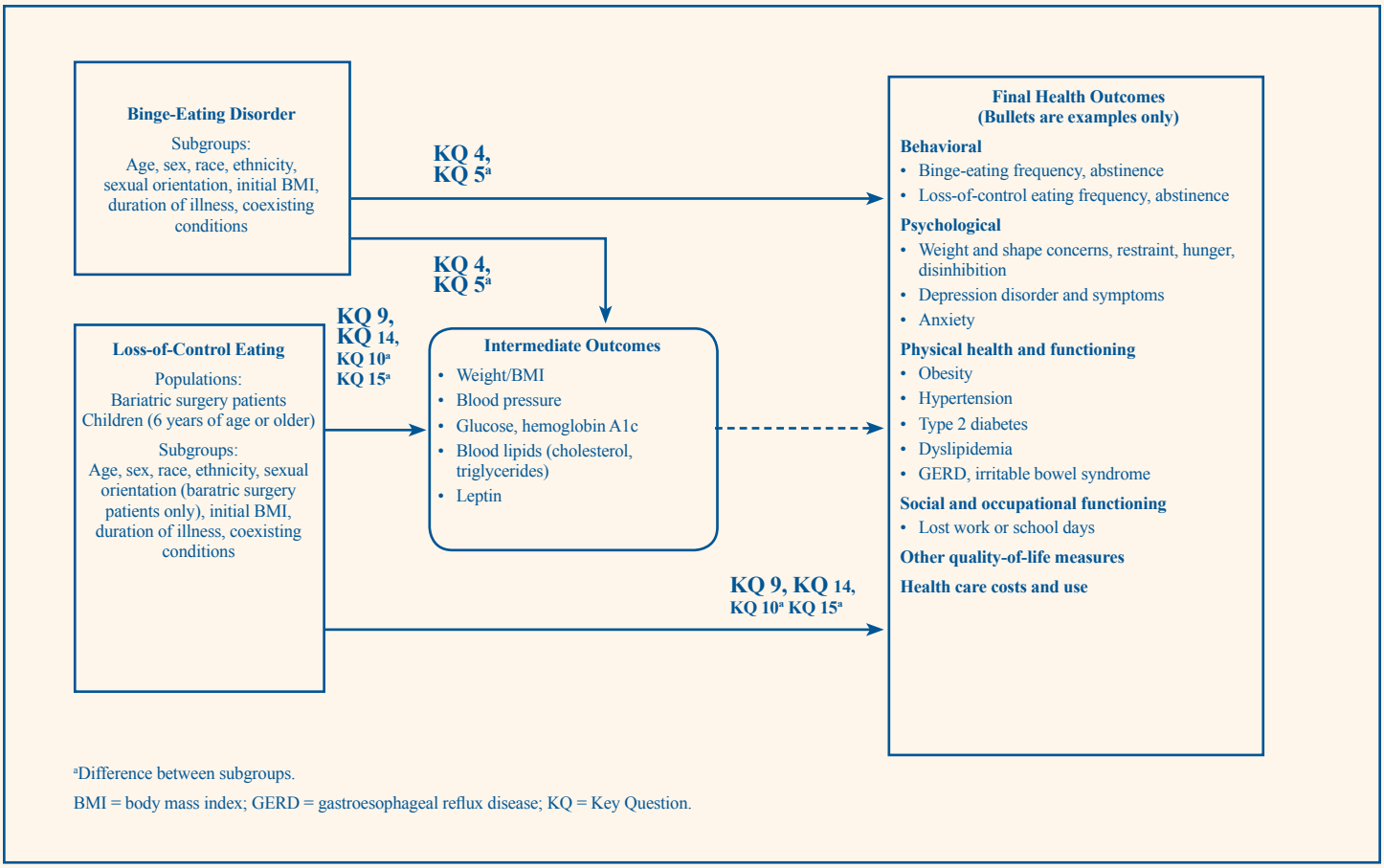


[a]Effectiveness of treatment.

[b]Differences between subgroups.

BMI = body mass index; GERD = gastroesophageal reflux disease; KQ = Key Question.

Figure B. Analytic framework for binge-eating disorder and loss-of-control eating: course of illness (outcomes of the disorders)



[a]Difference between subgroups.

BMI = body mass index; GERD = gastroesophageal reflux disease; KQ = Key Question.

Methods

Topic Refinement and Protocol Review

This topic and its KQs were developed through a public process. The Binge-Eating Disorder Association nominated the topic. The RTI International–University of North Carolina Evidence-based Practice Center (EPC) further developed and refined the topic with input from Key Informants in the field. The Agency for Healthcare Research and Quality (AHRQ) posted provisional KQs for public comment on January 13, 2014. We incorporated public comments and guidance from a Technical Expert Panel into the final research protocol (posted on the AHRQ Web site on April 4, 2014).

Literature Search Strategy

Search Strategy

We conducted focused searches of MEDLINE® (via PubMed®), Embase®, CINAHL (nursing and allied health database), Academic OneFile, and the Cochrane Library. An experienced research librarian used a predefined list of search terms and medical subject headings. The librarian completed the searches for the draft report on June 23, 2014; she conducted a second (update) search on January 19, 2015, during peer review.

We searched for relevant unpublished and gray literature, including trial registries, specifically ClinicalTrials.gov and Health Services Research Projects in Progress. AHRQ requested Scientific Information Packets (SIPs) from the developers and distributors of interventions identified in the literature review. We also requested Technical Expert

Panel members' and Peer Reviewers' recommendations of additional published, unpublished, and gray literature not identified by the review team. We included unpublished studies that met all inclusion criteria and contained enough information on their research methods to permit us to make a standard risk-of-bias assessment of individual studies. This could include, but was not limited to, conference posters and proceedings, studies posted on the Web site ClinicalTrials.gov, and U.S. Food and Drug Administration (FDA) medication approval packages. We included unpublished studies that met all inclusion criteria and contained enough information to permit us to make a standard risk-of-bias assessment. We searched reference lists of pertinent review articles for studies that we should consider for inclusion in this review, including our earlier review on this topic.[16-18]

Inclusion and Exclusion Criteria

We developed inclusion and exclusion criteria with a framework in mind that considered the relationship among the patient populations, interventions, comparators, outcomes, timing of outcome assessments, and settings (PICOTS). We considered only trials or studies written in English; additional evidence possibly available in non–English-language studies that had an abstract in English is also discussed.

The populations of interest are (1) individuals meeting DSM-IV or DSM-5 criteria for BED, (2) postbariatric surgery patients with LOC eating, and (3) children with LOC eating. We excluded studies of individuals with co-occurring anorexia nervosa or bulimia nervosa and studies of children younger than 6 years of age. We excluded trials with fewer than 10 participants and nonrandomized studies with fewer than 50 participants.

Treatments of interest include pharmacological interventions (e.g., antidepressants, anticonvulsants, attention-deficit hyperactivity disorder [ADHD] medications, and weight loss medications) and interventions that combine various psychological and behavioral techniques and principles to varying degrees (e.g., cognitive behavioral therapy [CBT], interpersonal psychotherapy [IPT], behavioral weight loss [BWL], dialectical behavioral therapy [DBT], and psychodynamic interpersonal therapy [PIPT]). We sought evidence on complementary and alternative medicine treatments but did not find any, and such interventions are not further discussed. Treatment combinations could involve psychological and behavioral interventions or psychological and behavioral with pharmacological interventions. Included studies had to have at least two groups. Acceptable comparisons included one of the other treatment comparisons, placebo, nonintervention, wait-list controls, or treatment as usual.

For psychological and behavioral interventions, we evaluated evidence by modality separately: individual and group therapy, and therapist-led and self-help approaches. The modalities involve a different therapist-patient relationship and level of health care resources; and only group therapy includes the influence of other patients suffering from the condition in the therapeutic process.

We specified a broad range of outcomes—intermediate and final health benefit outcomes and treatment harms (Figures A and B). We analyzed five groups of treatment effectiveness and course-of-illness outcomes: binge-eating outcomes, eating-related psychopathology outcomes, weight-related outcomes, general psychological outcomes (e.g., depression), and other (e.g., quality of life). Potential harms (also a broad range of minor to severe side effects or adverse events) varied across intervention types. Outcome differences for subgroups were evaluated for both treatment effectiveness and course of illness. We reported treatment outcomes at the end of treatment or later, but course-of-illness studies had a 1-year minimum followup from the diagnosis.

We included studies with inpatient or outpatient settings. We did not exclude studies based on geography.

Study designs included meta-analyses, systematic reviews, randomized controlled trials (RCTs), nonrandomized controlled trials, prospective and retrospective cohort studies, and case-control studies. We counted systematic reviews only if they provided information used in the evidence synthesis.

Study Selection

Trained members of the research team reviewed article abstracts and full-text articles. Two members independently reviewed each title and abstract using the predefined inclusion and exclusion criteria. Studies marked for possible inclusion by either reviewer underwent a full-text review. Two members of the team independently reviewed each full-text article. If both reviewers agreed that a study did not meet the eligibility criteria, it was excluded; each reviewer recorded the primary reason for exclusion. If reviewers disagreed, they resolved conflicts by discussion and consensus or by consulting a third member of the review team. We screened unpublished studies and reviewed SIPs using the same title/abstract and full-text review processes. The project coordinator tracked abstract and full-text reviews in an EndNote database (EndNote® X4).

Data Abstraction

We developed a template for evidence tables using the PICOTS framework and abstracted relevant information into the tables using Microsoft Excel. We recorded characteristics of study populations, interventions, comparators, settings, study designs, methods, and results. Six trained members of the team participated in the data abstraction. One reviewer initially abstracted the relevant data from each included article; a second more senior member of the team reviewed each data abstraction against the original article for completeness and accuracy.

Risk-of-Bias Assessment

We assessed risk of bias with three appropriate tools, described in more detail in the full report: (1) one for judging trials based on the Cochrane risk-of-bias tool for RCTs and summary judgments corresponding with EPC guidance; (2) one for evaluating risk of bias in non-RCTs and observational studies (modified from 2 existing tools); and (3) AMSTAR (A Measurement Tool To Assess Systematic Reviews) for assessing the quality of a systematic review. Two independent reviewers rated the risk of bias for each study. Disagreements between the two reviewers were resolved by discussion and consensus or by consulting a third member of the team.

Risk of bias is reported as a rating of low, medium, or high. RCTs with a high risk of bias are those with at least one major issue that has the potential to cause significant bias and thus might invalidate its results; such flaws include different application of inclusion/exclusion criteria between arms, substantial differences in arms at baseline, high overall attrition, differential attrition across arms that is not adequately addressed through analytic methods, or lack of control for concurrent treatment. An RCT may be evaluated as medium risk of bias, in contrast to low risk of bias, if the study does not have an obvious source of significant bias but, while it is unlikely that the study is biased because of the reported conduct in relation to other aspects of the trial, information on multiple bias criteria is unclear because of gaps in reporting. A key consideration in evaluating the risk of bias of cohort and case-control studies (only for our course-of-illness analyses) was control for critical potential confounding through design or statistical analyses. If critical information for making that assessment was not reported or was unclear, or if the conduct or analysis was severely flawed, we rated the study as high risk of bias.

To maintain a focus on interpretable evidence, we opted generally not to use trials with a high risk of bias in synthesizing treatment benefits. However, we did consider studies with high risk of bias in sensitivity analyses of our meta-analyses of treatment benefits and as allowable evidence for both treatment harms and course of illness.

Data Synthesis

For quantitative synthesis (meta-analyses to estimate overall effect sizes using Comprehensive Meta-Analysis, version 3.2), we had sufficiently similar evidence for placebo-controlled trials of second-generation antidepressants and lisdexamfetamine and for wait-list–controlled trials of therapist-led CBT. We did all other analyses qualitatively, based on our reasoned judgment of similarities in measurement of interventions and outcomes, and homogeneity of patient populations.

Strength of the Body of Evidence

We graded the strength of evidence based on the "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[19] This EPC approach incorporates five key domains: study limitations, directness, consistency, precision of the evidence, and reporting bias. Reviewers may also consider three optional domains if relevant to the evidence: increasing dose response, large magnitude of effect, and an effect that would have been larger if confounding variables had not been controlled for in the analysis.

Grades reflect the strength of the body of evidence to answer each KQ. A grade of high strength of evidence indicates that we have high confidence that the evidence reflects the true effect. Moderate strength of evidence indicates that we have moderate confidence that the evidence reflects the true effect. Low strength of evidence suggests that we have low confidence that the evidence reflects the true effect. Insufficient evidence signifies that the evidence is not available, that we are unable to estimate an effect, or that we have no confidence in the estimate of the effect.

Two reviewers assessed each domain independently and also assigned an overall grade for comparisons for each key outcome; they resolved any conflicts through consensus discussion. If they did not reach consensus, the team brought in a third party to settle the conflict.

Applicability

We assessed the applicability both of individual studies and of the body of evidence. For individual studies, we examined factors that may limit applicability (e.g., characteristics of populations, interventions, or comparators). Such factors may lessen our ability to generalize the effectiveness of an intervention for use in

everyday practice. We abstracted key characteristics of applicability into evidence tables. During data synthesis, we assessed the applicability of the body of evidence using the abstracted characteristics.

Peer Review and Public Commentary

Experts in BED and LOC eating, specifically clinicians and researchers specializing in pharmacotherapy treatment, psychotherapy and behavioral treatment, pediatrics, and evidence-based interventions, were invited to provide external peer review of the draft review. AHRQ staff (Task Order Officer and EPC Program Director) and an Associate Editor also provided comments. Associate Editors are leaders in their fields who are also actively involved as directors or leaders at their EPC. The draft report was posted on the AHRQ Web site for 4 weeks to elicit public comment. We responded to all reviewer comments and noted any resulting revisions to the text in the Disposition of Comments Report. This disposition report will be made available 3 months after AHRQ posts the final review on its Web site.

Results

We report results by KQ, grouped basically by intervention comparison (for treatment effectiveness and harms). We cover BED, LOC eating, and then course-of-illness findings in that order. Tables C–E summarize key findings and strength-of-evidence grades. The full report contains summary tables for results. Appendix D of the full report documents risk-of-bias assessments; Appendix E presents evidence tables for all included studies.

Literature Searches

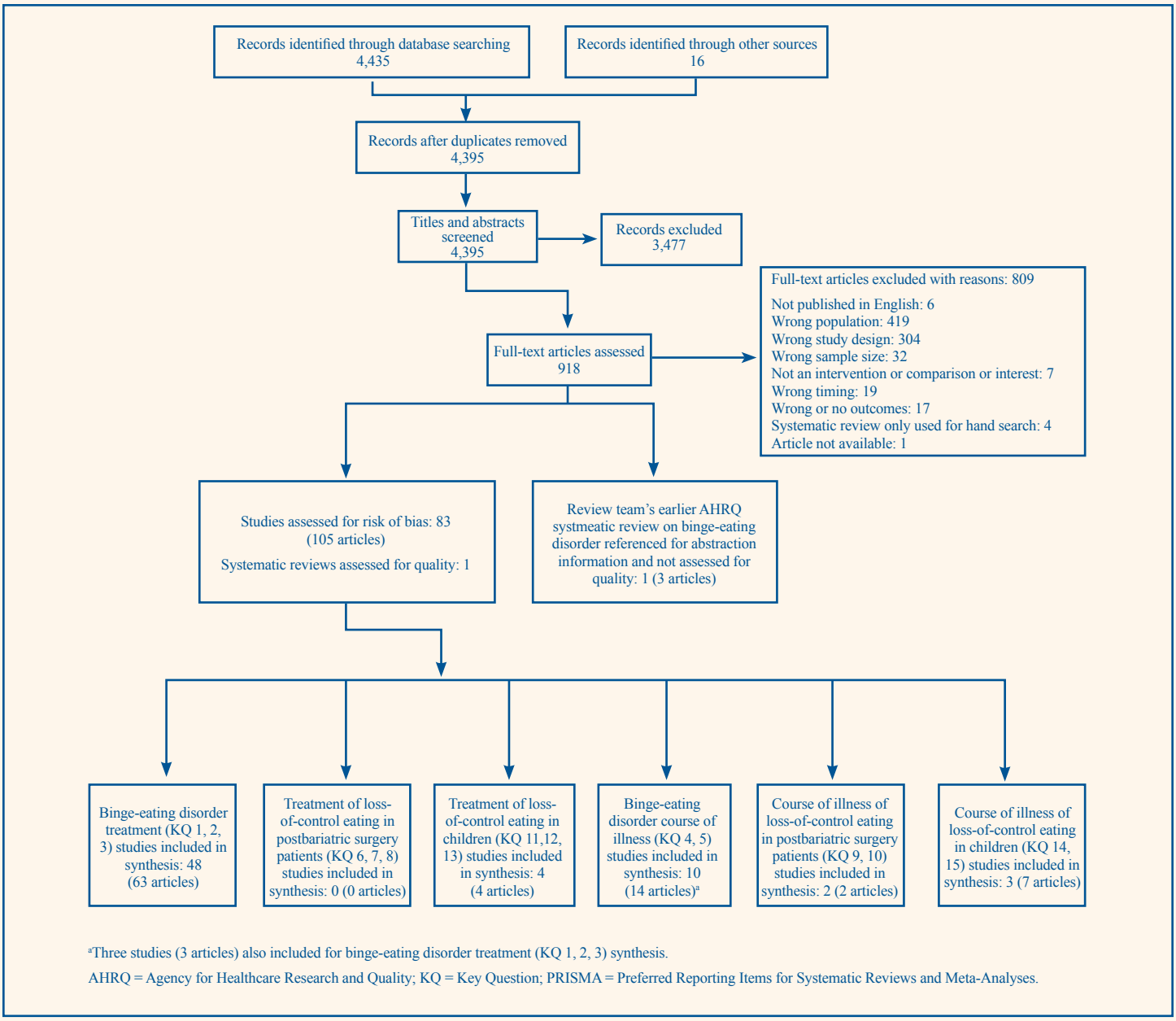
Figure C, a PRISMA [Preferred Reporting Items for Systematic Reviews and Meta-Analyses] diagram, depicts our literature search results. We identified a total of 4,395 unduplicated citations and determined that 918 met criteria for full-text review. We excluded 809 full-text articles based on our inclusion criteria and retained 105 articles reporting on a total of 83 trials or studies and 1 systematic review. Because we used some abstractions from our 2006 systematic review on eating disorders to develop some BED treatment and course-of-illness results, we consider that review as included evidence.[16-18] However, we reevaluated the risk of bias for all earlier included studies because we updated our assessment tools.

We did not use 19 studies in our main analyses of treatment benefits because of their high risk of bias. In keeping with standard approaches, however, we included one of these studies, which compared an antidepressant medication with placebo, in sensitivity analysis of our meta-analysis findings.[20] This was the only study with high risk of bias that reported on a treatment comparison that we evaluated through meta-analysis. We also used seven of the studies with high risk of bias in our assessment of treatment harms.[20-26]

We used 52 studies (67 articles) in our main analysis of treatment benefits (both BED and LOC eating). Fifteen studies (23 articles) met inclusion criteria for course-of-illness KQs. We used all 15 studies in that evidence synthesis, regardless of our risk-of-bias rating for the study.

Of the 20 fair- or good-quality studies on treatment for BED from our previous systematic review, 19 trials met the inclusion criteria for this review. One study was excluded because it used sibutramine, a treatment method no longer available in the United States.[27] Four studies[20,24,28,29] that we had rated as good or fair quality for the earlier review were newly rated as high risk of bias; we omitted them, therefore, from our main analyses. The earlier review also included three studies on BED course of illness that we have used here.[30-32]

Figure C. PRISMA diagram for binge-eating disorder treatment and course of illness



[a]Three studies (3 articles) also included for binge-eating disorder treatment (KQ 1, 2, 3) synthesis.

AHRQ = Agency for Healthcare Research and Quality; KQ = Key Question; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Key Question 1. Effectiveness of Interventions for Binge-Eating Disorder

For treatment effectiveness for BED, we address three broad categories of treatment: pharmacological, psychological or behavioral, and combination treatments.

For medications, the 18 included trials involved second-generation antidepressants, anticonvulsants, ADHD medications, an antiobesity drug, and a variety of other agents, including one dietary supplement. Among the antidepressants were several selective serotonin reuptake inhibitors (SSRIs) and several agents that primarily inhibit norepinephrine reuptake (i.e., norepinephrine-dopamine reuptake inhibitor [NDRI] or selective serotonin-norepinephrine reuptake inhibitor [SNRI]). Among the ADHD medications were lisdexamfetamine and atomoxetine.

In the category of psychological and behavioral treatments, the 23 included trials involved CBT, DBT, IPT, BWL, PIPT, and inpatient treatment.

Seven trials provided data on combination treatments, including pairings of CBT, BWL, hypocaloric diet, and diet counseling with either an antidepressant or an antiobesity medication. Two of the seven trials paired compound nonpharmacotherapy treatments (i.e., CBT plus BWL, CBT plus diet counseling) with an antidepressant. All trials testing a combination psychological plus pharmacological treatment arm also included a comparable combination placebo-controlled treatment arm (e.g., CBT plus antidepressant compared with CBT plus placebo).

Given the variability in outcome reporting and treatment comparisons, we were able to conduct meta-analyses only to measure the effectiveness on several outcomes of antidepressant treatments, as a class, compared with placebo; lisdexamfetamine compared with placebo; and therapist-led CBT compared with wait-list.

Pharmacological Interventions: Antidepressants Compared With Placebo

Eight RCTs (all placebo controlled) examined the effectiveness of antidepressants for treating BED patients. Of these, six involved an SSRI,[33-38] and one each involved an NDRI[39] or an SNRI.[40] In the six SSRI trials, two studied fluoxetine,[33,34] and one each studied citalopram,[38] escitalopram,[35] fluvoxamine,[36] and sertraline.[37] Assessments were conducted at the end of treatment.

As a class, antidepressants were associated with better binge-eating outcomes than placebo: abstinence (high strength of evidence for benefit), reduction in frequency of binge episodes per week (high strength of evidence for benefit), and reduction in binge days per week (moderate strength of evidence for benefit). Antidepressants were also associated with greater reductions in eating-related obsessions and compulsions (moderate strength of evidence for benefit). Weight reductions and BMI reductions were no greater with antidepressants (for both outcomes, low strength of evidence for no difference). Lastly, antidepressants were associated with greater reductions in symptoms of depression (low strength of evidence for benefit). The evidence was insufficient to evaluate outcomes for any specific antidepressant medication.

Pharmacological Interventions: Antidepressants Compared With Other Active Interventions

One trial involved a head-to-head comparison of two second-generation antidepressants (fluoxetine and sertraline).[41] The evidence was insufficient for concluding anything about treatment superiority.

Pharmacological Interventions: Anticonvulsants Compared With Placebo

Three placebo-controlled RCTs provided evidence about treating BED patients with anticonvulsants; two involved topiramate[42,43] and one lamotrigine.[44] Topiramate was associated with abstinence among a greater percentage of participants and with greater reductions in binge eating, obsessions and compulsions related to binge-eating, and weight (moderate strength of evidence for benefit); it also produced greater increases in cognitive restraint and reductions in hunger, disinhibition, and impulsivity (low strength of evidence for benefit). The evidence on the efficacy of lamotrigine was limited to one small trial (insufficient strength of evidence).

Pharmacological Interventions: Attention-Deficit Hyperactivity Disorder Medications Compared With Placebo

The included evidence consisted of four placebo-controlled RCTs of pharmacological interventions that were originally formulated for ADHD and were now being tested for treating patients with BED. One trial investigated the norepinephrine reuptake inhibitor atomoxetine,[45] which has been associated with weight loss; the other three studied the stimulant lisdexamfetamine.[46] The effectiveness of atomoxetine was examined in one small RCT (insufficient strength of evidence). Based on evidence from three RCTs, lisdexamfetamine was associated with abstinence among a greater percentage of participants, greater reductions in binge episodes per week, decreased eating-related obsessions and compulsions, and greater reductions in weight (high strength of evidence

for all of these outcomes). Depression measures were not consistently reported across the three studies; one of the studies found no difference from placebo (insufficient strength of evidence). Recently, lisdexamfetamine became the first medication approved by the FDA for treating BED patients.[47]

Pharmacological Interventions: Other Medications Compared With Placebo

Three placebo-controlled RCTs dealt with other pharmacological interventions. One trial each investigated the following: the sulfonic acid acamprosate, which is a mixed GABAA receptor agonist/NMDA receptor antagonist;[48] the μ-opioid antagonist ALKS-33 (also known as samidorphan);[49] and the dietary supplement chromium picolinate.[50] The strength of evidence is insufficient to determine effectiveness of any of these treatments because each was studied in a single, small sample trial.

Behavioral Interventions: Cognitive Behavioral Therapy Compared With No or Limited Intervention

CBT can be delivered in various formats; approaches include therapist-led, partially therapist-led, and self-help strategies (i.e., structured, guided, and pure). The two therapist-led approaches can involve either individual sessions (one-on-one) or group sessions.

Nine trials compared CBT with limited or no intervention.[51-59] Of 12 comparisons (in 7 separate trials) involving CBT and wait-list controls, 5 involved therapist-led CBT,[51-55] 2 involved partially therapist-led CBT,[54,55] 2 used structured self-help CBT,[54,55] 2 used guided self-help CBT including one Internet-based guide[56] and one in-person guide,[57] and 1 used pure self-help CBT.57 Two wait-list trials delivered CBT in an individual format[56,57] and five delivered CBT in a group format.[51-55]

Therapist-led CBT was related to various improved outcomes, including abstinence, binge frequency, and eating-related psychopathology (high strength of evidence for all outcomes). In contrast, reductions in BMI and symptoms of depression were not greater (both moderate strength of evidence for no difference). Similarly, partially therapist-led CBT was related to a greater likelihood of abstinence and reduced binge frequency (both low strength of evidence), but reductions in BMI and symptoms of depression were not greater (both low strength of evidence for no difference). Structured self-help was associated with reduced binge frequency (low strength of evidence) but no greater reduction in BMI or symptoms of depression (low strength of evidence for no difference).

Five small RCTs examined the effectiveness of guided or pure self-help CBT, but they differed in delivery format or comparator, and therefore evidence was insufficient for all comparisons and outcomes.

Behavioral Interventions: Cognitive Behavioral Therapy Compared With Cognitive Behavioral Therapy Variants

Seven trials compared CBT delivered in one format with CBT delivered in a different format.[54,55,57,60-63] Variations across trials resulted in four therapist-led comparisons: exposure versus cognitive restructuring,[60] CBT alone versus CBT plus ecological momentary assessment,[61] individual versus group,[62] and fully therapist-led versus partially therapist-led interventions.[54,55,63] Several self-help comparisons were also tested: one for guided self-help versus pure self-help[57] and two for therapist-led versus structured self-help.[54,63]

Only three of these comparisons were replicated in more than one trial. Binge-eating outcomes did not differ across comparisons of variations in therapist-led CBT, with one exception favoring therapist-led over structured self-help in one trial (low strength of evidence for no difference). BMI and depression outcomes did not differ across types of CBT (both moderate strength of evidence for no difference).

Behavioral Interventions: Cognitive Behavioral Therapy Compared With Behavioral Weight Loss

Four trials compared CBT with BWL approaches;[59,64-66] one also compared CBT and BWL (separately) with CBT plus BWL.[65] The CBT format varied across trials and included both therapist-led[64,65] and guided self-help.[59,66] For comparisons with therapist-led CBT, results were mixed. Binge frequency was lower in the therapist-led CBT arm (low strength of evidence), and BMI reduction was greater in the BWL arm at the end of treatment (moderate strength of evidence); the groups did not differ with respect to abstinence, eating-related psychopathology, or depression outcomes (low strength of evidence for no difference). Evidence on comparisons with guided self-help was insufficient because all comparisons were limited to single, small trials.

Behavioral Interventions: Cognitive Behavioral Therapy Compared With Interpersonal Therapy

Three trials compared CBT with interpersonal therapy strategies in treating patients with BED.[51,66,67] Two trials compared therapist-led IPT with either therapist-led CBT[68] or guided self-help CBT.[66] Another trial compared

therapist-led CBT with therapist-led PIPT.[51] Because trials differed in the intervention types that were compared, we could not synthesize results across trials (insufficient strength of evidence for all outcomes).

Behavioral Interventions: Cognitive Behavioral Therapy Combined With Diet or Weight-Loss Interventions

Three trials examined the use of CBT plus additional interventions involving either diet or weight-loss strategies (or both) in treating patients with BED. These involved two trials comparing CBT alone with CBT plus a diet or weight-loss intervention[65,69] and a single trial comparing CBT plus a low-energy dense diet with CBT plus general nutritional counseling. No significant differences were found for virtually any outcomes (insufficient strength of evidence in all cases).

Behavioral Interventions: Behavioral Weight Loss

Two trials tested BWL interventions for BED patients. These compared guided self-help BWL with an active control[59] and therapist-led BWL with therapist-led IPT.[66] Strength of evidence was insufficient because each comparison was limited to one small trial.

Behavioral Interventions: Psychodynamic Interpersonal Therapy Versus Wait-List

One small trial examined the effectiveness of therapist-led group PIPT.[51] Strength of evidence was insufficient for all outcomes.

Behavioral Interventions: Dialectical Behavioral Therapy

One trial evaluated therapist-led DBT against therapist-led active comparison-group therapy (insufficient strength of evidence for all outcomes).[70-72]

Behavioral Interventions: Inpatient Treatment Versus Inpatient Treatment Plus Active Therapies

Three trials examined treatment in an inpatient setting.[73-75] In each trial, patients received a standard inpatient care program and were randomized to additional active therapies. Two trials used virtual reality treatments that aimed to reduce body image distortions and food-related anxiety. However, these trials differed in several ways, so results were all based on single, small studies (insufficient strength of evidence for all outcomes).

Pharmacological Interventions: Combination Treatments Compared With Placebo and With Other Treatments

Evidence about combination interventions came from seven placebo-controlled RCTs. In all seven trials, investigators combined a medication with a psychological treatment; in two, they combined a medication with two psychological treatments.[34,76] Three trials used an antidepressant;[34,76,77] one, an anticonvulsant;[78] and three, an antiobesity agent.[79-81] The psychological interventions included CBT in three trials,[34,78,80] BWL in one trial,80 CBT plus BWL in one trial,[77] hypocaloric diet in one trial,[81] and group psychological support plus diet counseling in one trial.[76] The strength of evidence was insufficient to reach a conclusion concerning the effectiveness of any specific combination treatment because each combination was studied only in a single, small trial.

Key Question 2. Harms Associated With Treatments or Combinations of Treatments for Binge-Eating Disorder

Virtually all harms were limited to pharmacotherapy intervention trials (reported in 33 trials). Harms associated with treating BED patients and discontinuations from studies attributable to harms occurred approximately twice as often in patients receiving pharmacotherapy as in those receiving placebo. The number of serious adverse events was extremely low. Topiramate was associated with a significantly higher number of events involving sympathetic nervous system arousal (e.g., sweating, dry mouth, rapid heart rate) and "other" events (moderate strength of evidence), as well as a higher number of events related to sleep disturbance (low strength of evidence). Fluvoxamine was associated with greater gastrointestinal (GI) upset and sleep disturbances (low strength of evidence). Lisdexamfetamine was associated with a significantly higher likelihood of insomnia and headache (high strength of evidence), as well as greater GI upset, central nervous system arousal, and decreased appetite (moderate strength of evidence).

Key Questions 6 and 7. Effectiveness of Interventions (and Harms From Interventions) for Loss-of-Control Eating in Bariatric Surgery Patients

We found no evidence meeting our inclusion criteria that examined treatments or combinations of treatments for LOC eating among bariatric surgery patients.

Key Questions 11 and 12. Effectiveness of Interventions (and Harms From Interventions) for Loss-of-Control Eating in Children

Four small trials examined behavioral interventions for children with LOC eating.[82-85] One trial was a pilot for a larger trial by the same investigator group. The trials differed in the age range of participants (adolescents only or both adolescents and younger children), the definition of LOC eating that the investigators used to determine participant eligibility, treatment comparisons, and measures used to evaluate binge outcomes. With the exception of weight (low strength of evidence for no difference), strength of evidence was insufficient across all outcomes.

Key Questions 3, 8, and 13. Differences in the Effectiveness of Treatments or Combinations of Treatments for Subgroups

We found no evidence on differences by age, sex, race, ethnicity, sexual orientation, initial BMI, duration of illness, or coexisting conditions in any of our three populations of interest: patients with binge-eating disorder, bariatric surgery patients with LOC eating, and children with LOC eating.

Key Question 4. Course of Illness Among Individuals With Binge-Eating Disorder

Our evidence included 10 studies; all followed patients who had been identified through their earlier participation in a treatment study.[30,31,62,66,67,86-93] Factors that individual studies identified as being related to better outcomes included more rapid response to treatment, improvement in eating-related psychopathology, and improvement in non–eating-related psychopathology. Studies differed in the characteristics that the investigators had hypothesized might be related to better outcomes (insufficient strength of evidence). Binge outcomes were the most commonly reported outcomes across studies. Four studies reported weight outcomes (BMI), but results were mixed (insufficient strength of evidence). One study found an increased risk of miscarriage among women with BED (insufficient strength of evidence).[94] Finally, one study (of attempted suicides)[93] and a review article of three studies (of suicides)[92] found no evidence of increased risk of suicide among BED patients 5 years after treatment (moderate strength of evidence for no effect).

Key Question 9. Course of Illness Among Bariatric Surgery Patients With Loss-of-Control Eating

Two studies met our inclusion criteria but differed in the criteria they used for defining LOC eating before surgery.[32,95] One study found that LOC eating before surgery was related to LOC eating following surgery but not to weight loss or weight regain (insufficient strength of evidence across all outcomes because of a lack of clear and consistent findings in more than 1 study.)

Key Question 14. Course of Illness Among Children With Loss-of-Control Eating

Evidence concerning the course of illness among children with LOC eating behavior came from three longitudinal cohort studies.[96-102] Early adolescent binge or LOC eating predicted similar behavior in later adolescence in two studies (low strength of evidence). Evidence of additional outcomes was limited or inconsistent across studies (insufficient strength of evidence).

Key Questions 5, 10, and 15. Differences in Course of Illness for Subgroups

We found no evidence examining differences in the course of illness based on differences in sociodemographic or health characteristics (age, sex, race, ethnicity, sexual orientation, initial BMI, duration of illness, or coexisting conditions) in any of our three populations of interest: individuals with binge-eating disorder, bariatric surgery patients with LOC eating, and children with LOC eating.

Discussion

Key Findings and Strength of Evidence

We limit our discussion to key findings, chiefly on effectiveness (KQ 1) and harms (KQ 2) of common therapies for BED patients. Tables document main findings and strength-of-evidence grades (arrived at following AHRQ guidance). Other treatment results for BED and all treatment results for LOC eating can be found in the previous results section and in more detail in the full report. We comment briefly on course of illness in this section.

Key Question 1. Effectiveness of Treatments or Combinations of Treatments for Binge-Eating Disorder

Commonly studied treatments for BED patients are pharmacological agents and therapies that combine psychological and behavioral approaches. For outcomes

of pharmaceuticals (compared with placebo) and psychological and behavioral treatments (compared with wait-list or inactive controls), findings are limited to outcomes measured at the end of treatment. In contrast, patients enrolled in comparative effectiveness trials comparing two or more psychological and behavioral treatments or two or more formats of the same intervention tended to be assessed beyond the end of treatment, most commonly less than 1 year but in some instances 2 years or more.

Pharmacological Interventions

Table C summarizes the pharmacological interventions on which we had low, moderate, or high strength of evidence for clinical outcomes. Evidence based on meta-analyses pertains to second-generation antidepressants and lisdexamfetamine; evidence based on qualitative synthesis pertains to topiramate and lisdexamfetamine.

As a class, second-generation antidepressants were superior to placebo for achieving BED-specific and related clinical outcomes; the magnitude of the benefits generally was modest. Evidence was insufficient to demonstrate the effectiveness or comparative effectiveness of specific second-generation antidepressants for treating BED patients. Antidepressants were 1.67 times as likely as placebo to help patients achieve abstinence from binge eating (high strength of evidence). They reduced the weekly frequency of binge-eating episodes by approximately two-thirds of a binge episode per week (high strength of evidence) and approximately one binge-eating day (moderate strength of evidence). Even though patients improved, many did not achieve abstinence with antidepressants; 41 percent of those receiving antidepressants and 23 percent of those receiving placebo achieved abstinence.

For treating psychological aspects and correlates of BED, antidepressants helped reduce obsessive thoughts and compulsions related to binge eating and modestly improved symptoms of depression (low strength of evidence for benefit).

Overweight and obese patients treated with antidepressants did not lose significantly more weight during treatment than those who did not receive an antidepressant; BMI did not differ between groups (low strength of evidence for no difference in both cases). Given the limited impact on weight and the short length of treatment (6 to 12 weeks), finding no difference in the change in BMI at the end of treatment is not surprising.

Table C. Strength of evidence for pharmacological interventions to improve outcomes in binge-eating disorder

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
Second-generation antidepressants vs. placebo	MA of 8 RCTs (N = 416)	Antidepressants increased binge abstinence: RR, 1.67 (95% CI, 1.24 to 2.26; p = 0.001)	High for benefit
	MA of 7 RCTs (N = 331)	Antidepressants decreased the frequency of binge episodes per week: mean difference, −0.67 (95% CI, −1.26 to −0.09; p = 0.024)	High for benefit
	MA of 3 RCTs (N = 122)	Antidepressants decreased the frequency of binge days: mean difference, −0.90 (95% CI, −1.48 to −0.32; p = 0.002)	Moderate for benefit
	MA of 3 RCTs (N = 122)	Antidepressants decreased eating-related obsessions and compulsions based on— • Mean difference in YBOCS-BE: total, −3.84 (95% CI, −6.56 to −1.12; p = 0.006) • YBOCS-BE obsessions: −1.53 (95% CI, −2.69 to −0.37; p = 0.010) • YBOCS-BE compulsions: −2.31 (95% CI, −3.85 to −0.76; p = 0.003)	Moderate for benefit for total, obsessions, and compulsions
	MA of 4 RCTs (N = 182)	No difference in weight: mean difference in kg, -3.91 (95% CI, -10.14 to 2.32; p = 0.219)	Low for no difference
	MA of 6 RCTs (N = 297)	No difference in BMI: mean difference, −1.05 (95% CI, 2.64 to 0.55; p = 0.198)	Low for no difference
	MA of 3 RCTs (N = 142)	Antidepressants decreased symptoms of depression: mean difference, −1.98 (95% CI, −3.67 to −0.28; p = 0.022)	Low for benefit
Topiramate vs. placebo	2 RCTs (N = 468)	Topiramate increased binge abstinence	Moderate for benefit
	2 RCTs (N = 468)	Topiramate decreased the frequency of binge episodes	Moderate for benefit
	2 RCTs (N = 468)	Topiramate decreased eating-related obsessions and compulsions	Moderate for benefit
	2 RCTs (N = 468)	Topiramate decreased weight	Moderate for benefit
	1 RCT (N = 407)	Topiramate improved general and eating-related psychological functioning, as indicated by increases in cognitive control of eating and decreases in symptoms of psychological distress, susceptibility to hunger, and disinhibition of control over eating	Low for benefit

Table C. Strength of evidence for pharmacological interventions to improve outcomes in binge-eating disorder (continued)

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
Topiramate vs. placebo (continued)	1 RCT (N = 407)	Topiramate decreased impulsivity	Low for benefit
	1 RCT (N = 407)	Topiramate decreased disability in family and social domains	Low for benefit
Lisdexamfetamine vs. placebo	MA of 3 RCTs (N = 966)	Lisdexamfetamine increased binge abstinence: RR, 2.61 (95% CI, 2.04 to 3.33; p = 0.000)	High for benefit
	3 RCTs (N = 966)	Lisdexamfetamine decreased binge episodes per week	High for benefit
	3 RCTs (N = 966)	Lisdexamfetamine decreased eating-related obsessions and compulsions based on mean difference in YBOCS-BE total	High for benefit
	3 RCTs (N = 966)	Lisdexamfetamine decreased weight	High for benefit

BMI = body mass index; CI = confidence interval; MA = meta-analysis; RCT = randomized controlled trial; RR = risk ratio; YBOCS-BE = Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating.

Topiramate reduced the frequency of binge eating by approximately 1 binge day per week more than placebo; it helped more patients (BED, 58%; placebo, 28%) achieve abstinence from binge eating (moderate strength of evidence for benefit).Topiramate helped lower obsessive thoughts and compulsions related to binge eating by approximately 30 percent more than placebo and reduce greater general psychological distress symptoms by approximately 23 percent more than placebo (moderate strength of evidence for benefit). Among overweight and obese patients, those treated with topiramate lost, on average, approximately 10 pounds more (equivalent to ~4% more total body weight) than those who received placebo (moderate strength of evidence for benefit). Compared with placebo, topiramate also decreased patients' susceptibility to hunger as a trigger for binge eating, improved their general tendency to act less impulsively, increased their sense of cognitive control over their binge eating, and decreased disruptions in their social and family life (low strength of evidence for benefit).

Lisdexamfetamine improved binge-eating outcomes. Patients treated with lisdexamfetamine were 2.61 times as likely to achieve abstinence from binge eating as those who received placebo (high strength of evidence for benefit): across all study participants, 40 percent in the treatment arm, compared with 15 percent in the placebo arm, achieved abstinence. Patients treated with lisdexamfetamine also experienced a greater reduction in binge-eating days per week than those receiving placebo: point estimates of the differences in two Phase 3 trials were 1.3 and 1.7 fewer days, respectively (high strength of evidence for benefit). Lisdexamfetamine was associated with superior eating-related psychopathology outcomes, as measured through the Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating (YBOCS-BE) (high strength of evidence for benefit), and with weight reduction (high strength of evidence). However, data on depression and other psychological outcomes were too limited to be evaluated (insufficient strength of evidence).

Psychological and Behavioral Interventions

Table D summarizes the psychological and behavioral interventions for which we had low, moderate, or high strength of evidence for treatment benefits. We found evidence for all outcomes at the end of treatment and for some outcomes over periods as long as 6 years after treatment ended.

CBT reduced outcomes related to BED, measured as binge frequency and achieved abstinence, compared with those on wait-list. These benefits were apparent for four forms

of CBT (therapist led, high strength of evidence; partially therapist led, structured self-help CBT, and guided self-help CBT, all low strength of evidence). Evidence of the benefits of therapist-led CBT was particularly compelling; meta-analyses estimated a 4.95 times greater likelihood of abstinence (59% CBT; 11% wait-list) and a reduction of 2.3 binge episodes per week. For reducing general and eating-related psychological symptoms, therapist-led CBT reduced patients' susceptibility to hunger and eating concerns and improved their sense of control over eating (high strength of evidence); guided self-help CBT helped patients reduce global eating-related psychopathology (low strength of evidence). However, across the various forms of CBT, treatment was generally no better than wait-list for reducing weight or symptoms of depression (low strength of evidence for no difference). Collectively, this body of evidence suggests that some forms of CBT help patients with BED improve in several key behavioral and eating-specific psychological domains.

Table D. Strength of evidence for psychological or behavioral interventions to improve outcomes in binge-eating disorder

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
Therapist-led CBT vs. wait-list	MA of 4 RCTs (N = 295)	CBT increased binge abstinence: RR, 4.95 (95% CI, 3.06 to 8.00; p = 0.000)	High for benefit
	MA of 3 RCTs (N = 208)	CBT decreased the frequency of binge episodes per week: mean difference, −2.32 (95% CI, −4.56 to −0.09; p = 0.04)	High for benefit
	5 RCTs (N = 344)	CBT decreased eating-related psychopathology	High for benefit
	5 RCTs (N = 344)	No difference for BMI	Moderate for no difference
	5 RCTs (N = 344)	No difference for symptoms of depression	Moderate for no difference
Partially therapist-led CBT vs. wait-list	2 RCTs (N = 162)	CBT decreased binge frequency	Low for benefit
	2 RCTs (N = 162)	CBT increased binge abstinence	Low for benefit
	2 RCTs (N = 162)	No difference for BMI	Low for no difference
	2 RCTs (N = 162)	No difference for symptoms of depression	Low for no difference
Structured self-help CBT vs. wait-list	2 RCTs (N = 162)	CBT decreased binge frequency	Low for benefit
	2 RCTs (N = 162)	No difference for BMI	Low for no difference
	2 RCTs (N = 162)	No difference for symptoms of depression	Low for no difference
Guided self-help CBT vs. wait-list	2 RCTs (N = 122)	CBT increased binge abstinence	Low for benefit
	2 RCTs (N = 122)	CBT decreased binge frequency	Low for benefit
	2 RCTs (N = 122)	CBT decreased eating-related psychopathology	Low for benefit

Table D. Strength of evidence for psychological or behavioral interventions to improve outcomes in binge-eating disorder (continued)

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
Therapist-led vs. partially therapist-led CBT	2 RCTs (N = 158)	No difference in binge frequency or abstinence	Low for no difference
	2 RCTs (N = 158)	No difference in eating-related psychopathology	Low for no difference
	2 RCTs (N = 158)	No difference in BMI	Low for no difference
	2 RCTs (N = 158)	No difference in symptoms of depression	Low for no difference
Therapist-led vs. structured self-help CBT	2 RCTs (N = 158)	No difference in eating-related psychopathology	Low for no difference
	2 RCTs (N = 158)	No difference in BMI	Low for no difference
	2 RCTs (N = 158)	No difference in symptoms of depression	Low for no difference
Partially therapist-led vs. structured self-help CBT	2 RCTs (N = 164)	No difference in binge frequency or abstinence	Low for no difference
	2 RCTs (N = 164)	No difference in eating-related psychopathology	Low for no difference
	2 RCTs (N = 164)	No difference in BMI	Low for no difference
	2 RCTs (N = 164)	No difference in symptoms of depression	Low for no difference
Therapist-led CBT vs. BWL	2 RCTs (N = 170)	CBT decreased binge frequency more than BWL at end of treatment and up to 12-month followup	Low for benefit
	2 RCTs (N = 170)	No difference in abstinence	Low for no difference
	2 RCTs (N = 170)	No difference in eating-related psychopathology	Low for no difference
	2 RCTs (N = 170)	BWL decreased BMI more than CBT at end of treatment	Moderate for BWL benefit
	2 RCTs (N = 170)	No difference in symptoms of depression	Low for no difference

BMI = body mass index; BWL = behavioral weight loss; CBT = cognitive behavioral therapy; MA = meta-analysis; RCT = randomized controlled trial; RR = risk ratio.

We examined the comparative effectiveness of three different forms of CBT with each other: therapist-led CBT, partially therapist-led CBT, and structured self-help CBT. These comparisons are of interest, as they provide insight about the relative importance of therapist involvement in the effectiveness of CBT. Across comparisons, we found virtually no differences in binge-eating, BMI, or depression outcomes (low strength of evidence for no difference). All three of the CBT approaches were generally effective at helping patients both achieve binge abstinence and reduce binge frequency, most notably at end of treatment but throughout both short-term (6 month) and long-term (12 month) followup. Thus, although CBT variations generally did not differ in their ability to improve outcomes related to binge eating, they produced significant improvements in core outcome domains (regardless of treatment arm) over time.

We compared therapist-led CBT with therapist-led BWL treatment on outcomes assessed at the end of treatment and, in limited studies, for up to 6 years after treatment ended. CBT was superior to BWL for decreasing binge frequency at end of treatment and up to 12-month followup (low strength of evidence for benefit). BWL produced better BMI outcomes than CBT at end of treatment (moderate strength of evidence), but BWL patients tended to regain the weight they had lost during treatment. However, groups did not differ in abstinence, eating-related psychopathology, or symptoms of depression at end of treatment or at 12-month or 6-year followup.

Key Question 2. Evidence for Harms Associated With Treatments for Binge-Eating Disorder

We identified potential harms or side effects only for pharmacotherapy trials (comparisons with placebo). Table E summarizes the interventions for which we had low, moderate, or high strength of evidence for harms. Symptoms of sympathetic nervous system arousal were more common among patients who received topiramate than those who received placebo (moderate strength of evidence). Topiramate was also associated with headaches and sleep disturbances (low strength of evidence) and with a collection of other symptoms, including rash, high blood pressure, confusion, and taste aversion (moderate strength of evidence). Patients treated with fluvoxamine reported symptoms of GI upset and sleep disturbances more frequently than patients who received placebo (low strength of evidence). Patients treated with lisdexamfetamine more commonly experienced GI upset (moderate strength of evidence), sympathetic nervous system arousal (moderate strength of evidence), insomnia (high strength of evidence), headache (high strength of evidence) and decreased appetite (moderate strength of evidence).

Table E. Strength of evidence for harms of pharmacological interventions to improve outcomes in binge-eating disorder

Intervention and Comparator	Number of Studies (Sample Sizes, Number of Reported Events)	Outcome and Results	Strength of Evidence
Topiramate versus placebo	2 RCTs (N = 468, 94)	Topiramate and placebo: no difference related to GI upset	Low for no difference
	2 RCTs (N = 468, 243)	Topiramate: higher number of events related to sympathetic nervous system arousal	Moderate for harm
	2 RCTs (N = 468, 89)	Topiramate: higher number of events related to sleep disturbance	Low for harm
	2 RCTs (N = 468, 73)	Topiramate: higher number of headaches	Moderate for harm
	2 RCTs (N = 468, 179)	Topiramate: higher number of other events[a]	Moderate for harm

Table E. Strength of evidence for harms of pharmacological interventions to improve outcomes in binge-eating disorder (continued)

Intervention and Comparator	Number of Studies (Sample Sizes, Number of Reported Events)	Outcome and Results	Strength of Evidence
Fluvoxamine vs. placebo	2 RCTs (N = 105, 24)	Fluvoxamine: higher number of events related to GI upset	Low for harm
	2 RCTs (N=105, 22)	Fluvoxamine higher number of events related to sympathetic nervous system arousal	Low for harm
	2 RCTs (N = 105, 57)	Fluvoxamine: higher number of events related to sleep disturbance	Low for harm
Lisdexamfetamine vs. placebo	3 RCTs (N = 938, 119)	Lisdexamfetamine: higher number of events related to GI upset	Moderate for harm
	3 RCTs (N = 938, 342)	Lisdexamfetamine: higher number of events related to sympathetic nervous system arousal	Moderate for harm
	MA, 3 RCTs (N = 938, 78)	Lisdexamfetamine: higher likelihood of insomnia (RR, 2.66; 95% CI, 1.63 to 4.31; p = 0.00)	High for harm
	3 RCTs (N = 938, 111)	Lisdexamfetamine: higher likelihood of headache (RR, 1.63; 95% CI, 1.13 to 2.36; p = 0.009)	High for harm
	3 RCTs (N = 938, 66)	Lisdexamfetamine: higher number of events related to decreased appetite	Moderate for harm

[a]Includes confusion, depression, eructation, high blood pressure, language problems, rash or itching, respiratory illness, rhinitis, sinusitis, taste aversion, urinary hesitancy, bone fracture resulting from accidental injury, and other problems.
CI = confidence interval; GI = gastrointestinal; MA = meta-analysis; RCT = randomized controlled trial; RR = risk ratio.

Key Question 4. Course of Illness Among Individuals With Binge-Eating Disorder

Ten studies (trials or observational studies, including 3 rated high risk of bias) provided information on outcomes of BED patients 1 year or longer after their diagnosis; all involved only individuals who had participated in BED treatment studies. Investigators commonly reported binge outcomes, but they tended to offer different hypotheses about what factors might be related to better outcomes; these variables included more rapid response to treatment, improvement in eating-related psychopathology, and improvement in non–eating-related psychopathology. One study found that the odds of miscarriage were higher among women with BED (1 study, insufficient evidence); a review article (3 studies) and an additional study found no evidence of increased risk of suicide among BED patients 5 years after treatment (moderate strength of evidence for no effect.)

Findings in Relation to What Is Already Known

Our 2006 review, "Management of Eating Disorders,"[16-18] included evidence on treatment and course of illness for BED. Based on our qualitative analysis of eight RCTs, we concluded that medications improved clinical outcomes. Two later meta-analyses reached a similar conclusion. Stefano and colleagues[103] included seven (of our 8) RCTs and focused specifically on antidepressant medications; Reas and Grilo[104] included six of those RCTs and two new trials of SSRIs, and focused specifically on SSRIs. Those studies estimated similar effect sizes for abstinence (risk

ratio of nonabstinence from binge eating: 0.77 and 0.81, respectively), but they reached different conclusions about weight and depression outcomes.

For the current review, we excluded two of the eight RCTs from our earlier review (one because it was newly rated as high risk of bias and a second because it used a medication no longer available in the United States). Also, we included two newer antidepressant trials,[39,40] one anticonvulsant trial,[44] one trial of atomoxetine,[45] and three new trials of lisdexamfetamine[46,105-107] not included in either the 2008 or 2009 meta-analyses.

Based on this additional evidence, we confirmed our earlier conclusion about the effectiveness of second-generation antidepressants for binge abstinence and binge frequency. We also provided new findings regarding the effectiveness of second-generation antidepressants for eating-related obsessions and compulsions, weight, and depression outcomes. In the current review, we included one additional anticonvulsant RCT but were not able to add new information regarding effect size for anticonvulsant medications because of high variability among studies.

With regard to psychological and behavioral interventions, our previous review concluded that CBT effectively reduces binge frequency and increases binge abstinence, based on a qualitative synthesis of eight RCTs. For the current review, we excluded 2 of the 8 RCTs from our earlier review (newly rated as high risk of bias[28,29]) and added 16 new RCTs.[51-53,56,58,59,61,62,64-66, 69,70,74,75,108] Based on this newer body of evidence, we confirmed our earlier conclusion establishing CBT as an effective treatment for improving binge abstinence and reducing binge frequency; we also reported its effectiveness at reducing eating-related psychopathology. We provided new findings about the effectiveness of different forms of therapist involvement in CBT interventions and for promising interventions such as IPT and DBT.

For BED course of illness, our earlier review identified only three studies. Although the evidence base is larger for this review, the new studies provide little additional insight. They are mostly case series designs without comparisons or controls for potential confounding factors associated with outcomes, and they are limited to patients followed after treatment.

Our review is the only one that we have identified that has summarized the evidence on treatment and course of illness for bariatric surgery patients and children with LOC eating.

Implications for Clinical and Policy Decisionmaking

We had hoped to comment on the effectiveness and harms of specific pharmacological and psychological or behavioral treatments for BED and on the comparative effectiveness of specific treatments for BED. Unfortunately, the heterogeneity in approaches precluded offering much in the way of implications for clinical practice or policy decisionmaking. Key conclusions with meaningful ramifications for either clinical applications or policymaking follow.

For several key outcomes, we found clear evidence of benefits with second-generation antidepressants; however, we cannot comment on the effectiveness of any specific second-generation antidepressant. We confirmed previous observations of benefit with topiramate and presented new evidence of clear benefit from lisdexamfetamine. We also found strong evidence of benefit with therapist-led CBT for several key outcomes and support for the effectiveness of other forms of CBT (i.e., partially therapist-led CBT and guided self-help CBT).

Harms of psychological and behavioral treatments were rarely reported but commonly known side effects with topiramate, fluvoxamine, and lisdexamfetamine were reported. The FDA has determined that these three drugs are associated with potential risk during pregnancy; in particular, topiramate is associated with increased risk of oral clefts in newborns.[109] No pregnancy-related harms occurred in the included studies, in which women of childbearing age were overrepresented.[8] Nonetheless, clinicians may want to counsel women patients of childbearing age about the pregnancy risks of these medications in determining their long-term treatment plans.

Overall, based on the available evidence for both benefits and harms, clinicians may find second-generation antidepressants, topiramate, medications formulated for ADHD (notably lisdexamfetamine), and a few forms of CBT to be reasonable choices for the treatment of BED.

The superiority of a few CBT formats was determined for efficacy but not for comparative effectiveness; outcomes from CBT interventions were assessed in comparison with no intervention at all (wait-list control). Limited data emerged on the comparative effectiveness of various formats of CBT or comparisons between CBT formats and other approaches. Although virtually none of the available evidence showed superiority of one approach over another, we caution readers not to conclude that this implies that the various behavioral and psychological intervention

formats are identical in terms of outcomes; the point is that they are not significantly different. None of the included comparative effectiveness studies was designed to examine the equivalence or noninferiority of approaches.[110] These findings have implications for decisionmakers who may be considering the resources needed for therapist-led interventions relative to those for other, less therapist-intensive forms of CBT or other behavioral interventions. These considerations may be particularly relevant for broader community settings, such as rural areas that may have limited availability of specialized treatment for BED or LOC eating.

Data on other promising treatment options, such as IPT and DBT, were limited to single trials because investigators used a wide array of delivery formats. Clinicians may want to consider these treatments for some patients. The effect of IPT on binge abstinence may be particularly durable; one study found that at 4-year followup, binge abstinence was greater in IPT than CBT patients.

We had wanted to examine the potential impact of the DSM-5 changes to make the BED diagnostic criteria less stringent: the binge frequency criterion was lessened and the duration of illness shortened. Clinicians, patients, and policymakers might have considerable interest in knowing whether effective treatment options may differ in this newly included group of patients. Unfortunately, no study provided separate results for a patient population diagnosed according to DSM-5.

We also sought to provide useful evidence concerning effective treatments for two specific populations of individuals with LOC eating. Given the complete lack of studies for bariatric surgery patients and only inconclusive or inconsistent information about children, we cannot pose any definitive implications for clinicians or policymakers at this time.

Applicability

Population

Findings about BED treatment interventions are likely to be applicable to all adults age 18 and older with the disorder, but chiefly to overweight or obese women. We cannot comment on the applicability of treatment findings for specific subgroups of adults (even among women) or whether findings extend to BED patients diagnosed based on DSM-5 criteria (which are less stringent than those for DSM-IV). Also unclear is whether our findings apply to adolescents with BED or to various minority groups.

The evidence base about treating LOC eating was small for children and nonexistent for bariatric surgery patients. Thus, generalizing to child patient populations is probably inappropriate, and generalizing to bariatric surgery patients is impossible. A key drawback is that appropriate and consistent diagnostic criteria that clinicians might reliably use to identify LOC eating have not been established.

For BED course of illness, generalizing our findings to an untreated population would be inappropriate. We can, however, offer hypotheses about several ongoing concerns. In particular, untreated BED could likely become a chronic condition that might, in turn, result in deleterious mental and physical health effects. Left untreated, the condition may lead to or worsen other mental health concerns (e.g., depression or anxiety) or physical health conditions (e.g., diabetes or irritable bowel syndrome).

Interventions and Comparators

In general, we believe that the findings about selected second-generation antidepressants, topiramate, ADHD medications, and a few forms of CBT are applicable to the BED patient populations studied. Only lisdexamfetamine has FDA approval for treating BED (presumably taking both benefits and adverse events into account).

For most treatments, tested in only a single study, we cannot draw any clear implications for clinical or policy decisionmaking. This is true for classes of interventions and single agents, such as individual antidepressants. No evidence is available on complementary and alternative medicine approaches for either BED or LOC eating,

Outcomes

Although we cast a wide net for outcomes, our primary focus was on reductions in commonly measured BED symptomatology, including binge frequency, eating-related obsessions and compulsions, restraint, shape and weight concerns, weight, and depression. Investigators used a considerable array of different measures or instruments to assess these outcomes; this heterogeneity constrains our ability to conclude that findings can be generalized with confidence across all outcome categories of interest. We did not find sufficient information to draw any conclusions about treatment effectiveness for more global measures, such as quality of life or lost productivity; neither did we find evidence about treatment effectiveness as it relates to final health outcomes such as diabetes, gastric reflux, and irritable bowel syndrome. Given the scarcity of information about LOC eating, we can conclude little or nothing about the applicability of these trials to proposed or potential outcomes of treatment among bariatric surgery patients or children.

Timeframes

All trials of medications measured outcomes at the end of treatment, but many of these trials were relatively short; only two trials reported followup beyond the end of treatment.[111,112] Similar studies examining the efficacy of psychological and behavioral interventions measured outcomes at the end of treatment. Comparative effectiveness studies on different psychological or behavioral interventions or different intervention formats were more likely to include both short- and long-term followup; one trial extended to 6 years after the end of treatment. Generally, the applicability of these trials for understanding the long-term impacts of treatment (benefits or harms) is relatively limited because the long-term efficacy of the individual treatments has not been established; the applicability of these studies (especially the pharmacological trials) for short-term benefits may be somewhat stronger.

Settings

The evidence base for both BED and, in children, LOC eating was largely outpatient care, which is the standard of care in the United States. We found very limited evidence about inpatient therapies, and the patient populations in studies of inpatient care (all conducted in Italy) would be unlikely to be eligible to receive inpatient care in the United States. Of all the trials we included for either BED or LOC, most were conducted in clinical settings in North America (mainly United States but also Canada); evidence also came from studies conducted in Scandinavia or elsewhere in Europe.

Generally, apart from considerations relating to health systems and insurance for the few investigations done outside North America, results are applicable to U.S. patient populations. However, most studies were conducted in supervised settings generally associated with academic research and medical centers, where medication treatment was likely managed by a psychiatrist, and psychological and behavioral treatments were likely delivered by highly trained personnel. It is unclear whether our findings apply to the real-world settings in which individuals seek and receive treatment in their local community through contact with their primary care physician or other community-based providers who do not have specific expertise in BED treatment.

Limitations of the Review Process

For this review, we excluded non–English-language studies based largely on limitations of time and resources. However, we examined English-language abstracts of non–English-language studies to assess the potential size of the literature that would be missed through this approach. Based on this exercise, we concluded that by limiting our review to English-language studies only, we may have missed only one systematic review of exercise as treatment for BED patients.

Limitations of the Evidence Base

For all medications except fluoxetine, topiramate, and lisdexamfetamine; many psychological and behavioral studies; and all combination treatment studies, the evidence base for treatment efficacy comprised only single studies. The evidence base was extremely limited in scope and volume for treatment of LOC eating in children and nonexistent for bariatric surgery patients after surgery. Evidence about harms was limited because adverse events, serious adverse events, and study discontinuations clearly attributable to adverse events were not uniformly collected or reported in studies.

We also encountered a nontrivial number of trials or other studies with substantial drawbacks in methods. The problems involved randomization and allocation concealment, masking of outcomes assessors, attrition (or differential attrition), and questionable analytic techniques (e.g., no intention-to-treat analyses). Other issues in the overall evidence base included small sample sizes (and thus lack of power for determining intended effects), lack of clarity in defining the conditions (or not reporting data separately for DSM-IV and DSM-5 patients), short studies (e.g., outcomes measured only at end of treatment, which could be just a matter of weeks), and lack of information on statistical methods (or data on confidence intervals or similar information on statistical tests).

Research Gaps

Subgroups Studied

No study addressed differences in treatment outcomes among important subgroups defined by age, sex, race, ethnicity, or other relevant patient characteristics. Observational and cross-sectional studies have shown that binge eating may be more common among certain racial minorities, yet treatment studies have failed to address whether outcomes differ between groups defined by race. These gaps limit applicability to these important groups.

Secondary analyses of data from treatment studies have shed some light on factors that may be important for future consideration, including age and sex. Nevertheless, the specific analyses that were conducted did not address whether treatment effectiveness was the same or different in these subgroups. For instance, as in our earlier systematic review of eating disorders, we identified very

little information about the impact of treatments on either men or boys.

Moreover, despite the high comorbidity between BED and depression and between BED and obesity, no studies specifically compared outcomes in groups of patients defined either by baseline level of depression or by baseline weight status. Second-generation antidepressants have a small but significant impact on symptoms of depression in BED patients with low levels of depressive symptoms. Whether the small benefit of second-generation antidepressants is meaningful, or perhaps amplified, in BED patients with higher levels of depression warrants further study.

In light of growing awareness of LOC eating in children and concerns that LOC eating has negative health effects and predisposes to BED later in life, treatment studies focusing on children are needed.

Outcomes Measured (Benefits or Harms)

The evidence base was deficient for outcomes related to social and occupational functioning or quality of life more generally. It was similarly poor in relation to final health outcomes such as glucose intolerance or dysregulation that may predispose patients to diabetes and other chronic conditions. Also lacking is evidence of harms associated with psychological or behavioral treatments. A fourth critical gap concerns longer term benefits and harms for all single and combination treatment modalities.

Interventions

We found strong evidence that CBT is beneficial for patients with BED; however, that conclusion was limited largely to therapist-led CBT because of insufficient information regarding other CBT formats. At present, the body of evidence for CBT constitutes a collection of disparate studies testing variations in format; furthermore, the rationale for comparing different formats is not consistently grounded in an a priori mechanism of action.

The number of therapists with expertise in CBT for BED is limited. This limitation poses a challenge for implementation of our findings. One useful step might be to compare directly, in adequately powered head-to-head trials, whether therapist-led CBT is superior to other CBT formats. If modified versions that require less therapist involvement can be shown to be as effective as therapist-led CBT through equivalence or noninferiority trials, such information could help make CBT more scalable than it has been to this point. Findings might then guide the next generation of studies that are needed to move the field closer to an individualized approach to treatment. Those future studies should consider other psychological or behavioral interventions that have shown promise (IPT and DBT). In addition, they should be adequately powered to test for differences in outcomes across key subgroups (e.g., groups defined by age, sex, race, ethnicity, mental health comorbidities, and weight), for which a dearth of information still exists.

Second-generation antidepressants were beneficial in reducing symptoms of depression, and topiramate was beneficial for reducing symptoms of impulsivity. A head-to-head comparison of the effectiveness of these two treatment options on mood and impulse regulation outcomes might help clinicians and patients make first-line pharmacotherapy treatment choices based on individual patients' needs and preferences. Further examination of lamotrigine may also be warranted, despite the negative findings for abstinence in one small trial; in that trial, the lamotrigine response rate (50%) was similar to that of topiramate (58% percent), but the placebo response rate was extremely high (71%). Further examination of lamotrigine may also be justified because, owing to its unique biochemical structure and function relative to topiramate, it may be associated with fewer sympathetic nervous system and other side effects.[113,114]

Head-to-head comparisons involving pharmacological treatment, psychological treatment, and combination treatments are also needed to determine whether, as one study suggests,34 gains persist longer following psychological (CBT) or combination (CBT + fluoxetine) treatment than following pharmacological (fluoxetine) treatment alone. This information would help patients and providers optimize their plans to address both short- and long-term goals of treatment.

CBT comparative effectiveness evidence has focused on whether less specialized care can be as effective as more intensive services (e.g., those with substantial involvement of therapists); more studies of these comparisons are needed. In addition, studies of stepped-care models can elucidate whether and when a combination treatment or a shift to higher levels of care (e.g., intensive outpatient, partial hospitalization, residential treatment, or inpatient) is warranted for patients who are not responding adequately to conventional outpatient treatment.

Despite current interest in complementary and alternative medicine, neutraceuticals, and mindfulness-based interventions for regulating appetite, eating behavior, and weight, the literature is deficient regarding these types of interventions for BED. We searched clinical trial registries to determine whether additional evidence was available from newly completed but as- yet unpublished studies. We also checked for evidence of studies that were selectively

withheld from publication because of unfavorable outcomes (possible publication bias). Based on these activities, we did not determine that reporting bias was a concern.

We included as evidence a report of a Phase 2 trial of lisdexamfetamine dimesylate (Vyvanse®), one of two included medications originally formulated to treat patients with ADHD. In this trial, separate study arms compared dosages of 30 mg/day, 50 mg/day, and 70 mg/day with placebo. The FDA approved this medication for treatment of BED in January 2015, expanding significantly our earlier evidence base. The FDA approval was based on the results of two Phase 3 trials, limited to lisdexamfetamine dimesylate dosages of 50 or 70 mg/day (N = 773). We obtained data on these trials through the gray literature. Peer-reviewed publication of the Phase 3 trials would add to our confidence about the conduct and outcomes of these studies. In addition, the mechanism of action of lisdexamfetamine for treating BED patients is unknown, so whether similar results would emerge for other stimulants or other medications currently used to treat ADHD patients is unknown.

Deficiencies in Methods

Our 2006 review, "Management of Eating Disorders,"[16-18] identified several methodological issues within the BED treatment literature and recommended changes for future studies. Some of these deficiencies persist; they include inadequate reporting of randomization and allocation concealment and insufficient attention to treatment group differences in the use of cointerventions. These and other factors led us to change our risk-of-bias ratings (e.g., to high risk of bias) for some studies and, in turn, reduced the strength of the evidence for the current review.

The 2006 review also highlighted several critical needs for advancing the field. Our suggestions included conducting replication studies, doing longer term followup studies, and streamlining and standardizing outcome measures to eliminate reporting of false discoveries. Unfortunately, with few exceptions,[42,43,54,55] replication studies do not exist; thus, the evidence base remains insufficient to address whether gains achieved during short-term treatment persist after treatment ends. This gap is especially critical for pharmacological treatments, as patients and their providers seek to understand the need for ongoing medical management to maintain treatment gains.

The field would benefit from the development of universally accepted definitions of remission and recovery.[115] To reach this goal requires longer term followup periods with periodic reevaluation of a core set of psychological, behavioral, and physiological outcomes. Standard definitions of remission and recovery should consider a continuum approach rather than focus on just a fixed point in time.

We have two recommendations for improved designs. First, studies should implement a minimum 1-year followup period. Even longer periods of followup may be warranted to capture the remissions and improvements in illness that can occur long term. Similarly, longer trials might help clarify what treatments provide better outcomes with fewer side effects and are better for patients who do not fully recover but live with a chronic illness.

Second, future studies should include a reasonably limited set of eating-specific instruments (such as the Eating Disorder Examination questionnaire, the Three-Factor Eating Questionnaire, or the YBOCS-BE) and general psychological symptom (depression, anxiety, negative body image) self-report instruments. Adaptations of existing reliable and valid instruments[40] that are specific to binge eating might help to move the field closer to an understanding of the core determinants of recovery and relapse, but such adaptations should be used only if they are clearly described so that others can replicate their use. Such descriptions should include basic information on the reliability, validity, and reproducibility of these newer instruments.

Additionally, considering the perspective of the patient in defining remission and recovery is crucial. Using such preferences or values in developing consistent definitions of these types of patient-centered outcomes would be a major advance in this clinical area. Interweaving this information with reliable, validated measures would allow researchers and clinicians to generate a comprehensive set of parameters by which remission and recovery could be measured. Consistent and thorough reporting of these outcomes (e.g., fully descriptive data at each major assessment point) would help improve calibration of these instruments against each other, which is ultimately needed for future efforts to use meta-analysis to evaluate treatment effect size.

Further, there are several etiological and treatment considerations that might merit further study to better elucidate the onset, maintenance, and treatment of BED. For example, given the prevalence of underlying metabolic disorders (e.g., diabetes mellitus, polycystic ovary syndrome) in patients with BED, it would be useful to more fully examine the role of these disorders in the development and maintenance of BED. With regard to treatment, there may be utility in evaluating treatment

interventions originally developed for post-traumatic stress disorder, given the incidence of BED in those with trauma histories.

Finally, we recommend that studies continue to measure and report binge frequency as both discrete binge episodes and binge days per week. More data are needed to resolve whether one or the other is the better choice for assessing treatment effects.

Conclusions

Overall, we found the body of evidence to be small; often uneven across treatment types and comparisons; and, in some areas of interest, nonexistent. Nevertheless, we can conclude that antidepressants as a class, lisdexamfetamine, topiramate, and CBT effectively address major characteristics of binge eating, On the other hand, we were able to draw few conclusions regarding the comparative effectiveness of interventions or combinations of interventions. In addition, we found that harms were measured in only pharmacotherapeutic treatments. In light of the timing of this report so soon after publication of the DSM-5, the body of evidence may reasonably be expected to grow over the next few years.

Our meta-analyses provided strong evidence that second-generation antidepressants, lisdexamfetamine, and therapist-led CBT increase the likelihood of achieving abstinence. Meta-analyses also provided strong evidence that CBT and second-generation antidepressants reduce binge frequency and that second-generation antidepressants reduce obsessions and compulsions related to binge eating. Our qualitative assessments provided additional support for lisdexamfetamine (reduced binge frequency and obsessions and compulsions related to binge eating) and topiramate for treating BED patients as well. Overall, treatment benefits outweighed harms; harms were limited to medications and were severe and treatment limiting in very rare cases only.

Additional, adequately powered, multisite RCTs are needed to replicate encouraging findings observed to date only in single trials. Investigators should increase the sample sizes on which they base conclusions about treatment effectiveness; in designing comparative effectiveness studies, they should consider whether the goal is to determine whether treatment options are equivalent or superior.

The possible course of illness of LOC eating in children has been studied in three well- designed cohort studies that followed children through adolescence and into adulthood. Of particular concern in these studies is examining the important clinical and policy aspects of the role of early LOC eating on future risk of obesity and BED. The strength of conclusions that we could draw were limited by the diversity of definitions of LOC eating across both treatment trials and the longitudinal cohort studies. In particular, studies differed in the length of time that the adolescent or preadolescent respondents needed to manifest the behavior, varying from occurrence in the past year, at least once in the past 3 months, or at least weekly during the past year.

Several studies considered the relative role and importance of objective or subjective binge episodes. Distinguishing between these two constructs may be an important step for improving clinical understanding of the course of illness, in part because the frequency of subjective binge-eating behavior can be highly distressing for bariatric surgery and other patients. Furthermore, developing a common core of outcomes and a convention for reporting and analyzing those outcomes would greatly improve the capacity to compile aggregate data, compare findings across trials, and combine data from different treatment trials. These enhancements would in turn improve the ability of clinical and policy decisionmakers to understand risk factors more clearly and to develop treatment guidelines in these patient populations.

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Full Report

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