Comparative Effectiveness Review Disposition of Comments Report

Research Review Title: *Management and Outcomes of Binge-Eating Disorder*.

Draft review available for public comment from January 22, 2015 to March 4, 2015.

Research Review Citation: Berkman ND, Brownley KA, Peat CM, Lohr KN, Cullen KE, Morgan LC, Bann CM, Wallace IF, Bulik CM. Management and Outcomes of Binge-Eating Disorder. Comparative Effectiveness Review No. 160. (Prepared by the RTI International–University of North Carolina Evidence-based Practice Center under Contract No. 290-2012-00008-I.) AHRQ Publication No. 15(16)-EHC030-EF. Rockville, MD: Agency for Healthcare Research and Quality; December 2015. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

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#	Reviewer	Section	Comment	Response
1	Peer Reviewer #1	General comments	Should binge eating disorder be hyphenated? Most of us don't hyphenate it, but your review seems to prefer that.	Yes, throughout the report we hyphenate binge eating when referring to binge-eating disorder.
2	Peer Reviewer #1	General comments	Unfortunately and just recently (actually last week) the Food and Drug Administration in the U.S. approved Lisdexamfetamine (marketed as Vyvanse) for binge eating disorder, and one of the main studies on which that approval was based was published in psychiatry archives and available online. Given the fact that this change will markedly impact the field, particularly for physicians who are only interested in prescribing FDA approved medications for certain disorders, you may wish to rethink whether or not you wish to include these changes.	Yes, we are aware of a very recent publication based on findings from that trial. The article below has been added to the review. McElroy, S. L., Husdon, J. I., Mitchell, J. E., Wilfley, D., Ferreira-Cornwell, M. C., Gao, J., . . . Gasior, M. (2015). Efficacy and Safety of Lisdexamfetamine for Treatment of Adults With Moderate to Severe Binge-Eating Disorder A Randomized Clinical Trial. JAMA Psychiatry, 72(3), 235-246. doi: doi:10.1001/jamapsychiatry.2014.2162
3	Peer Reviewer #1	General comments	At times you refer to "binges." Most of us would prefer binge eating or binge eating episodes since "binges" can mean things other than food (e.g. alcohol). Therefore you might wish to standardize this and if you wish to continue to use binge, define it early as an abbreviation for binge eating episode.	We agree and have edited as such throughout the report.
4	Peer Reviewer #1	General comments	This is obviously a very thorough, well-written summary of the information. Unfortunately, the field has just changed in the last week. Thanks very much for allowing me to provide input.	Thank you. The final report will take into account not only the new lisdexamfetamine dimesylate (Vyvanse) treatment study but other studies that have been published after our original search.
5	TEP Reviewer #1	General comments	The report is succinct and well written. The target populations are clearly defined.	Thank you.
6	Peer Reviewer #2	General comments (ES)	ES-13 (Page 27 of 1120), Lines 6-13: A major absence in this report is omission of data about lisdexamfetamine, which was recently approved for the treatment of BED—in fact, it is the ONLY medication approved for the treatment of BED. One can argue that the published data on which the drug was approved is inadequate to reach conclusions on long-term safety and efficacy (indeed, the recently published study was relatively small and had only 11 weeks of treatment http://www.ncbi.nlm.nih.gov/pubmed/25587645). However, these data should be presented, even if only to say that more data on longer terms safety and efficacy are needed.	We have added this newly published study to our review during the peer review period. McElroy, S. L., Husdon, J. I., Mitchell, J. E., Wilfley, D., Ferreira-Cornwell, M. C., Gao, J., . . . Gasior, M. (2015). Efficacy and Safety of Lisdexamfetamine for Treatment of Adults With Moderate to Severe Binge-Eating Disorder A Randomized Clinical Trial. JAMA Psychiatry, 72(3), 235-246. doi: doi:10.1001/jamapsychiatry.2014.2162
7	Peer Reviewer #2	General comments (ES)	ES-3, line 22-23 (page 17-1120). It is stated that treatment of children is likely to include a role for parents. While this is true for treatment of other eating disorders, such as AN, in young children, it is NOT necessarily true for children/adolescents with BED. In fact, there are few, if any, treatment studies for binge or LOC eating in young (pre-adolescent) children, and in adolescents it is often the adolescent who	Thank you. We have revised the statement to say that it *may* include a role for parents.

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			is targeted for group IPT or CBT treatment, not the parent….	
8	TEP Reviewer #2	General Comments	Yes: this is a comprehensive, detailed, clear review, and the results should be useful for both clinicians and researchers. The key questions are appropriate and clearly stated.	Thank you
9	Peer Reviewer #3	General Comments	This review is generally well done and makes a good contribution. Most significant concern is the description of BED versus LOC eating. Generally LOC eating is considered to be an umbrella term under which BED falls as an extreme example. The authors use the terminology differently and need to be more explicit about this from the beginning (i.e., in paragraphs 1-3 of intro).	We appreciate the need to be clear about how we use the term "LOC eating" in our review. We have revised the introductory text with the intent of clarifying some of the key ways in which the term has been used differently across the literature and to emphasize our approach, which was not to define LOC eating but rather to include studies of persons determined to engage in LOC eating as defined by the original study authors.
10	Peer Reviewer #3	General Comments	Given the length and breadth of the report, bulleted key points are very useful.	We appreciate that the report is long. Instead of bulleted points, we have included a one page abstract and an executive summary. It is our intent that the executive summary provide a succinct presentation of the key points.
11	Peer Reviewer #3	General Comments	As some of the key questions could not be addressed due to lack of available data, this reviewer wondered whether those questions could be included as future directions rather than in the intro/method/results of the paper, which would allow for some streamlining of presentation of (already dense) materials.	In our presentation of the results, we believe that it is necessary to mention questions that could not be answered. We have tried to do that briefly.
12	Peer Reviewer #4	General Comments	The population and key questions are well defined and clearly stated.	Thank you
13	Peer Reviewer #5	General Comments	(1) I am not sure that "second generation antidepressants" constitutes a meaningful class. It's really a historical definition that includes a number of medications in different subclasses some of which have been studied in BED (SSRI, SNRI, NDRI) and some of which have not (NRI, NaSSA). The NLM definition is "a structurally and mechanistically diverse group of drugs that are not tricyclics or monoamine oxidase inhibitors." These medications have different mechanisms of action, different side effect profiles, etc. Stating that second-generation antidepressants as a class are superior to placebo both extends the findings to medication classes that have not been studied, and excludes some that have (e.g. TCA, as reported in the original 2007 review in one trial [Laederach-Hoffman et al., 1999]). Parenthetically, this is in contrast to "second generation antipsychotics" which is a much more mechanistically unified class. I think it would be preferable either states results with reference only to particular subclasses, or to use "antidepressants as a class" with acknowledgment that not all subclasses have been studied.	We acknowledge that the term "second generation antidepressants" is an imperfect solution to labeling the group of medications included in our meta-analyses because our analyses were not inclusive of all second-generation antidepressants; however, we feel the term "antidepressants" would be more confusing as it would imply the inclusion of tricyclic antidepressants and others that are widely known to not be second-generation antidepressants. We have provided additional explanatory text introducing the results of the pharmacological studies and believe this will help clarify the terminology we use.

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14	Peer Reviewer #5	General Comments	(2) Regarding KQ 9 (course of illness of loss-of-control eating among bariatric surgery patients), it seems that the literature on the prognostic significance of BED, i.e. impact of pre-op BED diagnosis on eating and weight outcomes, has not been included. Although, for reasons well described in the review, LOC eating is a more appropriate construct than BED for post-op patients, it may make sense to include BED as a form of LOC eating in pre-op patients, the post-op significance of which (in terms of both eating and weight) may still fall within the scope of the review. A somewhat older review on the topic is provided by Niego SH et al., Int J Eat Disord 2007; 40:349-59 and there are more recent papers as well.	We sought evidence on individuals who had been diagnosed with BED prior to bariatric surgery. Because of limited evidence, we also included evidence from studies of individuals with LOC eating diagnoses prior to surgery. The diagnostic criteria of each included study is clearly identified. For course of illness to be included in our review, a population needed to be followed for a minimum of one year post-diagnosis.
15	Peer Reviewer #6	General Comments	Yes, this report is clinically meaningful. It was good to see LOC in children and post bariatric surgery included in the report given that these are current issues in clinical practice. Target audience and population were well-defined. Key Q were appropriate and adequately stated.	Thank you
16	TEP Reviewer #3	General Comments	My view is that the report is clinically meaningful in that it describes the major treatment gaps and limitations for BED. The target population and audience are clearly and explicitly described, as are the key questions.	Thank you
17	Public Reviewer: Raquel Halfond American Psychiatric Association	General Comments	This draft report on management and outcomes of binge eating disorder was shared with members of the work group who developed the American Psychiatric Associations practice guidelines on eating disorders. The feedback that we received was very positive and our suggestions are minor ones. As lisdexamfetamine recently received FDA approval for binge eating disorder it would be important to update the information on studies of this medication pp. 187188. It may also be worthy of specific mention in the executive summary even though the findings are limited.	The McElroy (2014) report on the lisdexamfetamine Phase 2 trial has been added to the report. We have also added in various places throughout the report that this is the only medication that has received FDA approval for treating BED.
18	Public Reviewer: American Psychological Association members and staff	General comments	This is a very comprehensive review.	Thank you
19	Public Reviewer: American Psychological	General comments	Consider adding evidence profiles (including summary of findings tables) as an appendix to the report. This will allow guideline developers to make more immediate use of the review without additional intermediate steps.	Similarly, the EPCs conduct a strength of evidence evaluation for each major comparison and outcomes. We do not go the additional step of combining the findings for the purposes of making recommendations.

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	Association members and staff		These profiles could be developed using free online software provided by GRADE here: http://www.guidelinedevelopment.org/	In the EPC model, this is left to the guidance organizations.
20	Public Reviewer: Shire	General Comments	On January 30, 2015, the U.S. Food and Drug Administration expande approved uses of lisdexamfetamine dimesylate (Vyvanse) to treat mod to severe binge-eating disorder in adults. The drug is the first FDA-app medication to treat this condition. The FDA statement on the approval found here: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm We suggest inclusion of relevant information concerning lisdexamfetamine dimesylate (Vyvanse) in the Systematic Review inclu the structured abstract, the executive summary, the main body of the p and the following appendixes: • Appendix D. Risk of Bias Tables • Appendix E. Evidence Tables • Appendix F. Strength of Evidence Tables	The FDA press release of their approval presented at the link included in the comment refers to two Phase 3 trials. Because neither of these trials have been published in the peer review literature, we have added as evidence in the review available data that we abstracted from the clinicaltrials.gov website and the FDA approval package. Findings from the Phase 2 study were published in the peer review literature and we have included this evidence in the report as well.
21	Public Reviewer: Shire	General Comments	We request that you review and consider including the following articles and posters: **Publications:** • Efficacy and Safety of Lisdexamfetamine Dimesylate for Treatment of Adults with Moderate to Severe Binge Eating Disorder: A Randomized, Double-Blind, Placebo-Controlled Trial. McElroy SL, Hudson JI, Mitchell JE, Wilfley D, Ferreira-Cornwell MC, Gao J, Wang J, Whitaker T, Jonas J, M. JAMA Psychiatry. 2015 January. **Posters:** • Efficacy and Safety of Lisdexamfetamine Dimesylate in Treatment of Adults with Binge Eating Disorder: A Randomized, Double-Blind, Placebo-Controlled Trial. McElroy S, Mitchell J, Wilfley D, Gasior M, Ferreira-Cornwell C, Gao J, Wang J, Strakowski S, Hudson J. American College of Neuropsychopharmacology (ACNP 2012) • Lisdexamfetamine Dimesylate Safety and Efficacy on Binge Eating Days/Episodes and Behavior in Adults with Moderate to Severe Binge Eating Disorder. McElroy S, Mitchell J, Wilfley D, Gasior M, Ferreira-Cornwell C, Crow S, McKay M, Wang J, Hudson J. American Psychiatric Association (APA 2013) • Validation of the Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating to Support Use in Clinical Trials as a Measure of Treatment Benefit. Deal L, Wirth R, Herman B, Gasior	McElroy, 2015: included, added to our review for BED during the peer review period, 260 randomized McElroy, ACNP 2012: this report of the Phase 2 trial was excluded because it is duplicative to the Phase 2 results presented in the peer-reviewed publication. McElroy (2015) cited just above was included. . McElroy, APA 2013: this report of the Phase 2 trial was excluded because it is duplicative to the Phase 2 results presented in the peer-reviewed publication. McElroy (2015) cited just above was included. Deal, ASCP 2014-formerly NCDEU: The primary goal or this study was to validate the use of the YBOCS for BED. Outcome data is available in the poster but comparable data based on ITT analysis is provided in

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			M, McElroy S. American Society of Clinical Psychopharmacology (ASCP 2014 - formerly NCDEU) • Demographic, Psychiatric, and Medical Profile of a Study Population of Adults with Moderate to Severe Binge Eating Disorder: Data from a Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial. Hudson J, Mitchell J, WilfleyD, Gasior M, Ferreira-Cornwell C, Wang J, McKay M, Crow S, McElroy S. Eating Disorders Research Society (EDRS 2013) • Effects of d-Amphetamine Prodrug, Lisdexamfetamine Dimesylate on Impulsivity and Compulsivity in Treatment of Adults with Binge Eating Disorder: Data from a Phase 2 Randomized, Double-Bline, Placebo-Controlled Trial. McElroy S, Mitchell J, Wilfley D, Gasior M, Ferreira-Cornwell C, Crow S, McKay M, Gao J, Wang J, Hudson J. International Conference on Binge Eating Disorders . (ICED 2013)	McElroy et al.(2015), the peer-reviewed publication listed above. Therefore, the information in this poster was not added to the evidence base. Hudson, EDRS 2013: This poster was not included as evidence because it presents baseline data on participants included in the Phase 2 trial. This report did not include outcome data. Evidence from this trial was obtained from the peer-reviewed publication (McElroy et al., 2015) McElroy, ICED 2013: These are results from the Phase 2 trial, includes binge eating and YBOCS outcomes. This report of the Phase 2 trial was excluded because it is duplicative to the Phase 2 results presented in the peer-reviewed publication. McElroy (2015) cited just above was included
			• Dose Response Analysis of Lisdexamfetamine Dimesylate for Treatment of Binge-Eating Disorder. McElroy S, Reynolds J, Wang J, Gao J, Gasior M. American Society of Clinical Psychopharmacology (NCDEU 2013 - currently ASCP) **Publications Course of illness: Binge-Eating Disorder KQ 4 and KQ 5 (Pg 158-164)** • A Comparative Analysis of Role Attainment and Impairment in Binge-Eating Disorder and Bulimia Nervosa: Results from the WHO World Mental Health Surveys. Kessler RC, Shahly V, Hudson JI, Supina D, Berglund PA, Chiu WT, Gruber M, Aguilar-Gaxiola S, Alonso J, Andrade LH, Benjet C, Bruffaerts R, de Girolamo G, de Graaf R, Florescu SE, Haro JM, Murphy SD, Posada-Villa J, Scott K, Xavier M. Epidemiol Psychiatr Sci. 2014 Mar;23(1):27-41 • The Prevalence and Correlates of Eating Disorders in the WHO World Mental Health Surveys. Kessler RC, Berglund PA, Chiu WT, Deitz AC, Hudson JI, Shahly V, Aguilar-Gaxiola S, Alonso J, Angermeyer MC, Benjet C, Bruffaerts R, de Girolamo G, de Graaf R, Maria Haro J, Kovess-Masfety V, O'Neill S, Posada-Villa J, Sasu C, Scott K, Viana MC, Xavier M. Biol Psychiatry. 2013 May 1;73(9):904-14 • The Patient Experience with DSM-5 Defined Binge Eating Disorder: Characteristics, Barriers to Treatment, Implications for	McElroy, NCDEU 2013: This is a report of the results of the Phase 2 trial. Evidence on dose response in this trial was obtained from the peer-reviewed publication (McElroy et al., 2015) and this report was excluded because it did not provide any additional information. Kessler, 2014: excluded because the study design of looking at cross-sectional associations did not meet inclusion criteria for this review. Kessler, 2013: excluded because the study design did not meet inclusion criteria for this review. This study examined correlates of BED and we are examining outcomes from the course of illness. Herman, 2014: excluded because the study design did not meet inclusion criteria for this review; the study groups were too small to be evidence for course of illness. Ágh, 2015: excluded, this is a systematic review that did not match our key questions. However, we examined the reference list was hand searched for additional studies that we may have missed, none were identified.

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			Primary Care Physicians. Herman BK, Safikhani S, Hengerer D, Atkins N, Kim A, Cassidy D, Babcock T, Agus S, Lenderking WR. Postgrad Med. 2014 Sep;126(5):52-63. • Epidemiology, health-related quality of life and economic burden of binge eating disorder: a systematic literature review. Ágh T, Kovács G, Pawaskar M, Supina D, Inotai A, Vokó Z. Eat Weight Disord. 2015 Jan 9 • Automated identification of patients with a diagnosis of binge eating disorder from narrative electronic health records. Bellows BK, LaFleur J, Kamauu AW, Ginter T, Forbush TB, Agbor S, Supina D, Hodgkins P, DuVall SL. J Am Med Inform Assoc. 2014 Feb;21(e1):e163-8	Bellows, 2014: Excluded. This is not relevant as evidence of outcomes. This study examined a technique for examining electronic medical records to identify individuals with BED
			Posters Binge-Eating Disorder KQ 4 and KQ 5(Pg 158-164) • Estimating the Prevalence of Binge Eating Disorder in a Community Sample, Comparing DSM-IV-TR and DSM-5 Criteria. Cossrow N, Russo L, Ming E, Witt E, Victor T, Wadden T. American Psychiatric Association (APA 2014) • Survey of Binge Eating Disorder Recognition, Diagnosis, Treatment and Referral in US Physician Practices. Supina D, Herman B, Frye C, Shillington A, Mitchell J. American Psychiatric Association (APA 2014) • Communication between Psychiatrists and Patients with Suspected or Diagnosed Binge Eating Disorder: Differences in Perspective. Kornstein S, Keck P, Herman B, Puhl R, Wilfley D, DiMarco I, Charap E. American Psychiatric Association Institute on Psychiatric Services (APA-IPS 2014) • A Preliminary Conceptual Framework for the Patient-Reported Outcome Assessment of Binge Eating Disorder: Literature Review, Expert Insights, and Patient Interviews. Supina D, Shields A, Stokee J, Taylor F, Pompilus F, Delbecque L, Erder H. Eating Disorders Research Society (EDRS 2012) • Binge Eating Disorder Patient Characteristics and Barriers to Treatment: A Qualitative Study. Herman B, Safikhani S, Hengerer D, Atkins N, Kim A, Cassidy D, Babcock T, Lenderking W. American Psychiatric Association (APA 2014) • Characteristics of patients with BED compared to patients with EDNOS and patients without an eating disorder. Bellows B, Pawaskar M, LaFleur J, Kamauu A, Babcock T, Duvall S. American Psychiatric Association (APA 2014) • Using Natural Language Processing to Identify US Veterans with Binge Eating Disorder. Bellows B, DuVall S, Ginter T, Kamauu A,	Cossrow, APA 2014: prevalence estimates not relevant as evidence for the key questions of this review. Supina, APA 2014: survey of physicians, not relevant as evidence for the key questions of this review Kornstein, APA-IPS 2014: qualitative assessment of physician communication practices in identifying patients with BED based on DSM-5 criteria, not relevant to the key questions of this review Suprina, EDRS 2012: conceptual framework, not relevant for the key questions of this review Herman, APA 2014: qualitative study to understand cross-sectional characteristics of individuals diagnosed with BED, does not follow them over time and so not relevant to this review. Bellows, APA 2014: cross-sectional comparison with patients with eating disorder not otherwise specified, not relevant for this review. Bellows, ICPE 2013: identifying patients with BED prior to establishment of diagnostic criteria, not relevant to the key questions of this review, which are related to outcomes of treatment and course of illness

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			Supina D, Hodgkins P, Erder H, LaFleur J. International Conference on Pharmacoepidemiology & Therapeutic Risk Management (ICPE 2013) • Health Care Resource Utilization and Costs for Patients with AN, BN and BED. Supina D, Lewis-Beck C, McElroy S, Hodgkins P, Baser O. International Society for Pharmacoeconomics & Outcomes Research Annual European Congress (ISPOR-EU 2012) • Healthcare Costs of Patients with Binge Eating Disorder Compared to Patients with Eating Disorder not Otherwise Specified and No Eating Disorder. Bellows B, LaFleur J, Kamauu A, Pawaskar M, Supina D, Babcock T, Duvall S. International Society for Pharmacoeconomics & Outcomes Research Annual International Meeting (ISPOR 2014) • Humanistic and Economic Burden of Bulimia Nervosa and Binge Eating Disorder: A Systematic Literature Review. Ágh T, Kovács G, Kalo Z, Supina D, Pawaskar M, Vokó Z. International Society for Pharmacoeconomics & Outcomes Research	Supina, ISPOR-EU 2012, excluded, comparisons to patients without eating disorders in healthcare utilization, not relevant for this review. Bellows, ISPOR 2014: excluded, cross-sectional comparison with EDNOS and no diagnosis group, not relevant for this review. Agh et al: excluded. The poster presents results from a systematic review. We reviewed the references related to BED and did not find any additional articles that met our inclusion criteria.
22	TEP Reviewer #4	General comments	Indeed, Cochrane Reviews states, "Two studies is sufficient number to perform a meta-analysis, provided that those two studies can be meaningfully pooled and provided their results are sufficiently 'similar'" (citation noted below). As aforementioned, I believe the Peer Reviewer: Wilfley et al. (2002) and Wilson et al. (2010) trials are more than sufficiently similar to warrant this type of synthesis and strongly recommend they be synthesized in this report. Both studies utilized the gold standard assessment measure (EDE) to determine the same primary outcomes (days binged over past 28 days and abstinence rates) and had stringent procedures for interview and data collection. The treatments were well-defined and used manuals (the latter trial adapted from the former trial) and had sufficient oversight of treatment delivery. Ryan R; Cochrane Consumers and Communication Review Group. 'Cochrane Consumers and Communication Review Group: meta-analysis. http://cccrg.cochrane.org, June 2013	We consider Wilfley et al. (2002) to be group therapy and Wilson et al. (2010) to be individual therapy. For psychological/behavioral interventions, we evaluated evidence of individual and group modalities separately. The two approaches involve a different therapist-patient relationship and level of healthcare resources; and only group therapy includes in the therapeutic process the influence of other patients suffering from the condition. We have added a more explicit description of this a priori analysis approach decision to the methods section of the report. We do not combine studies quantitatively using meta-analysis unless we have 2 or more studies. However, we synthesize smaller bodies of evidence qualitatively. We similarly use qualitative synthesis to combine evidence in such cases as when the outcomes are measured using different metrics.
23	TEP Reviewer #4	General comments	These large trials laid the foundation for the funding of a third NIMH trial on disseminating IPT for the treatment of eating disorders to clinicians in college counseling centers (NIMH R01 MH095748; see attached for abstract). As such, the NIMH has deemed that they believe it is appropriate to disseminate IPT based on the results of these two earlier and very well-conducted trials. One of the main	We appreciate the additional information about these trials. In the results section, we have edited the text to better highlight the significance of the IPT results. We have made similar edits in the Discussion section that include pointing to the acceptability of IPT to the patient population.

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			reasons IPT was selected as the treatment for the current project is due to its high acceptability (see Wilson et al., 2010). As detailed in Wilson et al. (2010), patients reported both BWL and IPT to be more suitable than CBTgsh at session 1 and IPT to be more suitable than CBTgsh at session 4. Patients also expected IPT to be significantly more effective than CBTgsh both at the end of session 1 and session 4.	
24	TEP Reviewer #4	General Comments	A more minor note – please be sure to refer to interpersonal psychotherapy rather than interpersonal therapy throughout the report.	We have now changed the wording to "interpersonal psychotherapy."
25	TEP Reviewer #5	General Comments	The report, as a whole, is most beneficial in that it highlights the significant need for additional research to better understand effective treatments for BED generally and more specifically in subgroups including children/adolescents, LOC in children, and LOC in bariatric surgery	Thank you
26	TEP Reviewer #5	General Comments	Effective treatment is informed by an understanding of the cause(s) of illness and its co-morbid conditions. The report provides a glimpse of the limited understanding currently available to inform and develop treatment methods.	No response required.
27	TEP Reviewer #5	General Comments	The target population, audience, and key questions are appropriate and explicitly stated given the knowledge of BED at this time.	Thank you
28	TEP Reviewer #5	General Comments	Since a great amount of additional research is necessary, the report has limited clinical benefit to guide the treatment of BED and LOC currently.	We agree that there are a number of ways in which additional research is necessary. However, we believe that the report presents the clinical value of antidepressants, topiramate, CBT and lisdexamfetamine for BED. Results are more limited for LOC eating, where there are a number of things to learn, The report explicitly discusses the current limitations in treatment options
29	Peer Reviewer #1	Abstract	One thing that isn't completely clear to me is the issue of weight. In the structured abstract you refer frequently to weight (whether or not treatments would change weight). Not all patients with binge eating disorder of course, are overweight or obese, and most of the treatments for binge eating disorder were not designed for weight loss per se. However, increasingly it has become clear that weight loss is desirable for many patients with BED, and that the ideal treatment would usually incorporate weight loss effects. I might explicate this a little more detail early on to make it more clear to readers.	Virtually all of the patients in the BED trials were overweight or obese and so weight reduction was an outcome of interest. The text now reads: Topiramate and ADHD medications were associated with weight reduction in study populations that were virtually all overweight or obese.
30	TEP Reviewer #4	Abstract	In the Structured Abstract, it would be helpful if the reader were made explicitly aware of the four major categories of outcomes that were examined in this report (i.e., binge behavior, bing-eating-related psychopathology, physical health functioning, general	We have added the classifications to the results section of the abstract.

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			psychopathology) before specific results are presented.	
31	Peer Reviewer #5	Abstract	In the Abstract, the sentence under Results, lines 50-52, "Behavioral weight loss (BWL) treatment was superior to CBT for weight loss in the short term but was less effective in relation to weight loss or reducing binge-eating in the longer term" is a bit ambiguous. It is not clear "less effective" is with respect to CBT in the longer term or with itself (BWL) in the longer term vs. short term.	We have revised the text to read Behavioral weight loss treatment was superior to CBT for weight loss, measured at the end of treatment, but differences were not maintained in the longer term.
32	Public Reviewer: American Psychological Association members and staff	Abstract	The way the report objective is written in the abstract can give the mistaken impression that the report population is only bariatric surgery patients and children. Consider revising to clarify this point.	We have rewritten the text as follows: Objectives. To evaluate the effectiveness and the comparative effectiveness of treatments for patients with binge-eating disorder (BED) and for bariatric surgery patients and children with loss-of-control (LOC) eating.
33	Public Reviewer: Shire	Executive Summary	ES-3 Current Treatment Options for Binge-Eating Disorder We suggest including lisdexamfetamine dimesylate (Vyvanse) in the discussion and in Table B.	We have added the recently published trial of lisdexamfetamine (MeElroy, 2014) to our review.
34	Public Reviewer: Shire	Executive Summary	ES-7 Literature Search Strategy We appreciate that AHRQ will update the literature searches during peer review. We suggest that this article be added to the articles examined: McElroy SL et al JAMA Psychiatry. "Efficacy and Safety of Lisdexamfetamine for Treatment of Adults With Moderate to Severe Binge-Eating Disorder: A Randomized Clinical Trial." 2015 Jan 14.	This article was added during peer review.
35	Public Reviewer: Shire	Executive Summary	ES-11 – ES-15 Key Question 1. Effectiveness of Interventions for Binge-Eating Disorder Given that none of the sub-sections are applicable to lisdexamfetamine dimesylate (Vyvanse), we suggest the creation of a new subsection entitled Pharmacological Interventions: FDA Approved Treatments for Moderate to Severe Binge-Eating Disorder in Adults Compared with Placebo.	We have added the published peer reviewed trial of lisdexamfetamine (MeElroy, 2014) to our review. It was added to a section of the report that includes medications originally formulated for treating ADHD.
36	Public Reviewer: Shire	Executive Summary	ES-16 – ES-18 Key Question 1. Effectiveness of Interventions for Binge-Eating Disorder We suggest including lisdexamfetamine dimesylate (Vyvanse) in both the written discussion and Table C. We note that the results of clinical trials can be found on clinicaltrials.gov. The specific URLs are:	We have added the published peer reviewed trial of lisdexamfetamine (McElroy, JAMA Psychiatry, 2014) to our results review. The trial results presented in clinical trials.gov have been added to our discussion.

#	Reviewer	Section	Comment	Response
			https://www.clinicaltrials.gov/ct2/show/results/NCT01291173?term=vyvanse+binge-eating+disorder&rank=2 https://www.clinicaltrials.gov/ct2/show/NCT01718509?term=vyvanse+binge-eating+disorder&rank=4 https://clinicaltrials.gov/ct2/show/NCT01291173?id=spd489-208&rank=1	
37	Public Reviewer: Shire	Executive Summary	ES-20 Key Question 2: Evidence for Harms Assoicated with treatments for Binge-Eating Disorder We suggest inclusion of lisdexamfetamine dimesylate (Vyvanse) in the discussion.	These results have been added to our review.
38	Public Reviewer: Shire	Executive Summary	ES-20 – ES-21 Findings in Relations to What is Already Known We propose inclusion of lisdexamfetamine dimesylate (Vyvanse) in the discussion.	Lisdexamfetamine dimesylate (Vyvanse) has been added to the results and the discussion.
39	Public Reviewer: Shire	Executive Summary	ES-21 Implications for Clinical and Policy Descionmaking We recommend inclusion of lisdexamfetamine dimesylate (Vyvanse) in the discussion.	Lisdexamfetamine dimesylate (Vyvanse) has been added to the results and the discussion.
40	Public Reviewer: Shire	Executive Summary	ES-22 "We note, however, that no medications are currently approved for treating BED patients by the U.S. Food and Drug Administration." Please update the sentence/section to reflect the approval of lisdexamfetamine dimesylate (Vyvanse) for moderate to severe Binge-eating disorder in adults.	Lisdexamfetamine dimesylate (Vyvanse) has been added to the review.
41	Peer Reviewer #5	Executive Summary	On ES-8-9, under Risk-of-Bias, although the rating of high risk of bias is defined, it would be of interest to know how a rating of medium vs. low risk of bias was determined.	The determination of whether a study is low or medium risk of bias is based on specific criteria, but on a case by case basis, based on reviewer judgment. All of our decisions are included in the appendix to the report. For greater clarity, we have added the following sentence to the methods section of the ES and the main report. "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 information on multiple bias criteria, while unlikely to be biased because of the reported conduct in relation to other aspects of the trial, are unclear because of gaps in reporting."

#	Reviewer	Section	Comment	Response
42	TEP Reviewer #2	Executive Summary	I focused primarily on the Executive Summary which is excellent. The key findings/messages are clear.	Thank you
43	American Psychological Association members and staff Public	Executive Summary	Minor typo in the executive summary, the page numbering goes from ES 25 to ES 2 on the following page, then ES 3 and so forth.	Thank you. We have reviewed the numbering of the report for accuracy.
44	Peer Reviewer #7	Introduction	The report is clinically meaningful for those clinicians who treat Binge Eating Disorder, a newly recognized DSM 5 eating disorder. The information provided in great detail about Loss of Control eating is less helpful because this term is not clearly defined, (the report states on page 6, line 35, that it "has no consistently endorsed definition"), is not a recognized syndrome or disorder. LOC eating is a behavior that is subjective, not necessarily associated with overeating or binge eating, occurs on a continuum in the general population as well as in those who have undergone bariatric surgery and is not necessarily pathologic or associated with psychopathology or morbidity. The behavior of LOC eating was specifically examined in this review as it relates to children and in bariatric surgery patients.	We have revised the introduction to emphasize the varied manner in which the term 'LOC eating' has been used in the literature, including to describe persons reporting objective binge eating episodes as well as persons reporting subjective binge eating episodes; we have also sought to place more emphasis on our approach, which was not to impose a specific definition of LOC eating as a study inclusion criterion but rather to include studies in which participants were defined as having 'LOC eating' by the study authors. As the reviewer indicates, we focused our review on studies of children and bariatric surgery patients because these are populations of keen interest in the fields of psychiatry, psychology, and medicine, who are unlikely to meet criteria for BED.
45	Peer Reviewer #2	Introduction	Page 9 (54 of 1120) line 44-60: Patients with BED may present to their physicians for treatment of obesity, rather than with a complaint of binge eating, and may not admit to binge eating unless asked. PCPs may want to consider use of a screening tool, such as the PHQ-ED in patients believed to be at high risk: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2851838/	We have added text to the Introduction to incorporate this helpful insight.
46	Peer Reviewer #1	Introduction	On page 48 under "definition of loss-of-control eating" you mention that the "gut size" are significantly reduced. Most people are referring to the gastrointestinal tract in total when they talk about the "gut." I think you really wish to address the stomach size and capacity in this sentence.	Thank you; we have changed 'gut' to 'stomach'
47	Peer Reviewer #2	Introduction	Page 10, (55/1120) lines 3-16: Despite the concerns of the Health at every size movement that dieting worsens BED and that body acceptance is helpful, there is little evidence that behavioral weight loss treatments worsen binge eating. See, for example: Arch Intern Med. 2000 Sep 25;160(17):2581-9. Dieting and the development of eating disorders in overweight and obese adults. National Task Force on the Prevention and Treatment of Obesity.	We thank the reviewer for this comment. In response, we have added text regarding the findings of the National Task Force.

#	Reviewer	Section	Comment	Response
48	Peer Reviewer #2	Introduction	Page 3 (46-1120) line 5: The article cited for the prevalence of up to 30% should not be used for BED prevalence. The cited piece (I was an author) drew from data using a questionnaire for diagnosis of binge eating disorder QEWP) that was later found to be sensitive, but not specific. Later versions of the questionnaire note that it is a screening instrument, but must be followed up with a clinical interview of diagnosis. http://onlinelibrary.wiley.com/doi/10.1002/eat.22372/abstract The paper cited drew from two multisite field trials we conducted using the QEWP— Int J Eat Disord. 1993 Mar;13(2):137-53.Binge eating disorder: its further validation in a multisite study.Spitzer RL Matoff-Stepp S, Wadden T, Wing R, Marcus MD, Stunkard A, Devlin M, Mitchell J, Hasin D, Horne RL Robert L. Spitzer, Michael Devlin, B. Timothy Walsh, Deborah Hasin, Rena Wing, Marsha Marcus, Albert Stunkard, Thomas, Wadden, Susan Yanovski, Stewart Agras, James Mitchell and Cathy Nonas. Binge eating disorder: A multisite field trial of the diagnostic criteria (pages 191–203) Article first published online: 13 FEB 2006 |DOI: 10.1002/1098-108X(199204)11:3<191::AID-EAT2260110302>3.0.CO;2-S In addition, the high rates in obese individuals by the screening instrument (QEWP) were in patients seeking weight loss, primarily in specialized obesity treatment centers. Even using this screening instrument, BED rates in community samples with obesity were much lower (about 5%) and even those in commercial weight loss programs the prevalence was only about 15%. Therefore, when citing prevalence figures, you should use data that are obtained from clinical interview. References are: http://www.nimh.nih.gov/health/statistics/prevalence/eating-disorders-among-adults-binge-eating-disorder.shtml	We have clarified that the prevalence data we cite comes from the National Comorbidity study, as referenced by the reviewer. We feel it is important contextually to include mention of higher estimates of BED prevalence among obese individuals who presented for field- and community-based screening studies. Thus, we retained some of this information but have distinguished the sources of information. In addition, we have updated citations for BED prevalence among racial/ethnic minorities based on results from the National Latino and Asian American study (Nicdao et al., 2007)
49	Peer Reviewer #2	Introduction	Page 3, lines 18-26 (and throughout)—definition of LOC eating—throughout, LOC eating that may not meet the threshold for binge eating because amount of food is not considered objectively large (also called a "subjective bulimic episode" is noted as important only for children and for post-bariatric surgical patients. However, there is some evidence that LOC eating that does not meet criteria for binge eating is also important in adults who have not undergone bariatric surgery (see, for example http://www.ncbi.nlm.nih.gov/pubmed/19610126_)	We acknowledge that LOC eating is also important in other adult patient groups, such as those with anorexia nervosa binge-eating/purge subtype and those with bulimia nervosa. We now cite the study mentioned by this reviewer, to alert the interested reader to this related literature but sub-clinical BED is beyond the scope of this review.

#	Reviewer	Section	Comment	Response
50	TEP Reviewer #2	Introduction	Excellent.	Thank you
51	Peer Reviewer #3	Introduction	The definitions of binge eating, and loss of control eating need clarification. p. 1, Binge eating is defined by amount and by presence of loss of control. Loss of control is presented as a core feature in second sentence when in fact it's definitional. This should be corrected.	We have revised the text on LOC eating within the Introduction, giving greater attention to the relation of LOC eating to BED and greater emphasis to our approach, which did not attempt to define LOC eating, per se, but rather to include studies of LOC eating in two subgroups of current keen interest: bariatric surgery patients and children.
52	Peer Reviewer #3	Introduction	p. 2-3, I am not clear on the definition of LOC eating used in this review. LOC eating typically refers to objective binge eating (eating an objectively large amount of food + LOC) and subjective binge eating (eating a subjectively large amount of food + LOC). The authors have expanded the definition to also include those post-bariatric surgery who have LOC (it seems with or without objective/subjective large amount, as long as the amount/type is contraindicated). But LOC is typically described as the more umbrella term under which folks who meet criteria for BED would be an extreme example, rather than a mutually exclusive category distinct from BED. Given that this distinction and these two types of studies (BED and LOC) are at the foundation of this report it would be very helpful to provide more clarity on the distinction and whether they are considered to be overlapping in this study (and below, in the methods, in terms of study selection/inclusion). It may be useful to include a Venn diagram that shows OBEs/SBEs both falling under LOC eating, and BED being a small portion of those with OBEs (who may also have SBEs) and also that demonstrates folks with other types of eating disorders, and even those without eating disorders at all may have infrequent LOC eating. If instead the authors wish to focus on those who experience loss of control eating but do not meet full criteria for BED (which is what it seems they are focusing on in this latter group of LOC eating), I would suggest being very clear about that as this mixed group includes people with OSFED-BED (who endorse OBEs but not at the frequency/duration to meet BED), those with SBEs, and those post-bariatric surgery with LOC but by definition for the purposes of this report, excludes individuals meeting for full criteria BED.	Our intent was to highlight that the term "LOC eating" is used in many different ways throughout the literature. In the text, we have added language to clarify that LOC eating is not defined for the purposes of this review but rather is derived from the included studies and broader literature.
53	Peer Reviewer #3	Introduction	In the Table (p. 2) the distinction between LOC definition (b) and (c) should be clarified. Is the idea that the bariatric patient experiences LOC but of an amount that he/she may not think he/she had eaten too much but the amount eaten was contraindicated post-surgery? If yes, worth clarifying that (a) is an OBE, (b) is an SBE, and (c) is a LOC	We have revised the document by removing the LOC "definitions" from Table 1 and modifying the text under the heading "Loss of Control (LOC) Eating". Specifically, we revised the text that was previously ascribed to definition 'c' to clarify that within the bariatric surgery

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			episode in which the amount was contraindicated by post-surgical status but not necessarily subjectively large by patient report.	population LOC eating can be manifested as an excessive amount of food OR as a contraindicated type of food.
54	Peer Reviewer #3	Introduction	p. 10 – with regard to scope of review, what about adults with LOC eating who are not post-surgery (i.e., those endorsing SBEs)?	Adults with LOC eating who are not post-surgery and who do not meet the definition of BED are outside the scope of this review.
55	Peer Reviewer #3	Introduction	The ordering of the questions seemed a bit strange to me. Given that the Results are grouped by Effectiveness, Treatment Harms, and Course, I wondered if it would be more clear to have the questions numbered so that they are in order of how they are then answered in the results. (Also, as noted above in general comments, it may be more parsimonious to omit the questions that could not be answered due to lack of available data.)	Yes that would have been a reasonable alternative in our ordering of the key questions. We decided to group the questions by condition.
56	Peer Reviewer #3	Introduction	Minor: on p. 3, it is noted that one of the reasons it's hard to diagnose BED in kids is that there is no minimum age for diagnosis. While true that there is no minimum age for diagnosis, this is not what makes it challenging, rather the challenge is that we have some difficulty assessing LOC in kids, and kids have difficulty describing loss of control, and further, that energy needs are widely variable especially during periods of growth, which can complicate assessment of whether an amount is indeed objectively large. Part of why we choose to focus on LOC in kids is that there is evidence to suggest that it is the experience of LOC (independent of amount) that is associated with distress in kids.	Thank you for this insight; we have added text to include mention of the difficulty some children have in describing loss of control.
57	Peer Reviewer #4	Introduction	Overall, the introduction is well-written. One inconsistency I noted was that on p. 48, the authors suggest that LOC eating may be predictive of weight loss after bariatric surgery (lines 43-45), but on p. 54, the authors state that no evidence exists that patients with BED have poorer outcomes (lines 14-18). Perhaps the first mention of this can be clarified that LOC is thought of as a predictor, but evidence does not yet exist. Also, reference 107 is used for the lines on p. 54, but this does not seem to be the correct reference, as it refers to the STRATOB study, not a bariatric surgery study.	This text has been modified. One of the goals of the review is to summarize any evidence of whether LOC eating is related to weight outcomes among bariatric surgery patients. A related goal is to examine the evidence of outcomes among BED patients. Thank you for pointing out the erroneous citation. It has been corrected.
58	Peer Reviewer #6	Introduction	The introduction provides an excellent synthesis of the evolution of the BED diagnosis beginning with the DSM-IV and outlines the changes for DSM-5. The authors do a good job at describing the construct of LOC eating and how/why that is both an important and difficult construct to study	Thank you
59	TEP Reviewer #3	Introduction	No comments, the introduction was clear and concise.	Thank you

#	Reviewer	Section	Comment	Response
60	TEP Reviewer #4	Introduction	On p. 6, the authors indicate the challenges in assessing loss of control (LOC) eating, specifically in children and the post-bariatric adults. Please discuss LOC in adult non-post-bariatric individuals, and how individuals with a diagnosis of BED can experience subjective binge eating episodes in addition to objective binge eating episodes.	We have added text regarding the occurrence of LOC eating in other eating disorders (AN, BN) as well as text that brings to light the co-occurrence of subjective binge episodes (SBEs) and objective binge episodes (OBEs) in BED and the contribution of SBEs and LOC eating to overall distress among patients with BED.
61	TEP Reviewer #4	Introduction	Table 2, "Common diagnostic and outcome measures used in the included trials," is a very large table. It is currently organized alphabetically. It might be helpful to the reader to break the table into subsections to separate out different types of measures (e.g., diagnostic interviews, eating related symptoms, other psychologically relevant outcomes). In Table 2, the authors may also want to add the Clinical Impairment Assessment (CIA) questionnaire. This is a 16-item self-report questionnaire that measures severity of psychosocial impairment due to eating disorder features (Bohn & Fairburn, 2008).	We do not include the CIA because that was not use in any of the studies included in this review, as the title of the table indicates.
62	Peer Reviewer #7	Introduction	The literature review of treatments for BED is comprehensive and well done. Again, evaluating treatments for a behavior such as LOC eating that is not well defined and not a recognized disorder is problematic; this is an issue throughout this report. The authors state on page 16, Table 4" Because LOC eating has no commonly accepted definition, studies included in the review may define LOC using different diagnostic criteria". This is very problematic; LOC is not a diagnosis, and without uniform criteria, any review conducted by definition is not valid. This brings to the forefront the question of why such a review was even attempted considering these significant limitations.	We have edited this section of the report to clarify our rationale for focusing on post-bariatric surgery patients and children; despite the pitfalls that the reviewer points out, we believe this focus is justified from a public health perspective, given the growing numbers of obese patients undergoing weight-loss surgery and the very public concerns about childhood obesity.
63	Public Reviewer: Shire	Introduction	We suggest including lisdexamfetamine dimesylate (Vyvanse) in the discussion and in Table 3.	This study of this medication has been added to the report.
64	TEP Reviewer #5	Introduction	Introduction is clear and helpful.	Thank you
65	TEP Reviewer #4	Methods	On p. ES-7 and p. 15, the authors state, "We included unpublished studies that met all inclusion criteria and contained enough information to permit us to make a standard risk-of-bias assessment of individual studies." Please explain the process of identifying and receiving access to unpublished studies and data.	The text provided in the peer review draft report contained a description of the main sources of unpublished information; namely ClinicalTrials.gov, Health Services Research Projects in Progress (http://www.nlm.nih.gov/hsrproj/), and the European Union Clinical Trials Register (https://www.clinicaltrialsregister.eu/). Also, AHRQ requested Scientific Information Packets (SIPs) from the developers and distributors of the interventions identified in the literature review. We have added a sentence that we included other study information, such as conference

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				proceedings for studies that were identified through the registries listed above or through technical expert panel or peer reviewer recommendations.
66	TEP Reviewer #2	Methods	Yes: the criteria are sound and logical. The outcome measures (behavioral=binge eating, weight, and psychological) are entirely appropriate. I do not have sufficient expertise to comment on the statistical methodology.	Thank you
67	Peer Reviewer #3	Methods	Inclusion/exclusion. Inclusion/exclusion table (p. 16) is a bit confusing in terms of population. Where were children with binge eating disorder captured? It looks like they were not included in the BED studies, but it also looks like they would not have been included in the LOC studies due to the BED? If trials of children with frank BED were not included the rationale for their exclusion needs to be clear. Were there such studies that the authors excluded (if yes, how many)? Why were these not included?	Thank you for bringing this to our attention. We agree that this is confusing. We did not mean to exclude children who were diagnosed with BED but rather to create a lower bar for children and bariatric surgery patients. We have edited the text accordingly.
68	Peer Reviewer #3	Methods	Outcome definitions. Should LOC eating (operationalized as objective binge eating OR subjective binge eating) be included as an outcome of interest in the effectiveness and course analyses even for the BED studies? It would be important to know whether the BED treatments impact SBEs in addition to their efficacy in reducing OBEs, given that SBEs can still be quite distressing to patients. (Important from a clinical utility perspective.)	We have reported all outcomes that were included in study publications, including subjective binge episodes.
69	Peer Reviewer #4	Methods	The Methods section was largely clear. In the risk of bias section, it would be useful to mention some of the questions that are presented in the appendix so the types of issues being considered are clearer to the reader (without having to find the appendix at that moment).	We have added examples of questions included in the randomized controlled trial and observational study tools. The text also includes the major categories of risk that are included in assessments and the appendix that contains the full instruments.
70	TEP Reviewer #3	Methods	In my view the criteria were appropriately conservative and justifiable. My answer to the remaining methodological questions described above is yes.	Thank you.
71	Peer Reviewer #7	Methods	The inclusion and exclusion criteria for studies are justifiable and the search strategies are clearly stated and logical. The limitations of the search strategy are also clearly stated (only published English language studies included). The statistical methods appear appropriate, but best to have the question answered by a statistician which I am not.	Thank you
72	Peer Reviewer #6	Methods	The inclusion and exclusion criteria were justifiable. However, given the very large number of studies that were excluded from the report, I wonder if there may have been a way to include some of those studies and their findings. Given that BED is only a brand new diagnosis (only listed for further study in the previous DSM) - it makes sense that there	Through input from our technical expert panel, we decided that the focus of this review should be patients meeting BED DSM-IV or DSM-5 criteria. Given that DSM-5 criteria involved a relaxing of criteria compared to the earlier version, we were thus able to capture

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			are so many studies lacking adequate power and/or a rigorous study design. Perhaps there is a subset of those (excluded) studies that examined sub-threshold BED and those might be addressed in a separate category of "LOC eating in adults" (assuming that LOC eating was identified as a sub threshold condition and perhaps only frequency or duration was less than would have met criteria for full BED).	patients who might meet criteria for subthreshold DSM-IV BED. We looked for studies meeting DSM-5 even if not named as such (e.g., subthreshold DSM-IV BED) and found little evidence. We did not find any separate evidence. Based on the explanation above, we have not made any changes to the evidence base in the report based on the reviewer's comments; however we have added text to the Discussion to better elucidate our decision making process.
73	Peer Reviewer #6	Methods	Yes, the search strategies were explicitly stated and logical; definitions & diagnostic criteria for outcome measures and statistical methods were all appropriate.	Thank you
74	TEP Reviewer #4	Methods	On pp. 20-21, the authors detail that they graded the strength of evidence based on the EPC Methods Guide for conducting comparative effectiveness reviews (CERs). They state that the EPC approach incorporates five key domains: study limitations, directness, consistency, and precision of the evidence and reporting bias. Scores are given for the above domains and this is then translated into an overall grade for strength of evidence. Could the authors provide a bit more detail on this process – that is, the scoring system for each domain and how that translates to an overall grade? This would help the reader to better understand how grades for overall strength of evidence were made.	Developing a strength of evidence assessment is accomplished with the parameters of a framework but it is not a mechanistic process. The text contains the possible scores for each domain, that the domains are summarized into an overall strength of evidence (SOE) grade and the range of final grades. While extensive guidance is provided by AHRQ, grading strength of evidence cannot be a mechanistic process because of variations across bodies of evidence in relation to key substantive and methodological considerations. A report appendix includes domain scores and SOE grades for each comparison/outcome. The main results and discussion text contains tables highlighting key considerations in bodies of evidence. We have added the following text in response to the reviewer's comment: Grades for RCT bodies of evidence are provisionally considered as high strength of evidence and then may be downgraded based on concerns in one or more of the key domains. In contrast, bodies of evidence consisting of observational studies are provisionally assessed as low strength of evidence. Optional domains that can be included in the assessment if they are considered relevant can raise a strength of evidence grade. They include increasing dose-response, large magnitude of effect and an effect that would be larger if confounders had not been controlled in the analysis. Low study limitations can also

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				increase the strength of evidence in observational study bodies of evidence because these bodies of evidence begin with a lower provision strength of evidence grade because of heightened concerns about the risk of bias in the individual studies.
75	TEP Reviewer #4	Methods	3. Review methodology a. A fundamental issue results from the methodology chosen to govern this review. Although these methods are commonly used in these types of reports commissioned from AHRQ, there are some clear ways that they innately affect the conclusions. i. First, the criteria appear to be biased towards medication trials due to some of the criteria in grading system (e.g., providers and patients being blind). ii. Second, based on how some studies are presented in the review, which are viewed as being strong studies methodologically by top researchers in the field, it is easy to dismiss their findings (e.g., Telch et al. for DBT, IPT studies noted above). Thus, the conclusions can significantly misinform treatment providers and potential recipients. iii. Third, some additional information on the report methodology and the specific study designs could be included so that the reader can better judge the methodology and the scientific rigor of the study designs. This approach might also help inform which studies (although not yet replicated) have a higher likelihood of being replicated if repeated due to strong design.	3ai) We appreciate that behavioral interventions cannot be blinded from the patient and the provider (not applicable for risk of bias). It is key in these studies that the assessor is blinded. We looked for that information in studies. 3aii) We did not rank studies based on the research team's standing in the field. Studies evaluated as medium and low risk of bias were presented side by side, only high risk of bias were excluded from qualitative synthesis. However, we have reviewed the text to ensure that we have highlighted any low risk of bias studies, particularly if they included a large sample and would be applicable to a large cross section of clinicians. 3aiii) Inclusion and exclusion criteria in relation to study design are included in the report, as are risk of bias assessment criteria. The design of each study is included in the results. Details of the risk of bias assessment are included in an appendix and the final risk of bias rating is included in the report. The final risk of bias assessment is included in the report.
76	Public Reviewer: Shire	Methods	We appreciate that AHRQ will update the literature searches during peer review. We suggest that this article be added to the articles examined: McElroy SL et al JAMA Psychiatry. "Efficacy and Safety of Lisdexamfetamine for Treatment of Adults With Moderate to Severe Binge-Eating Disorder: A Randomized Clinical Trial." 2015 Jan 14.	This article was added during the update that is incorporated while the study is receiving peer review.
77	TEP Reviewer #5	Methods	This reviewer is not qualified to consider the methods.	No response required.
78	TEP Reviewer #4	Results	On p. 25, the authors state, "we preserved the term "remission" to reflect a more sustained, global state of change marked by the absence not only of binges but of other BED criteria for an extended period of time." Please specify exactly what other "BED criteria" are being referred to and what is meant by an "extended period of time." This would help the reader to be clear on exactly what the authors mean when they say "remission" in the current report.	The text was edited to read "In doing so, we preserved the term "remission" to reflect a more sustained, global state of change marked by the absence not only of binge eating but of other features/criteria that can linger after the cessation of binge eating. For example, remission would include the absence of distress regarding binge eating, feelings of disgust after overeating or eating alone because of embarrassment.

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				Although not defined in DSM-5, this sustained global state would reasonably persist beyond the one month window typically reported in studies.
79	TEP Reviewer #1	Results	If the report authors had found differences by subgroup, it would have been important to look at these more in depth. The absence of research to support differences point to the need for further study. As eating disorders overall predominantly affect women, any further sub-analyses among women would be very helpful to the field.	For each one of our conditions, we looked for studies of treatment in subgroups. We found few. By virtue of the trialist decisions, most of the trials are mostly all women.
80	TEP Reviewer #2	Results	inevitably, new information has emerged since the report was drafted and after last summer when the "window" for publication of studies closed. Specifically, a major event in this field is the publication of a placebo-controlled trial of lisdexamfetamine (Vyvanse) for BED, and FDA's approval of this medication for BED. I am not sure how to handle---maybe it is just outside the scope/timeframe of this report, but it's a big deal (see page 36, lines 22-23).	We have added this newly published study to our review during the peer review period. McElroy, S. L., Husdon, J. I., Mitchell, J. E., Wilfley, D., Ferreira-Cornwell, M. C., Gao, J., . . . Gasior, M. (2015). Efficacy and Safety of Lisdexamfetamine for Treatment of Adults With Moderate to Severe Binge-Eating Disorder A Randomized Clinical Trial. JAMA Psychiatry, 72(3), 235-246. doi: doi:10.1001/jamapsychiatry.2014.2162
81	Peer Reviewer #3	Results	Broadly speaking, it would be preferable to lead with the psychotherapies and then move into pharmacotherapy. If the authors wish to keep as-is, please justify the order.	We had no particular rationale for the order of presentation; however, because no other reviewer took exception to the current order, we respectfully elect not to change it, as this would dictate substantive edits that would tax the resources of the project.
82	Peer Reviewer #3	Results	There are certainly a lot of details in the results section, as appropriate. It would be helpful to include mean frequency of binge eating (or LOC eating) pre- and post-treatment in addition to quantifying abstinence rates.	We have included that information in our summary tables when it was presented in the included articles.
83	Peer Reviewer #3	Results	With so many tables and complex findings, it would be helpful to have more frequent bulleted key point summaries throughout Results.	Throughout the results sections we have included key findings for particular treatment comparisons. Each generally includes a bulleted list of findings.
84	Peer Reviewer #3	Results	p. 151, K7 – Could you say more about the lack of evidence for/against psychopharm interventions for LOC eating in bariatric patients? Is it that no studies have investigated this?	Correct. No study was found that met our inclusion criteria.
85	Peer Reviewer #3	Results	Again, better to omit the questions that cannot be answered from the intro/meth/results and include in future directions in discussion.	Yes, we appreciate that the report is long but having decided on particular key questions, we need to briefly comment that there is no evidence. If we do not do that, it may not be clear that the information was not skipped over.
86	Peer Reviewer #4	Results	I thought the authors were complete in their presentation of the studies and the findings. The information was presented consistently from one section to the next, and the rationale in the text for strength of	Thank you.

#	Reviewer	Section	Comment	Response
			evidence was supported by the information in the tables.	
87	Peer Reviewer #4	Results	One question I had - IPT had stronger outcomes over time for effectiveness in decreasing binge episodes. I understand that there is insufficient evidence based on the small number of studies. However, this information seems important and worthy of mention in the summary, as most readers will likely not read into the full report, with a note that there more studies are needed to support the finding.	We agree and we have expanded our mention of IPT in the Implications for Clinical and Policy Decisionmaking and the executive summary
88	Peer Reviewer #4	Results	p. 70, line 15, "we also used" should be "We also used..."	Correction made.
89	Peer Reviewer #4	Results	p. 71, line 22, why are there 2 citations (122 and 124) when saying that the authors included "one high risk of bias anticonvulsant study." I believe 124 should be removed.	Correction made.
90	Peer Reviewer #4	Results	p. 74, line 26 reference for McElroy et al. 200(83) in the table - the year should be '2000'	Correction made.
91	Peer Reviewer #4	Results	p. 92, line 14 "... to the end of treatmer were differed significantly" - were should be removed from the sentence.	Correction made.
92	Peer Reviewer #4	Results	p. 96. line 45, there should be a space between, "...(table 14).No trial..."	Correction made.
93	Peer Reviewer #6	Results	There is a tremendous amount of detail provided and I found that the studies included were very well described. As suggested in the previous section, perhaps there is a way to summarize what is known about alternative therapies such as DBT and mindfulness based meditation as treatments for binge eating. Since BED is a new diagnosis and funding for research has likely been limited in the past, it is not surprising that so many treatment studies has insufficient evidence and did not meet the reporting criteria. I think a table summarizing these insufficient studies could be helpful for understanding the full state of the field and for designing future studies.	We include in the discussion chapter treatment options that we believe have been inadequately studied and are potential directions for future research.
94	TEP Reviewer #3	Results	As a review the amount of detail presented was appropriate, and with earlier explanation of inclusion / exclusion criteria there was sufficient information about the different treatments to separate them from each other. The figures and tables were extremely helpful and providing a clear summary of the text. I am not aware of any studies that met infusion criteria that were not included.	Thank you
95	Peer Reviewer #7	Results	Is the amount of detail presented in the results section appropriate - YES? Are the characteristics of the studies clearly described YES? Are the key messages explicit and applicable YES? Are figures, tables and appendices adequate and descriptive YES? Did the investigators overlook any studies that ought to have been included or conversely did they include studies that ought to have been excluded? The	We added the McElroy study about treatment with lisdexamfetamine dimesylate (Vyvanse) during the peer review period. McElroy, S. L., Husdon, J. I., Mitchell, J. E., Wilfley, D., Ferreira-Cornwell, M. C., Gao, J., . . . Gasior, M. (2015).

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			authors state on page 232 that they searched the clinical trial registries and found several RCTs of lisdexafetamine in progress ((McElroy et al). The results of these trials have now been published (Current Psychiatry 2015, March 14(3) 41-42). Most importantly, lisdexafetamine (Vyvanse) has now been approved by the FDA for the treatment of Binge Eating Disorder. The details of the RCTs that were presented to the FDA leading to the approval are available and need to be thoroughly reviewed in this document. These data change some of the conclusions reached by the authors.	Efficacy and Safety of Lisdexamfetamine for Treatment of Adults With Moderate to Severe Binge-Eating Disorder A Randomized Clinical Trial. JAMA Psychiatry, 72(3), 235-246. doi: doi:10.1001/jamapsychiatry.2014.2162
96	Public Reviewer: Shire	Results	Binge-Eating Disorder: Overview Please update the section to reflect the approval of lisdexamfetamine dimesylate (Vyvanse).	This updated information has been added.
97	Public Reviewer: Shire	Results	Key Question 1. Effectiveness of Interventions for Binge-Eating Disorder Given that none of the sub-sections are applicable to lisdexamfetamine dimesylate (Vyvanse), consider the creation of a new subsection entitled Pharmacological Interventions: FDA Approved Treatments for Moderate to Severe Binge-Eating Disorder in Adults Compared with Placebo. The sub-section could include several tables such as: • Characteristics of included intervention studies • Outcomes of trials • Strength of evidence for outcomes A description of studies paragraph could precede the tables with a detailed synthesis following the tables.	We have combined results for lisdexamfetamine dimesylate (Vyvanse) with those of another medication that was also formulated to treat ADHD.
98	Public Reviewer: Shire	Results	KQ2: Harms Associated with Treatments or Combination of Treatments: Pharmacological Interventions We propose that you include lisdexamfetamine dimesylate (Vyvanse) in the discussion and in Table 46 and Table 47.	We have added reported harms from lisdexamfetamine dimesylate (Vyvanse) to our results for KQ2.
99	Public Reviewer: Shire	Results	KQ 4 and KQ5: Course of illness: Binge-Eating Disorder We recommend updating the text of this section with the references on epidemiology and health economic and outcomes research related information provided in the attachment.	We did not find that any of the analyses that were provided to the EPC during peer review met our inclusion criteria for our analysis of course of illness.
100	TEP Reviewer #4	Results: CBT v IPT	1. Interpretation of interpersonal psychotherapy (IPT) findings a. Regarding the IPT trials, the authors state: "Trials differed in the intervention types that were compared. Consequently the evidence did not allow for synthesis across studies (evidence was insufficient for all outcomes)" (p. 104). As one of the treatment developers, I would like to clarify that the treatments used in the Wilfley et al. (2002) and Wilson et al. (2010) trials were the same in terms of content; they only differed in their delivery (mixed format (group + individual) vs.	We have thoroughly reviewed the methodology and treatment descriptions in both the Wilfley et al. (2002) and Wilson et al. (2010) trials and agree that both utilized the same IPT intervention; however, the differences in the way the intervention was delivered: one all individual therapy and one primary group therapy (e.g., 19, 60-minute individual sessions in Wilson versus 20, 90-minute group sessions + 3 individual sessions in

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			individual format). As stated in Wilson et al. (2010), "Interpersonal psychotherapy for BED was formulated by Wilfley (cites the 2002 paper). It was based on the treatment developed by Klerman et al. for depression, and Fairburn later adapted it for the treatment of bulimia nervosa" (p. 96). Wilfley et al. (2002) used 20 weekly group sessions and 3 individual sessions. Wilson et al. (2010) used 19 50-60 minute sessions. The versions of interpersonal psychotherapy evaluated in these two trials are essentially identical in terms of their content and only differ in their format of delivery. As noted, even in the mixed-format treatment, participants had individual sessions with a therapist in addition to participating in group treatment sessions. Drs. Wilson and Agras would attest to the similarities of these treatments as well. In addition, samples (both large in size) were similar across the trials (i.e., mean age in the 40s, mean BMI in the mid-30s, 80%+ female, primarily White). Primary outcome measures used were the same and assessed via the gold standard assessment in the field (Eating Disorder Examination). Undoubtedly, I believe these trials allow for synthesis given the strong methodological rigor and similarities. Furthermore, the reductions in binge eating and abstinence rates are among the highest reported in the treatment literature for BED for CBT/CBTgsh and IPT. Additionally, abstinence rates obtained for IPT and CBT (therapist-led and guided self-help CBT) are virtually identical, and are robust and durable over time and are consistent with other clinical trials of CBT for BED. It appears that there was confusion regarding potential differences between the treatments used in these two trials which resulted in their findings not being synthesized. It is strongly recommended that the results of these studies are synthesized (i.e., the results from the two studies of IPT should be pooled); it is a huge disservice and oversight to patients and scientists to have the results of these two studies disregarded. IPT is a robust treatment--patients who suffer from BED report high liking of the treatment and reliably achieve marked benefit in both the short- and long-term.	Wilfley) precluded combining or synthesizing the data from the two trials in a meta-analysis. This is an analytic decision that is consistent with how we dealt with data from other interventions in this report (e.g., CBT, BWL). Thus, based on clinical judgment-driven hypotheses, our decision was not to combine studies that use the same intervention with these different modes of delivery. We found that IPT was associated with high percentages of abstinence in participants and have therefore brought out these findings in the report. We discuss the significance of the IPT results in the revised Discussion section.
101	TEP Reviewer #4	Results: CBT v IPT	These studies were both published in Archives of General Psychiatry (now JAMA Psychiatry), which has a 2014 impact factor of 13.8, with extremely strong results for IPT: i. Wilfley et al. (2002), funded by NIMH R29 MH051384, which randomized 162 individuals, found that binge eating recovery rates were equivalent for CBT and IPT at post-treatment (79% vs. 73%) and at 1-year follow-up (59% vs. 62%). While dietary restraint decreased more quickly in CBT, IPT had equivalent levels by all later follow-ups at 4, 8, and 12 months. This study thus suggested that IPT was a	Both trials mentioned here are included in the review of the evidence for behavioral interventions. We have made efforts to further highlight the significant findings associated with IPT.

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			viable alternative to CBT for the treatment of BED. ii. Wilson et al. (2010), funded by NIMH R01 MH063862, which randomized 208 individuals, found that there was no difference between IPT, behavioral weight loss (BWL), and guided self-help CBT (CBTgsh) on remission from binge eating post-treatment. However, at 2-year follow-up, both IPT and CBTgsh resulted in greater remission from binge eating than BWL but that outcomes for IPT and CBTgsh were very similar (odds ratios: BWL vs. CBTgsh, 2.3; BWL vs. IPT, 2.6; CBTgsh vs. IPT, 1.2). This study suggested that IPT and CBTgsh are significantly more effective than BWL in eliminating binge eating after 2 years and that outcomes for IPT and CBTgsh are extremely similar. All outcomes were assessed using the EDE and demonstrated substantial and long-term efficacy of CBTgsh and IPT for BED consistent with 2 year follow-up data from other clinical trials (over 60% abstinence rates at 2-year follow up; See Figure 2. Page 98) (Devlin et al, 2007 published in Obesity). Of particular note is the fact that this trial was conducted at two sites – one with more experience in IPT (Washington University in St. Louis) and one with less experience in IPT (Rutgers). Despite this, there was an absence of any treatment differences across sites, showing that the efficacy of IPT was shown even at a site without a strong background or allegiance to this treatment. Detailed descriptions about the treatments, treatment delivery, treatment providers, training in treatment delivery, individuals who delivered treatment, training in these treatments, supervision of treatment delivery, and assessment of treatment integrity are presented in Wilson et al. (2011) "Allegiance Bias and Therapist Effects; Results of a Randomized Controlled Trial of Binge Eating Disorder" (published in Clinical Psychology).	
			Further, I disagree with the study being labeled as having moderate bias. The reasons stated include: "downgraded from low overall b/c of lack of reporting of baseline differences, especially use of medications; also no measure of adherence." Information about the groups at baseline is presented in the paper (means and SDs) so the similarity of these groups could be determined by the authors of this report. Although information about distribution of use of antidepressants and other medications is not included in the paper, it is clearly noted that participants taking antidepressants were only included provided they had been on a stable dosage for at least 2 months. Adherence ratings were presented in the main outcome paper as well as in Wilson et al. (2011) "Allegiance Bias and Therapist Effects; Results of a Randomized Controlled Trial of Binge Eating Disorder" (published in Clinical Psychology), which suggested that adherence rated on a 7	The risk of bias (ROB) rating was rated as medium given that the report of baseline differences was presented in the manuscript, but it was unclear whether any of the baseline data in the table/text represented statistically significant differences. This information would be especially important in the case of antidepressant use at baseline as these would be considered co-interventions that could influence the overall results. Other factors contributing to the ROB rating were the overall dropout rate and differential dropout rate between groups.

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			point scale was high and consistent across all treatments (IPT 6.3 (.7); BWL 6.1 (.8); CBTgsh 6.2 (.7). Given this clarifying information, I hope the authors agree that the bias assessment for this study should be reconsidered.	We have thus edited the text in Appendix D to amend our concerns about adherence and to instead point to the baseline differences and differential dropout.
102	TEP Reviewer #4	Results: combination treatments for BED	2. Recommendations for psychotropic medications a. In comparison to psychological treatments, psychotropic medications have not been found to have durable effects for the treatment of BED. This notion does not appear to have been captured in the review but should indeed affect the recommendations the authors make. i. For example, Grilo et al. (2012), funded by NIDDK R01 DK49587 and published in Journal of Consulting and Clinical Psychology, found that at 12-month follow-up, remission rates were 3.7% for fluoxetine-only, 26.9% for CBT + fluoxetine, and 35.7% for CBT + placebo. Thus, the authors found that CBT + placebo was superior to fluoxetine-only and that adding fluoxetine to CBT did not enhance findings compared to adding placebo to CBT. These findings demonstrate the longer-term effectiveness of CBT, but not fluoxetine, through 12 months after treatment. Findings such as these are critically important to discuss in this report, as patients need to be aware what treatments may only lead to shorter-term solutions (i.e., psychotropic medication) vs. longer-term recovery (i.e., psychological treatments such as CBT and IPT). From my understanding of the results presented in the report and on which the recommendation for various psychotropic medications were drawn, the positive results for various medications are observed over only very short-term periods (e.g., 6-16 weeks). This is extremely problematic—BED is a chronic condition warranting treatments that produce marked and sustained outcomes.	"Under "Deficiencies in Methods," we had previously stated that ". . . 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 on-going medical management to maintain treatment gains." We have now added text to support these statements. Specifically, under "Gaps in Interventions," we state, "Head-to-head comparisons involving combination treatments are also needed to determine whether, as one study, Grilo (2012) suggests, gains persist longer following psychological (CBT) or combination (CBT+fluoxetine) treatment than pharmacological (fluoxetine) treatment. This information would help patients and providers optimize their plans to address both short- and long-term goals of treatment." In addition, in the Results, where we report on the cited trial, we highlight the 12-month differences in abstinence between the CBT and fluoxetine treatment arms.
103	TEP Reviewer #4	Results	There is now an indication for Vyvanse so the statements on pp. 7 and 185 should be adjusted accordingly. It will also be important to include the evidence from which this indication was given earlier in the review instead of just in the conclusion (p. 187) now that the paper is available in JAMA Psychiatry.	We have edited all of information we had earlier reported on lisdexamfetamine dimesylate (Vyvanse).
104	TEP Reviewer #2	Results	The findings regarding BWL are of interest and possible importance. For example, page 34, lines 9-12, indicating that BWL yields more weight loss, but less change in binge eating than CBT. This is potentially important in two regards: (1) BWL should be much more routinely available in the community than CBT. And, my hunch is that will be less expensive as it is less specialized; (2) it raises the important question of the patient's primary goal of treatment: the	We have now added statements to the Implications for Clinical and Policy Decisionmaking section that better incorporate the findings of both BWL and IPT.

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			behavior or the weight. I am sure this varies, but it may be an important point for the clinician to discuss with the patient. For these reasons, I was a bit disappointed that BWL is not mentioned at all (I don't think) in the Implications for Clinical Decision Making (page 35).	
105	TEP Reviewer #5	Results	From the viewpoint of this non scientifically trained reviewer, the detail, characteristics, and key messages are explicit and applicable. No known additional studies given the current scope.	Thank you
106	TEP Reviewer #4	Results and Discussion	Given these strong results and clear methodological rigor of the two large-scale studies of IPT, its high acceptability to patients, and the fact that NIMH has now funded a large R01 trial to disseminate this treatment, I believe this suggests that there is sufficient evidence for the efficacy of IPT and that IPT should be better highlighted in this report as a viable treatment option for BED. More studies on CBT have certainly been conducted but the results of promising treatments (like IPT) that simply have not had as many trials conducted should not be discounted, given the two large scale studies of IPT that have been conducted. Indeed, the 2010 study was funded by NIMH as a "definitive" trial, as it was a follow up of the 2002 study that had already documented the robust and sustained outcomes achieved by IPT, that were equivalent to those obtained with the "gold-standard" CBT treatment for BED. The 2010 paper replicated once again the robust and long-lasting effects of IPT, in a large-scale multi-center study. I am unsure what additional evidence or replication studies the authors of the current report would be looking for in order to make the conclusion that IPT is a first-rate treatment option for BED.	The results of the IPT trials have now been better highlighted both in the Results section as well as in the Discussion. We have made efforts to point to the robust and sustained binge-related outcomes and also included the importance of patient choice/acceptability in the Clinical and Policy Decisionmaking section.
107	TEP Reviewer #4	Results/Discussion	3. Review methodology b. Overall, it is recommended that the authors take into consideration the status of clinical practice and research and make sure that the conclusions are consistent with the actual risk of harm and known benefits to various treatments and to highlight treatments (like IPT) that have demonstrated robust results (with no contrary evidence provided). If the authors feel more research is needed for definitive studies like the two published IPT studies in Archives of General Psychiatry (2002; 2010), it would be important to spell this out. NIMH is loath to fund additional studies to evaluate treatments that have shown robust findings across two, large scale well-controlled studies. These two studies cost the government millions of dollars to address the question of how well IPT works for BED, in both the short- and long-term. Robust and sustained outcomes were achieved in both studies. It would also be helpful to provide information on effect sizes	We have now included data in the text to help contextualize the magnitude of the IPT results. We have also now more explicitly discussed the IPT results and highlighted their sustainability over long-term follow-up.

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			within the text would help readers form more educated opinions.	
108	TEP Reviewer #2	Discussion	one section related to Key Question #1 discusses the outcome of forms of CBT vs wait-list control. (e.g., page 27, line 22; page 32, Table D). The descriptions are appropriate. The issue I would raise is that a wait-list control group is an extremely low bar: superiority indicates only that doing something is better than doing nothing. Without some other credible treatment, such results provide no support for the *specific* benefits of CBT, or whatever the single active treatment is. I wonder if a comment along such lines might be appropriate.	We have now added a statement indicating that the benefits of CBT were only in relation to waitlist control and thus the specific benefits of CBT were not found within this review.
109	TEP Reviewer #2	Discussion	Basically, yes: clearly stated. But, see comments above.	Thank you
110	Peer Reviewer #2	Discussion/ Conclusion	When discussing potential risk of harm from medications, it should be noted that topiramate is a teratogen that leads to a higher incidence of oral clefts. This is particularly important because many women with BED are of childbearing potential.	Thank you for this insight. In response, within the Discussion, we added text under "KQ2. Evidence for Harms . . ." and under "Implications for Clinical and Policy Decisionmaking"
111	Peer Reviewer #3	Discussion/ Conclusion	p. 177 – could you also give the mean binge frequency pre- and post-treatment when summarizing? That may be a helpful complement to the abstinence rates. p. 181 – can we include a bullet of the comparison between psychopharm and CBT? What should clinicians start with?	In the Results section, we provide this context, indicating the mean change over time and final mean binge frequency for the treatment groups. We also added this sentence to the Discussion: "Binge frequency was approximately 5 episodes per week prior to treatment and approximately 1.5 and 2.1 episodes per week after treatment in those receiving antidepressants vs. placebo, respectively." We have added the following to clinical and policy implications: "While the effect size for abstinence was larger for therapist-led CBT than for lisdexamfetamine, second-generation antidepressants, and topiramate, the comparator arm differed (waitlist for CBT, placebo for medications). Therefore, the true difference in the magnitude of the effect size between the psychological intervention and the pharmacological interventions is not known. For this reason, we cannot make an empirically-driven recommendation regarding first-line treatment."
112	Peer Reviewer #3	Discussion/ Conclusion	p. 194, "Therefore, based on the available evidence for both benefits and harms, clinicians may find antidepressants, topiramate, and CBT to be good choices for the treatment of BED. However, the comparative effectiveness of these and other treatments remains unclear and constitutes an area in need of further study. Head-to-head trials are needed to help decisionmakers identify best options for first-	For emphasis, we have included this conclusion in the executive summary and well as the discussion

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			line and adjunct treatments, including trials that compare the effectiveness of different antidepressants, of antidepressants with other medications and with CBT, and of different modes of delivery of CBT. In particular, comparing different modes of delivery of CBT could be helpful to those making decisions that affect patient access to specialized treatment." This statement (above) feels critically important and should be highlighted somehow.	
113	Peer Reviewer #3	Discussion/ Conclusion	With regard to further studies, would it be worth mentioning the need to study whether and when to use higher level of care (e.g., intensive outpatient, partial, or residential treatment) in individuals with BED whose binge eating is intractable or causing distress/impairment enough to severely compromise functioning?	Under "Gaps in Interventions," we added the following text: "In addition, studies of stepped-care models are needed to elucidate whether and when combination treatments or a higher level of care (e.g., intensive outpatient, partial hospitalization, residential treatment, inpatient) is warranted for those not responding adequately to conventional outpatient treatment."
114	TEP Reviewer #1	Discussion/ Conclusion	Geography was not limited for the study in terms of article selection. Geography in the context of impact on treatment outcomes i.e. rural/urban location was not considered in the original framework. This could be an important variable for further research.	We have added to the Discussion the concern that specialized care for BED may be harder to obtain in rural areas and therefore, forms of behavioral treatment that require less direct care services are an important consideration. We have included the following statement in the discussion section: "These findings have implications for decisionmakers who may be considering the relative resources needed for therapist-led rather than 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.
115	TEP Reviewer #1	Discussion/ Conclusion	Research gaps are significant for BED and LOC. This cannot be overstated. Standard definitions of remission and recovery require a continuum approach rather than a fixed point in time. The longevity of illness as a predictive factor for recovery is important to further study. Longitudinal research is needed; one year follow up end points often used in research may not capture the remissions and improvements in illness over a longer period of time, nor the treatments that are better suited to patients who do not fully recover but essentially are living with a chronic illness.	We have added text concerning the need for long term follow-up to better understand those whose BED may persist as a chronic condition.

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116	Peer Reviewer #4	Discussion/ Conclusion	Overall, the authors presented the conclusions clearly. I agree with them that they should include the new study by McElroy et al on the use of lisdexamphetamine (Vyvance) in the report, which should be available now.	We have added this study during the peer review period.
117	Peer Reviewer #4	Discussion/ Conclusion	Same question regarding IPT- the findings were not presented for IPT in the discussion. I believe it may be helpful to mention that the effects of this treatment were examined, but there was insufficient evidence, as clinicians may be looking for this in this section.	We have now better incorporated the findings for IPT in the Discussion section.
118	Peer Reviewer #6	Discussion/ Conclusion	The major findings are well stated and the efficacy of second generation antidepressants (and topiramate) as well as therapist led CBT are well-described.	Thank you
119	Peer Reviewer #6	Discussion/ Conclusion	The future research section is clear and can be easily translated. However, I think the addition of a table or an outline that highlights categories of suggested future studies (e.g. A. Pharmacological: comparisons of multiple medications B. Therapeutic: non-therapist led CBT using similar methods and outcomes measures C. RTC of treatment for LOC eating before/after bariatric surgery etc) could be a very helpful way of visualizing what is lacking from the current state of the literature. I consider myself to be fairly up to date and knowledgeable about the BED literature and I was surprised to find how much of what we do know is considered scientifically insufficient. Funding agencies and clinical researchers would benefit from having an actual list of what is missing, unknown, unsupported, etc so that future study proposals can be designed with those aims in mind and funds can be directed at filling the current gaps.	We respectfully prefer to not use an outline style to present our suggestions for future research. Our approach was to use clearly identifiable sections of text.
120	TEP Reviewer #3	Discussion/ Conclusion	The implication that the current state of the science is inadequate was clear. The future research section was clear and consistent with the previous 2006 AHRQ eating disorders review. On page Es-23 (second paragraph the statement is made that comparing different formats is not consistently grounded in a priori mechanisms of action was thought by this reviewer to be a critical comment, that if adopted would benefit the science by providing a additional treatment target (the other target would be the traditional clinical symptom) that could be grounded in more basic or biological science. This would allow for a greater ability to interpret negative or marginal results by determining if the more fundamental treatment target was actually engaged. Another suggestion for the conclusion is that a set of common eating disorder data elements be developed and incorporated into future studies which would increase the ability to compare across different treatment trials.	We have added the following statement to the Conclusion. “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 and compare across or combine different treatment trials.”

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121	TEP Reviewer #4	Discussion/ Conclusion	On 184, when providing information about which medications might be treatment options for BED, it will be important to include that none of these are actually FDA-approved for the treatment of BED, extremely clear information on side effects, how established guidelines have not recommended this as a first line pharmacological treatment, and how any effects of these medications have not been shown to be durable.	We have added to the discussion that lisdexamfetamine dimesylate (Vyvanse) is the only medication that has been approved by the FDA and that an additional understanding of treatment options over a longer period of time will add to guideline development.
122	TEP Reviewer #4	Discussion/ Conclusion	The conclusions appear to state that it is very difficult to draw any conclusions. They also distinguish the support for antidepressants vs. topiramate. However, previously in the discussion section they seem to be equally recommended as pharmacological treatments. Also, failing to mention what some of the promising other treatments are (e.g., IPT which has been shown to have similar effects as CBT, DBT showing early promise) can mislead practicing treatment providers.	We have revised the conclusions so that we more clearly state that we found support for several treatment options, antidepressants, lisdexamfetamine, topiramate, and CBT. IPT and DBT are discussed earlier in the chapter. The evidence from these treatments was too sparse to reach definitive conclusions about their effectiveness.
123	TEP Reviewer #4	Discussion	b. One of the strongest recommendations is that topiramate should be used as a pharmacological treatment for BED. This medication never received approval from the FDA for the treatment of BED due to its negative side effects. As detailed in McElroy et al. (2007), topiramate was associated with paresthesia, upper respiratory tract infections, taste perversion, difficulty with concentration/attention, and other memory difficulties significantly more than a placebo. Thus, the authors should take care to be very clear about the negative side effects that have been found to be associated with this medication and the implications this has for clinical practice.	In the revised text, we clearly state that Lisdexamfetamine is the only FDA-approved medication for the treatment of BED and we also point out that topiramate has teratogenic potential.
124	TEP Reviewer #4	Discussion	It might be worth mentioning the timing of this report as a limitation. With DSM-5 recently published, it is unknown how much research is actively being conducted that will surface over the next several years utilizing the revised criteria and potentially collecting longer-term outcome data.	We have added the following paragraph to the implications for clinical and policy decisionmaking: “We wanted to comment on the potential impact of the DSM-5 change in the diagnostic criteria for BED. The binge frequency criterion has been lessened and the duration of illness has been 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, we found no studies that provided separate results for a patient population diagnosed according to DSM-5.”
125	TEP Reviewer #4	Discussion	On p. 153, the authors indicate the three trials investigating LOC eating among children they included in this review all differed in how they defined this construct. In the “Key Points” section, it may be helpful to include a sentence or two indicating the need for the field to develop a more universally accepted definition and therefore assessment tool for researching LOC eating in particular.	We have added to this point to the conclusions concerning the definition. We do not necessarily agree that there is a need for one assessment tool. “Greater consensus is needed concerning the necessary minimum criteria for determining LOC eating in children, including frequency and duration and whether the criteria should differ by the age of the child.”

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126	TEP Reviewer #4	Discussion	On p. 6, the authors highlight the difficulty in assessing LOC, for various reasons (e.g., lack of definition standardization, subjective vs. objective LOC, etc.). Given these challenges, it might be helpful to elaborate on the different ways researchers assessed LOC and make suggestions for improvement.	We have included a summary of the approaches that researchers have used to assess LOC eating. We have added the following sentence to the conclusions. .“Greater consensus is needed concerning the necessary minimum criteria for determining LOC eating in children, including frequency and duration and whether the criteria should differ by the age of the child.”
127	Peer Reviewer #7	Discussion/ Conclusion	Are the implications of the major findings clearly stated YES? Are the limitations of the review/studies described adequately ? YES	Thank you
128	Peer Reviewer #7	Discussion/ Conclusion	In the discussion, did the investigators omit any important literature? Yes- see my comments above regarding lisdexafetamine.	The published study of lisdexafetamine has been added to the review.
129	Public Reviewer: Shire	Discussion/ Conclusion	Discussion: Key Question 1. Effectiveness of Interventions for Binge-Eating Disorder We recommend updating the text of this section with information concerning lisdexamfetamine dimesylate (Vyvanse) as well as Table 63.	The published study of lisdexafetamine has been added to the review.
130	Public Reviewer: Shire	Discussion/ Conclusion	Discussion: Key Question 2: Harms Associated with Treatments or Combination of Treatments: Pharmacological Interventions We advise updating the text of this section with information concerning lisdexamfetamine dimesylate (Vyvanse) as well as Table 65.	The published study of lisdexafetamine has been added to the review.
131	Public Reviewer: Shire	Discussion/ Conclusion	Pages 183 – 184 Findings in Relation to What is Already Known We suggest also updating this section.	The published study of lisdexafetamine has been added to the review.
132	Public Reviewer: Shire	Discussion/ Conclusion	Implications for Clinical and Policy Decisionmaking We propose that you include lisdexamfetamine dimesylate (Vyvanse) in the discussion.	The published study of lisdexafetamine has been added to the review.
133	Public Reviewer: Shire	Discussion/ Conclusion	The report states, “For nearly all medications…the evidence base was limited to single studies.” It would be helpful to list those medications for which there were multiple studies.	We have revised this sentence to point out the “exceptions” (lisdexamphetamine, fluoxetine, and topiramate)
134	Public Reviewer: Shire	Discussion/ Conclusion	“We found reports of several related RCTs (Phase 2 and Phase 3)….among individuals with BED.” We hope that the information that we have provided will be helpful in the including updated information on lisdexamfetamine dimesylate (Vyvanse).	We have included the Phase 2 trial in our review. We did not have published findings from the two Phase 3 trials but we have added confirming information that we found on clinicaltrials.gov
135	Public Reviewer: Shire	Discussion/ Conclusion	We suggest inclusion of updated information on lisdexamfetamine dimesylate (Vyvanse) in the text of this section.	The published study of lisdexafetamine has been added to the review.
136	Peer Reviewer #6	Discussion	The report was well-structured and clearly presented. For policy makers, researchers and practitioners, a bullet-point list of current	In this chapter, rather than bullets we respectfully decided to present our conclusions with greater detail. A

#	Reviewer	Section	Comment	Response
			treatment recommendations and recommendations for future studies could be beneficial. The report goes into great detail about all of the studies and how the recommendations were determined, but having a one page summary without the explanations could be helpful.	more brief synopsis of our discussion and conclusions can be found in the executive summary.
137	TEP Reviewer #3	Discussion	The answer to the first two questions is yes, unfortunately the state of the science does not readily lend itself to informing policy decisions.	We agree with this observation and believe we have appropriately called attention to it under "Research Gaps" and "Implication for Clinical and Policy Decisionmaking"
138	TEP Reviewer #4	Discussion/ Conclusions	1. As discussed in this review, I am extremely concerned that the conclusions from this report cannot be used to soundly inform policy and practice decisions. As detailed in the General Comments, I am particularly troubled about the following three points, and how recommendations in this version of the report would negatively impact patients who suffer from BED: a. The inaccurate portrayal of IPT findings b. The misguided recommendations for psychotropic medications given that they have not been shown to have durable effects c. The strong recommendation for topiramate given its side effects	Within the Policymaking section, we have added the following: "Of critical importance is whether any of the medication treatments produce durable benefit without side effects that compromise adherence." Also, elsewhere in the chapter, we have added text to address the potential teratogenic effects of topiramate.
139	Public Reviewer: Raquel Halfond American Psychiatric Association	Discussion	In discussing methodological deficiencies p. 188 a broader definition is needed to address the factors that constitute symptom improvement remission and recovery. In addition to recommending continued reporting of both discrete binge episodes and binge days per week in clinical trials the text mentions the need for a core set of psychological behavioral and physiological outcomes. We concur and would specifically note the importance of assessing and understanding the impact of poor body image and shame in individuals with binge eating disorder. It would also be valuable to discuss definitions of improvement from a patient centered standpoint i.e. what constitutes improvement for them in their view. We appreciate the opportunity to review the draft report and hope these comments are helpful. For follow up on these comments please contact our American Psychiatric Association representative.	We have added the following to our discussion of the definition of remission and recovery: "Additionally, it is important to consider the perspective of the patient in defining remission and recovery and to use this perspective in the development a consistent definition. Interweaving this information with validated and reliable measures would allow researchers and clinicians to generate a comprehensive set of parameters by which remission and recovery could be measured."
140	TEP Reviewer #5	Discussion	Major findings are clear and limitations described adequately. Future research is clear based on the scope of the report, but there are considerable lapses in areas that warrant ongoing research that are not part of the report.	So noted.
141	TEP Reviewer #5	Discussion	It is this reviewers opinion that future research and reports should consider additional questions including: 1)the role of restriction/dieting in developing/maintaining the binge cycle or LOC 2)the role of	We agree with the reviewer and have incorporated some of these additional questions into the Deficiencies in Methods section of the report.

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			underlying metabolic disorders (ex: PCOS) in the development/maintenance of BED; 3)treatment outcomes of approaches utilized for PTSD given the incidence of BED in war veterans and victims of bullying and other types of traumas; 4) role of acceptance and addressing body image & weight stigma issues in outcomes.	
142	TEP Reviewer #1	Clarity and Usability	The report is very well organized. The results clearly suggest the need for new investment in BED and LOC research.	Thank you
143	Peer Reviewer #2	Clarity and Usability	In general it is well organized and can provide useful information--especially on what research is needed in the future	Thank you
144	Peer Reviewer #3	Clarity and Usability	BED has been well-studied and is focus of this report. LOC eating in children and in bariatric patients has received less attention and is a secondary focus. The LOC eating IN CHILDREN AND BARIATRIC patients should be qualified as such (as it is not LOC eating more broadly, which includes BED, sub-BED, etc.).	We have clarified this in the text.
145	Peer Reviewer #3	Clarity and Usability	Suggest omitting questions that are not answerable due to lack of data. This would help to streamline the manuscript.	We appreciate that this can get bulky in the text but we believe that it is our responsibility to transparently report by separately stating those questions that we sought to address but could not.
146	Peer Reviewer #3	Clarity and Usability	Suggest ordering questions by how they are presented in results.	We believe that this approach would add to the bulk in the text because some of the questions could not be answered.
147	Peer Reviewer #3	Clarity and Usability	Suggest leading with psychotherapy and then reporting on pharmacotherapy in the results.	We respectfully decline to re-order the report.
148	Peer Reviewer #3	Clarity and Usability	Conclusions are somewhat buried in Discussion and should be more clearly bulleted.	We have revised the discussion section so that the conclusions are more clearly identified.
149	Peer Reviewer #4	Clarity and Usability	Yes, the report was clearly structured and can be used to inform practice decisions. One point made in the Summary - Conclusions - p. 46, line 45, "bariatric surgery patients..." should be, "persons seeking bariatric surgery," as I believe this study was assessing persons before surgery.	Our goal was to examine treatment and outcomes in individuals who had undergone bariatric surgery because of limitations in their eating capacity due to the surgery.
150	Peer Reviewer #4	Clarity and Usability	In the summary, p. 24, line 47, I was wondering how risk of bias was determined. As this is the section that most readers will see (and may not go to the full document) more explanation may be needed here. It may just mean including the rationale for this particular study as high for risk of bias.	We do not believe that there is sufficient room in the ES to discuss individual risk of bias assessments and we direct the reader to the risk of bias appendix.
151	Peer Reviewer #4	Clarity and Usability	p. 27, line 50, it seems that references are needed after "...and two for therapist led versus structured self-help."	These references have been added.
152	Peer Reviewer #4	Clarity and Usability	p. 32, 2nd line "... antidepressants lost a modest amount more weight," seems awkward. Please consider changing the wording.	This text has been deleted based on additional analyses conducted during peer review.

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153	Peer Reviewer #4	Clarity and Usability	There is a tracked change that appears on p. 328, line 32.	Correction made.
154	Peer Reviewer #5	Clarity and Usability	In general, the organization is a strong point of the manuscript. Unfortunately, the variability in approaches has been such that there are few firm conclusions that can be drawn with regard to implications for clinical practice or policy. The need for greater standardization across studies, and for multicenter collaborations is clear.	We have brought those considerations forward in the discussion.
155	Peer Reviewer #7	Clarity and Usability	Is the report well structured and organized? YES Are the main points clearly presented? YES Can the conclusions be used to inform policy and/or practice decisions? The report needs to be updated to include the recent findings regarding efficacy of psychostimulants to treat BED.	Thank you. This study was added to the report during the peer review period.
156	TEP Reviewer #5	Clarity and Usability	The report is well structured and organized and the main points are clearly presented. The applications and conclusions highlight the inability of the current body of evidence to truly inform practice decisions. The small amount of evidence highlighted by the report will not favorably influence decisions and policies made by payers because of the largely inconclusive nature. This will compromise access to quality care for patients.	Thank you.