

Comparative Effectiveness Research Review Disposition of Comments Report

Research Review Title: *Comparative Effectiveness of Bariatric Surgery and Nonsurgical Therapy in Adults With Metabolic Conditions and a Body Mass Index of 30.0 to 34.9 kg/m²*

Draft review available for public comment from October 19, 2012 to November 16, 2011.

Research Review Citation: Maglione MA, Maggard Gibbons M, Livhits M, Ewing B, Hu J, Ruelaz Maher A, Li Z, Perry T, Shekelle PG. Bariatric Surgery and Nonsurgical Therapy in Adults With Metabolic Conditions and a Body Mass Index of 30.0 to 34.9 kg/m². Comparative Effectiveness Review No. 82. (Prepared by the Southern California Evidence-based Practice Center under Contract No. 290-2007-10062-I.) AHRQ Publication No. 12(13)-EHC139-EF. Rockville, MD: Agency for Healthcare Research and Quality. June 2013. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Research Review

The Effective Health Care (EHC) Program encourages the public to participate in the development of its research projects. Each comparative effectiveness research review is posted to the EHC Program Web site in draft form for public comment for a 4-week period. Comments can be submitted via the EHC Program Web site, mail or email. At the conclusion of the public comment period, authors use the commentators' submissions and comments to revise the draft comparative effectiveness research review.

Comments on draft reviews and the authors' responses to the comments are posted for public viewing on the EHC Program Web site approximately 3 months after the final research review is published. Comments are not edited for spelling, grammar, or other content errors. Each comment is listed with the name and affiliation of the commentator, if this information is provided. Commentators are not required to provide their names or affiliations in order to submit suggestions or comments.

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.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 2	Executive Summary	p. ES-2, and elsewhere: While the time intervals defining short-term vs. long-term outcomes are clearly described in the protocol for this report, their definitions are not as clearly indicated in the report itself	We have clarified in the text.
Peer Reviewer 2	Executive Summary	p. ES-4: it would be helpful to have SOE ratings organized by KQ	We have organized the Executive Summary (ES) according to the topics in the key questions. We discuss efficacy and comparative effectiveness findings (KQ 1, 2, and 5) first, then adverse events findings (KQ 3 and 5). We feel this organization makes more sense from a reader's perspective. We do not feel it is necessary to restate the key questions verbatim in the results section.
Peer Reviewer 2	Executive Summary	p. ES-6: Please clarify outcomes and time frame for the following statement: <ul style="list-style-type: none"> • Short-term outcomes: There is moderate strength of evidence that bariatric surgery is an effective way to treat diabetes in patients with BMI of at least 30 kg/m² but less than 35 kg/m² in the short term. • Does the following statement fall under the moderate rating stated in the sentence above? - At one year, surgery patients show significantly greater weight loss than can be expected from diets, exercise, or other behavioral interventions 	We give the SOE for the body of evidence for each key question rather than for individual health measures. This is because the key questions ask whether specific surgical procedures are effective in "treating diabetes" as a whole, taking all outcomes into consideration, including blood sugar, cholesterol, blood pressure, weight etc. Regarding time frame, "short term" includes up to 2 years.
Peer Reviewer 2	Executive Summary	p. ES-6: Please clarify outcomes and time frame for the following statements: <ul style="list-style-type: none"> • Taking into consideration the entire body of evidence, we rate the SOE as moderate for RYGB, LABG, and sleeve gastrectomy for treatment of diabetes and metabolic conditions in patients with a BMI of between 30 and 34.9, in the short term (up to 2 years). • For BPD, both the number of studies and their sample sizes are much lower in this population; thus the strength of evidence for this procedure is rated low 	Again, we give the SOE for the body of evidence for each key question rather than for individual health measures. This is because the key questions ask whether specific surgical procedures are effective in "treating diabetes" as a whole, taking all outcomes into consideration, including blood sugar, cholesterol, blood pressure, weight etc. As stated in your comment, short-term is up to two years. Regarding the BPD statement in your comment, the SOE is for efficacy in treating diabetes in the short term.
Peer Reviewer 2	Executive Summary	p. ES-7: it would be helpful to have the # of trials and SOE included in Table A	This is information stated in the accompanying text. We feel that too much information in an Executive Summary table can be distracting.
Peer Reviewer 2	Executive Summary	p. ES-8: please clarify SOE for long-term adverse events (insufficient?)	Yes, insufficient.
Peer Reviewer 5	Executive Summary	Need to discuss adverse events by surgical procedure as they differ	Adverse events are discussed by procedure in detail in the results section; we have added important points to the executive summary.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 5	Executive Summary	Not clear if studies that only reported weight outcomes for the target groups were included	We included studies that reported any of the following outcomes: weight loss/ BMI change, glucose, lipids, blood pressure, quality of life, complications, or adverse events. We have clarified this in the Methods.
Peer Reviewer 5	Executive Summary	Racial, demographic and other patient factors box – should have race as one of the listed categories	Thanks for catching; we have added race.
Peer Reviewer 5	Executive Summary	Need to discuss why same BMI cut-off used for Asians (e.g Ramachandran trial)	The BMI cut-off was decided during a year long "topic refinement" period which included group discussions with key stakeholders including consumers, health care providers, payer representatives, and policy makers from around North America. BMI (at least 30 but under 35) was selected primarily because bariatric surgery is reimbursed by private and public payers (in the US) for patients with BMI of at least 35 with comorbidities. At the start of evidence report development, because of the dearth of studies in this BMI range, the TEP suggested we not exclude any studies based on ethnicity or location.
Peer Reviewer 5	Executive Summary	This is not very clear, do you mean that if the average BMI for participants was between 30 and <35 you included the study? Need to provide further clarification throughout and why you included Dixon trial for example.	We have clarified on page 4 of the Executive Summary: We expect the risk of weight to be similar for a person with a BMI of 29.5 kg/m ² and a person with a BMI of 31.5 kg/m ² , yet our key questions deal with the latter and not the former. Indeed, the published literature does not always conform to the same threshold specified in the key questions. We judged that studies that included substantial number of patients within the threshold of our key questions, but perhaps also some outside the range, were still informative, and were included. Thus, if a study included patients with a BMI of 29 kg/m ² - 37 kg/m ² we judged that it would be more informative to the key questions to include rather than exclude it. Similar decisions were made about the presence of impaired glucose tolerance and the clinical diagnosis of diabetes.
Peer Reviewer 5	Executive Summary	Not sure why Finnish Diabetes Prevention Programme is not included – needs to be explained as people will expect it to be included. Unclear why Finnish Diabetes 'new' trial – it came out before DPP and also has long term follow-up data, should feature on page 34	We have revised the text to state that earlier findings from the Finnish DPP are included in prior systematic reviews. On page 35 (now 36) we present long-term results published after those reviews.
TEP 3	Executive Summary	remove 'a')	Correction made.
TEP 3	Executive Summary	change 'of' to 'between'	"Of" is correct usage

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Commentator & Affiliation	Section	Comment	Response
TEP 3	Executive Summary	change 'cases' to 'case'	Correction made.
TEP 3	Executive Summary	change 'bypass' to 'banding'.	Correction made.
Peer Reviewer 1	Introduction	Very complete	None needed
Peer Reviewer 3	Introduction	The introduction is good except for the "Medication" section (page 2). There is a part about diabetic medications and there are quite a few studies on GLP-1 agonist that show weight loss and improvement in blood sugar control. Would recommend putting this in the Introduction. this is mentioned in the body of the article (table 8) Since Liraglutide has a good chance of being approved for weight loss in the future would bring it up earlier	We have added descriptions of these drugs to the introduction.
Peer Reviewer 4	Introduction	Under Medications, you may wish to make a reference to the most commonly used obesity drug, Phentermine which is only approved for short-term use. Many other medications are used off-label for obesity so some acknowledgement of this might also be useful	We have added mention of Phentermine along with several other drugs.
Peer Reviewer 4	Introduction	May also wish to include under the bariatric surgery section that "Gastric Sleeve" also is referred to as Sleeve Gastrectomy. Noticed that the authors seemed to switch between these terms at times	We have stated this in the introduction, in the paragraph describing this procedure.
Peer Reviewer 5	Introduction	Should also mention low-glycaemic index and Mediterranean diets, which are being increasingly used in type 2 diabetes. Better also to say that there are other behavioural approaches used besides just CBT (which would be best not to call a form of education). Should mention exenatide and liraglutide.	We have rewritten the introductory section on "Conventional therapies" to include these interventions.
Peer Reviewer 7	Introduction	Well done!	None needed

Commentator & Affiliation	Section	Comment	Response
TEP 2	Introduction	<p>Bariatric Surgery The general statement regarding the mechanisms by which gastric bypass, LAGB and gastric sleeve induce weight loss is over-simplified and out of date. The restrictive aspect of LAGB clearly limits the quantity of solid food that a patient can consume at a single meal, but this may or may not be the predominant mechanism by which LAGB induces weight loss. As the authors correctly note later, gastric bypass generates minimal, if any, malabsorption of macronutrients. The statement regarding "...significant changes in hormones and neurosignals..." might be better stated as "...from the gastrointestinal tract to the central nervous system lead to hunger control and satiety." While the mechanism(s) of action of gastric bypass have not been conclusively demonstrated, this is a reasonable presumption and therefore a fair statement for the introduction. The matter of "...an aversion to high-carbohydrate foods..." could also be described as a learned behavior change, which may be an important mechanism for both LAGB as well as gastric bypass.</p>	<p>We have revised the descriptions of surgical procedures per the suggestions. TEP member #2 has reviewed and agreed with the revised section.</p>
TEP 2	Introduction	<p>LAGB The statement regarding adjustment of the gastric outlet according to a patient's weight loss is over-simplified and at times incorrect. Decision making regarding LAGB adjustment must be based on clinical symptoms and eating behavior, rather than weight loss, as a primary parameter. It is entirely possible to tighten a band, such that a patient turns to maladaptive consumption of high calorie liquids because solid foods are not tolerated.</p>	<p>We have revised the descriptions of surgical procedures per the suggestions. TEP member #2 has reviewed and agreed the revised section.</p>

Commentator & Affiliation	Section	Comment	Response
TEP 2	Introduction	<p>Gastric sleeve The mechanism by which gastric sleeve induces weight loss is not clear. At least one study has demonstrated increased or rapid gastric emptying following gastric sleeve resection, leading to a possible mechanism of neural-hormonal phenomena similar to gastric bypass.</p> <p>The attention given to addition of ileal interposition in this introduction, as well as later in the report, is inappropriate in the opinion of this reviewer. The role of ileal interposition as a component of a complex procedure with sleeve or as an independent procedure is uncertain at best. Ileal transposition is not listed as one of the procedures for which the literature search was done.</p> <p>More appropriate would be a more concise description of biliopancreatic diversion with duodenal switch. This procedure is a modification of the BPD described below in the introduction.</p> <p>Gastric sleeve was initially described as the first stage in a two stage BPD/DS procedure for very high risk patients. When substantial weight loss was observed with the first stage alone, consideration was given to application of the gastric sleeve as an independent procedure. The statement regarding "...followed by a malabsorptive procedure such as gastric bypass..." is incorrect. Gastric bypass is not a malabsorptive procedure, as noted above. The BPD does have a component of malabsorption. It is not established, however, that malabsorption is the primary mechanism by which weight is lost. The intestinal bypass of the past, a procedure that was abandoned due to complications from malabsorption, was shown to induce weight loss primarily by reduced nutrient intake.</p>	We have revised the descriptions of surgical procedures per the suggestions. TEP member #2 has reviewed and agreed the revised section.
TEP 2	Introduction	In 1991 the NIH conducted a consensus conference on bariatric surgery. It was the report from the consensus conference in 1991 that established the accepted criteria for bariatric surgery. Formal NIH guidelines were not published until 1998, at which time the consensus conference recommendations were re-stated due to a lack of evidence to confirm or refute the recommendations of the consensus conference.	We have revised this section.
TEP 2	Introduction	In summary, the introduction is problematic because it contains inaccuracies which are clumsy at best. The very high quality of the remainder of the report should not be compromised by the introduction.	We have revised the introduction extensively.

Commentator & Affiliation	Section	Comment	Response
TEP 4	Introduction	Regarding description of bariatric procedures- for gastric bypass- it is THE most common procedure and dumping is relatively rare.	We have reworded to state that some patients may experience this. Original wording stated many patients will experience.
Peer Reviewer 1	Methods	Methods are appropriate	None needed
Peer Reviewer 2	Methods	p. 6: Technical Expert Panel – this section is written in future tense	This section is written in the past tense.
Peer Reviewer 2	Methods	p. 6: Analytic Framework, first sentence – deleted “will be documented” from end of sentence	Unclear why; we have left in sentence
Peer Reviewer 2	Methods	p. 8: 2nd paragraph, 1st sentence – typo, “dissecting, comparing	We have deleted “dissecting”
Peer Reviewer 2	Methods	p. 8: 3rd paragraph, 1st sentence – typo, “- as in our prior Evidence Report a surgical and nonsurgical weight loss therapies in more obese patients.”	We have changed “a” to “on”
Peer Reviewer 5	Methods	Weight loss is as much an indirect outcome as HbA1c, since the ultimate aim of weight loss is to improve comorbid conditions.	Weight loss is an intermediate outcome in terms of being on the pathway to improvement in comorbid conditions, however we treat weight loss as a health outcome since it is something patients can feel and has its own benefits in terms of self-image.
Peer Reviewer 5	Methods	Date for sending out for review – is this correct? I only got in November.	We sent to AHRQ and its Scientific Resource Center in September 2011. They reviewed before forwarding to you.
Peer Reviewer 5	Methods	64 articles not retrievable – this is a very large number, is this because you had such a short timeframe? Needs an explanation.	This number decreased significantly during the review period, as new materials arrived. In addition, we went back and rejected many at title and abstract review as being beyond the scope of project. The remaining irretrievable studies are primarily conference abstracts.
Peer Reviewer 5	Methods	Need to provide units for the fasting blood glucose, HbA1c	HbA1c is reported as percentage of total hemoglobin. We have made this clear in the text and tables.
Peer Reviewer 5	Methods	Need to head Weight change % with (SD)	We have added.
Peer Reviewer 5	Methods	I found the methods very confusing, as they were inadequately described	We have revised for clarity.

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Peer Reviewer 5	Methods	The inclusion criteria for types of participant (? mean BMI in study, range of BMI in study, types of conditions) are nowhere stated. Why is Dixon study included?	We discuss the BMI range under Study Inclusion in the Methods section: We expect the risk of weight to be similar for a person with a BMI of 29.5 kg/m ² and a person with a BMI of 31.5 kg/m ² , yet our key questions deal with the latter and not the former. Indeed, the published literature does not always conform to the same threshold specified in the key questions. We judged that studies that included substantial number of patients within the threshold of our key questions, but perhaps also some outside the range, were still informative, and were included. Thus, if a study included patients with a BMI of 29 kg/m ² - 37 kg/m ² we judged that it would be more informative to the key questions to include rather than exclude it. Similar decisions were made about the presence of impaired glucose tolerance and the clinical diagnosis of diabetes.
Peer Reviewer 5	Methods	There are no statistical methods - e.g. how was absolute change calculated, e.g. 3.1 for gastric bypass from 5 studies on pages 23-25	We have clarified in the text. For each study that provided sufficient information, we calculated the mean change from baseline to followup, where a negative mean change indicates a decrease in outcome measure (e.g. BMI). We used these estimates to calculate a weighted mean change within surgery type and outcome.
Peer Reviewer 5	Methods	Need to head Weight change % with (SD)	We have added.
Peer Reviewer 5	Methods	It looks like individual drug and lifestyle studies were only discussed in detail if they were not covered by systematic reviews - this needs to be made clear in the methods	This is correct. We have revised in the methods section.
Peer Reviewer 5	Methods	23 line 4 Do you mean table 6 for the right?	Yes, we have corrected.
Peer Reviewer 6	Methods	Inclusion and exclusion criteria are justifiable. I agree with the decision to include studies that predominantly include patients with a BMI in the eligible range. The outcomes of interest are relevant. Methods appropriate for analysis.	None needed
Peer Reviewer 7	Methods	Appropriate	None needed
TEP 1	Methods	Please note the ethnicity issue again. Data for Korea (Lee) and India (Shah) seem to provide better results and this may be related to greater fattness and weight related disease risk. This could be compared with the poorer results when compared with BMI > 35 in italians	We have added more discussion of the ethnicity issue.

Commentator & Affiliation	Section	Comment	Response
TEP 2	Methods	The methods for inclusion and exclusion criteria are clearly defined. Some may feel the inclusion of case series is less strict than a systematic review might be, but under the circumstances the methods are appropriate. As the authors note, there are insufficient RCT's on which to base conclusions.	None needed
TEP 2	Methods	The results section is excellent. It is challenging to describe the results of the studies given the variable quality of the studies and related findings. This reviewer is not aware of any studies that were excluded that should have been included. The limitations of the included studies are well-described and defined.	None needed
TEP 3	Methods	remove 'dissecting'	Correction made.
TEP 4	Methods	Complications of nonsurgical complications should be reported as well including readmissions and need for additional medications	Unclear comment. Do you mean "nonsurgical interventions"? If so, we discuss adverse events associated with medications.
Peer Reviewer 1	Results	Yes this is appropriate. The results are written concisely and tables are provided with the specific data	None needed
Peer Reviewer 2	Results	p. 16, Table 2: are the outcomes listed in the footnote of this table (i.e., BMI, HbA1c, and glucose) the outcomes for rated KQ1 rated finding statements?	Again, the SOE for efficacy refers to "treating diabetes" as a whole, taking into consideration ALL related outcomes.
Peer Reviewer 2	Results	p. 17: With respect to following statement, was the difference between the 2 groups significant? Fasting blood glucose was lower in the surgical patients at 24 months compared to the medical group.	Yes.
Peer Reviewer 2	Results	p . 17, line 50: please define conventional therapy for this study	We added that conventional therapy focused on weight loss via lifestyle change. Each patient had at least one visit every six weeks with a member of a team including an MD, nurse, dietician and health educator.
Peer Reviewer 2	Results	p. 17, 3rd paragraph, 2nd sentence: consider restating this sentence so that it mirrors the statement about Dixon et al. study and the presentation of information in Table 3.	The paragraphs describing the O'Brien and Dixon studies have parallel structure; they differ somewhat because they report different outcome measures. The language was reviewed by a professional editor.
Peer Reviewer 2	Results	p. 17, line 51: the fasting blood glucose values (105.2 versus 139.6) are not included in the fasting blood glucose entry for Table 3 and don't seem to derive from the values included in Table 2	We have updated our analyses to include new studies identified during the review period, so this comment is no longer relevant.
Peer Reviewer 2	Results	p. 17-18: Why is the Chiellini study not included in Table 3? Was this factored into evidence rating? If it was not considered, please state that. If it was considered, please include in Table 3	Table 3 displays data for the RCTs that compare bariatric surgery with non surgical interventions. The Chiellini study is a small cohort study, not an RCT. Chiellini is now described in the results section on small cohort studies. All included studies, regardless of design, were taken into consideration in determining the strength of evidence.

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Peer Reviewer 2	Results	bottom paragraph/Table 3: p-values for Dixon, et al. study inconsistent in text vs. table (.0001 vs. .001).	Thanks for catching. We have corrected to .001.
Peer Reviewer 2	Results	p. 17, bottom paragraph: States that fasting blood glucose significantly lower in surgery patients vs. medical group but gives no p value or other indication of significance.	Significance is indicated by the 95% confidence intervals, which are presented in the same sentence. In addition, the table displays the p value of .002.
Peer Reviewer 2	Results	p. 19, Table 3: O'Brien: <ul style="list-style-type: none"> • Weight Change: include the table figures in the narrative or put % in table. • Why are DBP, lipid levels and QOL not included in Table 3 for O'Brien study? 	The table includes the variables considered most important to our stakeholders per our topic refinement discussions, i.e. diabetes outcomes such as fasting glucose, HbA1c, remission / resolution, and weight loss. These choices were made prior to data collection. Blood pressure, cholesterol, and QOL from the O'Brien study are discussed in the accompanying text.
Peer Reviewer 2	Results	p. 19, Table 3: would be useful to have baseline BMI for each study included in table	We have added this to the table.
Peer Reviewer 2	Results	p. 20, 1st paragraph: <ul style="list-style-type: none"> • Diabetes type 2 outcomes, sleeve gastrectomy group– discrepancy: In text, P=0.001; in Table 4, P=0.02. • Data not included in Table 4: HbA1c decreased by 4.2 percentage points in the gastric bypass versus 3.0 percentage points in the SG patients (P<0.05). 	P = 0.02 is correct, we have made this change.
Peer Reviewer 2	Results	p. 20, 2nd paragraph, discrepancy: <ul style="list-style-type: none"> • “At 24 months postoperative, both groups achieved weight loss: 22.7 kg/m2 (II-DSG) versus 22.2 kg/m2 (II-SG)...” • In Table 4, II-SG weight loss is listed as 22.1. 	Per feedback on the draft report from our Technical Expert Panel, we have removed these studies from our analyses, as they used an experimental procedure (ileal interposition).
Peer Reviewer 2	Results	p. 20, 2nd paragraph – discrepancy between text and table 4: II-DSG had statistically significantly greater....and mean fasting blood glucose (99.06 +/- 20.87 versus 114.6 +/- 34.5; P=0.008).	This study has been removed, as it used an experimental procedure.
Peer Reviewer 2	Results	p. 23, 1st paragraph: Should this read Table 5 and 6? Or are tables 5 and 6 labeled incorrectly?	Should read Table 5 and 6. We have corrected.
Peer Reviewer 2	Results	p. 23, Medication Needs: Why was it decided to include data for LAGB patients discontinuing medication at 0-3 months in the table, but not the 3-6 month or 6-12 month data? [study 26]	We have revisited our decisions regarding which time points to use and revised our tables accordingly.
Peer Reviewer 2	Results	p. 23, BMI, 2nd paragraph: The intervention (sleeve gastrectomy) for the following statement is not indicated: Postoperative BMI was much lower than the earlier one year followup (22.7 kg/m2)	We have revised this section with our updated results; this sentence has been removed.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 2	Results	p. 23, blood glucose: for improvements in HbA1c values seen in studies that measured out to one year or more, either give baseline or report the change in value instead of just giving final value. Studies that measured out to one year or more reported continued improvement in HbA1c values. They decreased to postoperative values of 5.8 percent for BPD to 6.3 percent for gastric sleeve.	We have revised this section with our updated results; this sentence has been removed.
Peer Reviewer 2	Results	p. 23, blood glucose: consider moving the following statement to an earlier position in the paragraph to let the reader know at the outset that LAGB is not included in the finding statements. There were no LABG studies that reported HbA1c data.	This report has already been edited by a professional editor, and we prefer to leave it as it stands now.
Peer Reviewer 2	Results	p. 23, blood glucose: Please make it clear whether LAGB is included in the findings referenced in the passage that begins “Studies that reported data on plasma glucose also demonstrated significant metabolic improvements, most patients had....” (last 4 sentences of paragraph).	We have revised this section with our updated results; this sentence has been removed.
Peer Reviewer 2	Results	Table 5: • It might aid the reader to include reference numbers. • While I like the way the table is grouped by follow-up, It would be helpful to also have a column with the actual number of months of followup included..	We have added the column you suggested. It is labeled “Followup Range.”
Peer Reviewer 2	Results	p. 30, last paragraph: some readers might interpret the following passage as exercise, diet, lifestyle, etc. better than surgical. Is that what is meant? Evidence has shown that exercise, diet, lifestyle, and behavioral interventions are associated with significant weight loss and better blood sugar outcomes (e.g., decreasing HbA1c or fasting glucose) among adult patients with pre-existing type 2 diabetes	We did not mean to imply that non-surgical interventions lead to “better” blood sugar outcomes than bariatric surgery. We have replaced “better” with “improved.”
Peer Reviewer 2	Results	p. 32-33, systematic reviews on diabetes medications section: it might improve readability and ease burden on reader to include a summary paragraph at the end of this section	We have inserted a summary paragraph, as suggested.
Peer Reviewer 2	Results	p. 34, short term outcomes: with respect to the following statement, “While both behavioral interventions and various medications have been shown to lower HbA1c levels significantly, the decreases reported in bariatric surgery patients at one year are greater,” please clarify whether this is a conclusion that should be given a SOE rating and if yes, please provide SOE	We give SOE for the “body” of evidence for each key question; rather than for each health outcome. The SOE refers to evidence as to whether the surgery is effective in “treating diabetes” as a whole, taking all outcomes into consideration, including blood sugar, cholesterol, blood pressure, weight etc.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 2	Results	p. 36, short term outcomes: please list specific outcome(s) for following statement. In sum, there is moderate strength evidence that bariatric surgery is an effective way to treat diabetes in patients with BMI of at least 30 but less than 35 in the short term	Again, we give SOE for the “body” of evidence for each key question; rather than for each health outcome. The SOE refers to evidence as to whether the surgery is effective in “treating diabetes” as a whole, taking all outcomes into consideration, including blood sugar, cholesterol, blood pressure, weight etc.
Peer Reviewer 2	Results	p. 36, Short term outcomes: With respect to the following statement: “And with the exception of exenatide, diabetes medications do not cause significant weight loss,” please state the SOE for the following intervention/outcome pairs or explain why the statements are not rated: <ul style="list-style-type: none"> • Exenatide / weight loss. • Other diabetes medications (presumably as a group) / weight loss 	Please see above.
Peer Reviewer 2	Results	p. 36: It is not clear if the moderate strength of evidence refers to the outcomes listed in the subsequent statements, e.g., : At one year, surgery patients have shown significantly greater weight loss than can be expected from diet, exercise, or other behavioral interventions	Please see above.
Peer Reviewer 2	Results	p. 15, 2nd paragraph, 1st sentence – typo (delete comma after patients?), “is that the patients, contributing data at...”	
Peer Reviewer 2	Results	p. 20, 1st paragraph – typo, “Diabetes type 2 remission defined as fasting plasma glucose levels...” (should the word is be inserted b/w remission and defined?).	We have added "was" before "defined"
Peer Reviewer 2	Results	p. 21, Table 4: <ul style="list-style-type: none"> • superscript next to DePaula (40) is running into next line. • 2nd column: II-DSGI (should that read II-DSG). • Use of comma b/w value and standard deviation is not consistent. 	We have corrected these typos.
Peer Reviewer 2	Results	p. 23, 1st paragraph: it might aid the reader to spell out IGT	We have spelled out Impaired Glucose Tolerance
Peer Reviewer 2	Results	p. 36, short term outcomes: In sum, there is moderate strength evidence that bariatric surgery is an effective way to treat diabetes in patients with BMI of at least 30 but less than 35 in the short term. <ul style="list-style-type: none"> • The word “of” missing from sentence above. • Missing units. 	We have added "kg/m ² " for BMI units
Peer Reviewer 2	Results	p. 38, Table 9: it would be helpful to have the reference numbers included in this table	We don't think this is necessary in a summary table.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 3	Results	fine but I would make one change. This is a very large not easily read paper (it is written well but just alot of info). Less is better I would strongly recommend removing the section on BPD. This is not a recommended surgery (NIH), I agree it is being done but in very small numbers and yet a significant number of cases of malpractice revolve around this surgery. Unfortunately the data collection (as noted by the author) is weak and very little is published about the problems after this procedure	We agree that this report is lengthy; thus, we have submitted a shorter summary as a journal article. In addition, AHRQ has contracted with Baylor University to develop consumer and provider pamphlets. Regarding BPD, the included surgical procedures were selected during a year long topic refinement process. Key stakeholders, including consumers, physicians, and payers wanted BPD included. We are not in a position to remove it now.
Peer Reviewer 4	Results	Results and details seem appropriate. Not aware of additional studies that should have been included. As noted above, noticed a tendency to switch between sleeve, sleeve gastrectomy and gastric sleeve in the language. May consider using one term.	Thank you, we have revised to use consistent language.
Peer Reviewer 4	Results	The inclusion of the last study in the results which fell outside of the parameters of the review was somewhat troublesome to me. Although it clearly demonstrates the need for better long-term data on LAGB, it may bias readers through not detailing some of the additional limitations of the study (surgical band techniques used and less follow-up care typically seen in Europe)	We have moved this study from the results section to the discussion section, where it is more appropriate.
Peer Reviewer 5	Results	Better labelling of some of the tables is required	We have updated the tables for clarity.
Peer Reviewer 5	Results	I am unclear why the Finnish Diabetes Prevention Programme is excluded from detailed discussion, particularly as there are long-term data comparable to DPP	On page 36 we discuss the long term results of the Finnish DPP.
Peer Reviewer 5	Results	The case series of patients with BMI < 30 isn't within the scope of the review	We have removed this study from the report.
Peer Reviewer 5	Results	How is absolute change calculated, e.g. 3.1 for gastric bypass from 5 studies – I can find no stats methods described. Need to clarify if this is fasting glucose.	We have clarified in the text. For each study that provided sufficient information, we calculated the mean change from baseline to followup, where a negative mean change indicates a decrease in outcome measure (e.g. BMI). We used these estimates to calculate a weighted mean change within surgery type and outcome.
Peer Reviewer 5	Results	What is flumamine – not an easily recognised drug name.	A study on “flumamine” (Fang, 2001) was included in a meta-analysis (Gillies, 2007) on drugs to delay or prevent type 2 diabetes in patients with IGT. We were unable to access the original study, which was published in China.
Peer Reviewer 5	Results	Need hbA1c units	HbA1c is measured as percentage of total hemoglobin, as we made clear in the tables and text.
Peer Reviewer 5	Results	Confusing, these two sentences contradict each other	We removed the second sentence. This was an editing error.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 5	Results	Why is UKPDS included in the review but also under excluded studies for BMI > 35 on page 115 and elsewhere in the excluded refs?	The UKPDS publications listed under “excluded for BMI >35” should have been listed as excluded as “duplicate publications” reporting the same study data. We have made this correction.
Peer Reviewer 5	Results	Insert ‘at’ the instead of ‘that’	Correction made.
Peer Reviewer 5	Results	‘upgraded’ instead of ‘upgrade’	Correction made.
Peer Reviewer 6	Results	Studies clearly described and key messages are solid I would describe the strength of the evidence for KQ3 as low instead of moderate because the definitions of the complications are inconsistently applied across studies and there is likely to be reporting bias given that rigorous methods for capturing complications were not often reported	We updated the adverse events analysis with eight new studies identified during the review period. We also removed several South American studies of ileal interposition, as this procedure is consider experimental. The new results lead to a strength of evidence of low for KQ3.
TEP 1	Results	The statements remission or resolution and meaningless without definition. Lipids change with time after surgery HDL initially falls and then risen. Cholesterol is not reduced in relation to weight loss but related to the type of procedure. Obesity related change in lipids are HDL-C and triglycerides not total cholesterol of LDL-C	We have added definitions of remission or resolution to the text where they were provided in the studies. However, not all studies provided definitions. We agree that such outcomes are not as useful as outcomes that have a precise definition, and so state in the report. We agree with you regarding cholesterol and triglycerides outcomes; we have rewritten this section. Still, we can only discuss the outcomes that the studies provide. We acknowledge that there may be reporting bias as to what measures authors selected to publish.
TEP 1	Results	The systematic review and subsequent reports from the non-surgical outcomes cross BMI limits of 30-35. As there are no long term data on surgery in this BMI range but clear data on bigger folk from the SOS study then it seems misleading to not these longer term findings in the context of diabetes prevention, treatment and hard endpoints. Yes they may not extrapolate down to BMI 30 - 35 but the audience need to know of their existence	We agree. We mention the positive results in higher BMI patients in the Introduction and Discussion sections.
TEP 1	Results	There is an Australian cohort study mentioned in the discussion. I think this is the one that extracted data for the US BOLD database - a retrospective study	We could not find any reference to an Australian cohort study in the Discussion section. We do discuss the U.S. BOLD study and two Australian RCTs in the Discussion section. In the results section, we also discuss a cohort of Australian patients.
TEP 2	Results	Page 17, line 17: The O'Brien RCT is a laparoscopic adjustable gastric banding study, not bypass.	We have corrected.

Commentator & Affiliation	Section	Comment	Response
TEP 2	Results	As noted above, the ileal transposition procedure gets quite a bit of coverage in this report, suggesting that it is a standard or clinically available procedure in current bariatric surgical practice. This is clearly not the case, as the combination of a relatively high operative complication rate and questionable efficacy indicates that this procedure is presently investigational at best.	We have removed ileal interposition from our analyses. We have clarified in the text that this procedure is experimental.
TEP 2	Results	The wording describing post-operative weight loss is not precise. Patients who have a higher preoperative weight in general lose more weight (measured in kg) but experience a lower percent of either total or excess body weight lost. This difference is exaggerated among low BMI patients as relatively modest weight loss yields a considerably higher percent weight loss figure than is seen for the higher BMI groups	We use change in BMI and percent of either total or excess body weight lost whenever data was provided. Unfortunately, some studies only reported total weight change in kg.
TEP 3	Results	change 'gastric bypass' to 'intestinal bypass'	Not found. Page 26 is a table that does not include the word "bypass"
TEP 3	Results	change 'weighted' to 'weighed'	Correction made.
TEP 3	Results	add 'behavioral changes' or 'behavioral modifications'. This is the most important thing, if not the only thing, that patients learn from support groups, rather than diet and exercise	Change made. However, one could argue that changing diet and increasing exercise are types of behavior modification.
TEP 4	Results	Would be consistent about reporting weight loss eg medical weight loss is reported as absolute kg lost while surgical weight loss is reported as bmi change which makes it appear equivalent- would suggest using total body weight loss for better comparison	We agree, however, we can only use what was reported in the original studies. Outcomes reported include percent excess weight loss, mean weight loss in kg or pounds, changes in BMI, etc. We tried to be as consistent as we could. Thus, in summary tables A and 9, we convert decrease in BMI to weight loss in kg for a patient 5 foot 6 inches tall. We hope this example gives the reader a way to compare results across intervention types.
Peer Reviewer 1	Discussion /Conclusion	It is clear that weight loss is greater and more sustainable with all types of surgery than lifestyle. While longer metabolic outcomes are needed, most people would be surprised if there were not an advantage to surgery. However, opening bariatric surgery to those with BMIs between 30-35 would potentially impact a lot of people. The part I don't see here relates to the impact of surgery on long-term quality of life. It is clear that the physiological adverse events are minimal but how about quality of life. Before recommending bariatric surgery to this large group of people I believe we need much more of this type of information. It was not addressed in the paper	We agree. One RCT that reported post-surgery quality of life in the short term; no long term surgery studies reported this outcome. We have added this as an area where more research is needed.

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Peer Reviewer 3	Discussion /Conclusion	looks good to me but again would recommend removing the parts about BPD or just stick with what you have said about not having enough data to make any good descisions on BPD	The included procedures were selected during a year long "topic refinement" period which included group discussions with key stakeholders including consumers, health care providers, payer representatives, and policy makers from around North America. Many stakeholders were interested in BPD; thus, we report the small amount of information we found.
Peer Reviewer 5	Discussion /Conclusion	These are OK, but even more emphasis needs to be placed on longer-term outcomes. It is even more likely that people who are not particularly obese before surgery will eventually have lower BMIs than those people who are far more obese before surgery. Thus people with a BMI < 35 could prove to be more at risk of long-term nutritional complications, although possibly at less risk from the surgical procedures themselves	We have added this as future research need.
Peer Reviewer 7	Discussion /Conclusion	The major findings are well described, as well as the limitations in the data. The appropriate literature is concluded, and discussed. Though the general theme of the document is to compare "this to that" in the discussion there should be room to discuss the potential combined effects of surgery and the additive effect of optimal medical management if surgery is less than 100% successful in the short, intermediate and long term. Also there should be mention of the potential benefits of "postponing" if not "curing" metabolic diseases. Presently, there is no specific reason to doubt that for example glycemic control achieved through medical or surgical means leads to differing outcomes based specifically on that parameter. The medical literature does supply this evidence in the long term, as well as the natural history of the disease process as the individual ages and pathology matures. Long-term data for surgery is needed to validate this, but should not override common sense as we develop our data and treatment options.	We have made this point in the discussion.
TEP 2	Discussion /Conclusion	This reviewer believes the discussion and conclusion are excellent as written	None needed
TEP 4	Discussion /Conclusion	Yes- clear and complete	None needed
Peer Reviewer 2	Summary and Discussion	p. 46, typo: ...or peripheral arterial disease., Importantly	We removed the comma
Novo Nordisk Inc.	Conclusion	The Conclusion Should More Robustly Acknowledge the Safety and Effectiveness of Non-Surgical Therapies.	We have stated this as accurately as we feel possible.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 2	Future Research	p. 48, 3rd paragraph: It is not clear to what specific outcomes this passage is referring or for what (if any) comparator. Taking into consideration the entire body of evidence, we rate the strength of evidence as moderate for RYGB, LABG, and sleeve gastrectomy for treatment of diabetes and metabolic conditions in patients with a BMI of between 30 kg/m ² and 35 kg/m ² , in the short term (up to 2 years)	The outcome is "treatment of diabetes" at up to two years. SOE for sleeve gastrectomy was reduced to low in the final version, as several studies using sleeve with experimental procedures were removed.
Peer Reviewer 2	Future Research	p. 48, adverse events: please specify the SOE for long term adverse events (insufficient?). Please specify the SOE for short-term adverse events (moderate). Would aid the reader to specify long term vs. short term time frames.	SOE is insufficient for long term, low for short term adverse events.
Peer Reviewer 2	Future Research	p. 49, 1st paragraph, future research: should the following passage be in the conclusions section? There is insufficient evidence that bariatric surgery is effective in preventing the clinical consequences of diabetes-microvascular and macrovascular endpoints such as diabetic retinopathy, kidney failure, and myocardial infarction	We have already included this sentence. We don't see a problem stating this in the future research section as well, as it refers to an evidence gap.
Peer Reviewer 2	Future Research	p. 49, last paragraph, typo – comma at end of first sentence	We removed the comma
Peer Reviewer 7	Future Research	There should be more emphasis on the merging of the required data elements to satisfy the needs of the various stakeholders in these diseases. Much of the paucity of metabolic data in the surgical literature is due the fact that surgeons rather than endocrinologists or internists designed the surgical weight loss studies. As we move to "metabolic" rather than "weight loss" as our primary objective, new ways of presenting the outcome data need to be developed and standardized so that long-term data initiated now will be useful in 10 years. Bold, the LABS consortium and other data bases which have been implemented should help to support the need for long term robust outcome data for surgery. Planning to include nontraditional data sets(such as low BMI patients) need to be encouraged rather tahn discouraged in order to collect the long term data needed to make valid evidence based assessments for treatment in these populations as therapeutic surgical options develop.	We agree and mention this in our Future Research section.
TEP 1	Future Research	The second last paragraph in future research seem out of place	We feel that the BOLD (Bariatric Outcomes Longitudinal Database) provides an excellent source of data on American bariatric surgery patients with diabetes of IGT in our BMI range. Suggesting analysis and publication of such data does not to us seem out of place in this section.

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Commentator & Affiliation	Section	Comment	Response
American College of Surgeons	Future Research	<p>When we examine the emerging scientific literature on the subject, there are a modest number of randomized trials currently underway examining the impact of the Roux-en-Y gastric bypass or other bariatric surgical procedures versus best medical management in the treatment of T2DM in the BMI 30-35 population.</p> <p>However, as your report suggests, these trials are difficult and the issue of randomization to surgical procedures represents a significant hurdle. Most potential subjects have a strong preference for specific surgical procedures, making trial design and accrual a challenge. Most importantly, the biggest hurdle in conducting such work is obtaining funding for the clinical care of subjects who undergo bariatric surgery in this BMI range, which falls outside of the range for which insurers consider bariatric surgery an allowable benefit. Most trial budgets do not allow for this level of financing, and as such this has contributed directly to difficulties in doing such work. Finally, although the NIDDK has funded several such pilot and feasibility trials to date, the periods of funding for these grants have not allowed for obtaining the long-term follow-up called for in your report. All of these factors, to date, prevent the conducting of a clinical trial that can produce strong evidence to support the effectiveness and safety of bariatric surgery in this population.</p>	We emphasize these concerns in our Future Research Section.
American Dietetic Association	Future Research	<p>ADA believes the long-term benefits, cost-effectiveness, and risks of bariatric surgery in individuals with type 2 diabetes should be studied in well-designed controlled trials with optimal medical and lifestyle therapy as the comparator. Similarly, ADA advocates for more long term research studies on the person with diabetes five or ten years post-bariatric surgery (e.g. are the blood sugars or A1C still in good control).</p>	We emphasize the need for long-term studies in our future research section.
American Society for Metabolic & Bariatric Surgery	Future Research	<p>The ASMBS agrees that further research is needed to demonstrate the positive longterm effects of bariatric surgery on the clinical endpoints of micro and macrovascular disease and mortality in the BMI 30-34.9 group. However the high rates of improvement in metabolic syndrome demonstrated after surgery in the lower BMI group suggests that this patient population will experience similar improvements in vascular disease and mortality to those well documented in the higher BMI group.</p>	No response needed.
Novo Nordisk Inc.	Structured Abstract	<p>The Review's Structured Abstract Should Further Highlight the Risks of Bariatric Surgery and the Limitations of Gathering Applicable Data.</p>	We have done this as well as possible, given the limited word count and format requirements.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 5	Appendix	DPP is not excluded	The DPP (Diabetes Prevention Program) is included in our results; however, some publications from DPP were excluded. Separate journal articles from the same study are excluded as “duplicates” if they report the same data.
Peer Reviewer 1	Clarity and Usability	The physiological impact is clear but not the psychological impact	Unfortunately, no included studies reported these outcomes.
Peer Reviewer 4	Clarity and Usability	Excellent report. Content will be very useful to consumers who are considering such procedures	None needed
Peer Reviewer 5	Clarity and Usability	The limited detail on inclusion criteria and confusing detail on study inclusion are not helpful to the user	We have added detail on inclusion criteria.
Peer Reviewer 6	Clarity and Usability	Overall, this is an excellent report. Well written, thorough, and clearly presented.	None needed
Peer Reviewer 7	Clarity and Usability	The report is well structured and usable to define policy and future research.	None needed
TEP 1	Clarity / Usability	The main points/findings are at no point put in a text box and each summarized in 1-2 sentences. I think this is needed in both the executive summary and in the summary	We appreciate your feedback. We are required to use a specific template per AHRQ. The template is continually being refined and updated; we will pass along your suggestion.
TEP 2	Clarity / Usability	The conclusions can and presumably will be used to inform policy whereby access of patients with BMI 30-34.9 with diabetes or other metabolic conditions to bariatric/metabolic surgery will continue to be limited. This will continue to result in a lack of U.S. trials as research funds are inadequate to fund the cost of the surgery itself. This creates an unfortunate but apparently unavoidable “catch 22” wherein the research necessary to address the deficiencies in present literature, particularly in the U.S., cannot be done.	This comment is directed more towards funding agencies than to the authors of this report and we are not so sure that this report will perpetrate this catch-22. We clearly state the need for comparative long-term studies.
TEP 4	Clarity / Usability	Yes- clear and complete	None needed
Peer Reviewer 1	General	The main conclusions are appropriate and not unexpected. I believe most people in the field realize that all of the bariatric surgery procedures produce better and more sustainable weight loss than lifestyle. It would be surprising if this were not the case in those with BMI 30-35. However, it is difficult to do randomized trials of surgery and the report concludes it would be nice to have more physiological outcomes after surgery over the long term. The biggest missing piece is the impact on overall quality of life (QOL).	We concur. Unfortunately, very few studies reported quality of life outcomes. One RCT of LAGB versus nonsurgical treatment measured QOL using the SF-36; we note those results in the text.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 2	General	Throughout report: Would be helpful to have intervention/outcome pairs listed with strength of evidence.	In some instances, the outcomes and the timing that went into the consideration of the SOE are discussed in the remainder of the paragraph. In other instances, we listed the outcomes that provided the main evidence for the SOE for the conclusion.
Peer Reviewer 3	General	yes, very well defined and meaningful key question appropriate and explicitly stated	None needed
Peer Reviewer 4	General	Well written report. From my consumer perspective, believes it meets all the questions appropriately	None needed
Peer Reviewer 5	General	I found this confusing as the target population was not explicitly defined - what is meant by metabolic conditions? Appears to be diabetes and prediabetes (but then on page 109 studies are excluded because they are not diabetes, so presumably prediabetes excluded)? I would consider fatty liver disease, metabolic syndrome, etc. conditions that would fall under 'metabolic conditions'.	The target population has BMI of at least 30 but less than 35 and the metabolic conditions of diabetes or impaired glucose tolerance (IGT). We have clarified in the text and on the list of excluded studies.
Peer Reviewer 6	General	The report is timely and important. The objectives are clearly stated and clinically relevant.	None needed
Peer Reviewer 7	General	This report summarizes the available data on one of the more important present and future health issues confronting modern society. Our present guidelines for bariatric surgery are almost 20 years old and reassessing indications and objectives through available evidence is an important topic. All key questions are appropriately addressed. Gaps and limitations are present due to data limitations. As we move forward in treating these patients with the disease of obesity and its associated comorbidities is is going to be important to effect a paradigm change in thinking of these operations as treating metabolic derangement rather than treating excesses of weight. This change will help clarify the design of the research and the perception of successful outcomes.	None needed
TEP 1	General	There is an important distinction between conventional well established surgery and some novel anti-diabetes procedures. RYGB, LAGB, BPD and now SG would be considered conventional and established. The others not. The DePaula procedures are very novel and certainly not accepted conventionally. They should not be classified as sleeve gastrectomy	We have removed the ileal interposition studies (i.e. DePaula) from our analyses as this procedure is indeed experimental.

Commentator & Affiliation	Section	Comment	Response
TEP 1	General	When talking about this BMI range, ethnicity needs to be discussed very early on. Risk of metabolic disease, degree of fatness and distribution of fat vary. One cannot really discuss this BMI range without this enormous consideration. BMI cut points for action were designed for whites.	This issue is discussed in the applicability section.
TEP 1	General	The cessation of medications for a condition is no indication that the cessation is appropriate. Assumptions that disease is cured leads to stopping diabetes, blood pressure and lipid altering therapy without it necessarily being clinically relevant	We agree. The vast majority of the studies that reported medication cessation regularly measured and reported corresponding data on serum glucose, HbA1c, blood pressure, cholesterol, etc. However, there were two studies (Sultan, 2009; Parikh, 2006) that did not. We now note this in the text.
TEP 1	General	There is the same approach to nCPAP for treating OSA rarely is a diagnostic test performed to confirm cessation appropriate	We don't understand this comment.
TEP 1	General	With weight loss lipid changes are poorly understood and the review should note the very unusual rise in triglycerides after BPD - Scopinaro	We have added mention of this finding.
TEP 1	General	I would have ignored any studies that did not provide biochemical evidence of change in diabetes of lipids and ignored blood pressure statements unless accompanied by actual measures	If you are referring to the studies reporting on diabetes resolution or medication cessation, the vast majority regularly measured and reported corresponding data on serum glucose, HbA1c, blood pressure, cholesterol, etc. However, as we note above, there were two studies (Sultan, 2009; Parikh, 2006) that did not. We now note this in the text. Due to the dearth of studies in the target population, we did not exclude these studies, but instead take their limitations into consideration in our conclusions.
TEP 2	General	Given the prevalence of BMI 30-34.9 with diabetes and the potential for bariatric surgery to impact this combination of conditions, the report is clinically meaningful. The target population and audience for the report may not be explicitly defined but this is not a problem, as the report is pertinent to all involved in healthcare planning and decision making. The key questions are appropriate.	None needed

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Commentator & Affiliation	Section	Comment	Response
TEP 3	General	<p>There are 2 major issues with the manuscript.</p> <p>1. The definition of sleeve gastrectomy as defined on page 22 in the Glossary is incorrect. Sleeve gastrectomy refers purely to the "surgical weight-loss procedure in which the stomach is reduced to about 15% of its original size by surgical removal of a large portion of the stomach". It does not involve any intestinal manipulation nor any variations as the present definition on page 22 states. Any variation which includes intestinal bypass is a completely separate, and more importantly experimental operation, which is not recognized by either the ASMBS nor the Surgical Review Corporation (which certifies Center of Excellence status). The authors have included 8 references which discuss ileal interposition (2 variations) in conjunction with sleeve gastrectomy, specifically 7 DePaula references (34-40) and 1 by Kumar (41). The ileal interposition operation, either with sleeve gastrectomy or diverted sleeve gastrectomy, is an operation of its own and once again, is entirely experimental. It is not the sleeve gastrectomy portion that is represented and reflected in the outcomes, but rather the intestinal manipulation. Therefore the outcomes that the authors present in this manuscript for sleeve gastrectomy are inaccurate because they include ileal interposition outcomes data rather than just pure sleeve gastrectomy data. This affects both reported weight loss and health outcomes, as well as complication/side-effect outcomes. Since the health outcomes are very impressive for ileal interposition, it is important to include in the manuscript; however it is imperative that the authors not only separate this group of operations as completely different operation from the LAGB/RYGB/sleeve/BPD, but also state that these are experimental operations. This change affects several areas of the manuscript including but not limited to paragraphs on page 16, 19,22, 26, 38,42, 46,47,48,49, 64, 70,</p>	<p>We have revised the description of sleeve gastrectomy per your comments. We have removed the ileal interposition studies from our analyses, and stated that it is experimental.</p>

Commentator & Affiliation	Section	Comment	Response
TEP 3	General	<p>2. The authors have clearly stated the inclusion and exclusion criteria for publications included in this analysis. However, they strayed from their initial intent and method by including one published paper by Himpens (page 67) which shows 12 year outcomes of 82 (out of initial 151 patients) gastric banding (LAGB) European patients with initial BMI > 35, which had unusually high complication rates and abnormal outcomes as compared to a multitude of similar cohort patients. The authors recognize the possible non-applicability of studies performed outside of the US, as stated on page 68, line 55, but fail to make this statement on page 67 after summarizing the Himpens paper. If the authors are interested in long-term outcomes of bariatric surgery on all cohorts which do not fit into the inclusion criteria of this manuscript, then it is only fair and unbiased, to include all the other scientific papers that have similar profiles, for example Vertruyen et al (page 143, line 3) and Carelli et al (Safety of the laparoscopic adjustable gastric band: 7-year data from a U.S. center of excellence. Carelli AM, Youn HA, Kurian MS, Ren CJ, Fielding GA. Surg Endosc. 2010 Aug;24(8):1819-23. Epub 2010 Feb). In addition, the authors included non-scientifically published 'information' that was printed in the Los Angeles Times which was not scientifically validated (page 69, line 13-20). Although concerning, scientists should understand the paparazzi nature and financial motivation of journalism, and consider removing this from what is a scientifically rigorous analysis. If the authors are interested in media reports of outcomes of bariatric surgery and non-surgical therapy in adults with metabolic conditions and BMI 30-34.9, then an entire search and analysis of all media reporting must be performed and included into this manuscript.</p>	<p>We mention the Himpens cohort because this is the longest followup we identified. This is stated in the text. Vertruyen and Carelli do not have this length of followup. The media reports are mentioned in the "discussion" section, as an example of the often heard concern that published studies from academic medical centers of any procedure may themselves be a biased sample of patients and surgeons compared to results obtained in community practices. We do not include this type of information in our analyses.</p>
TEP 4	General	<p>Excellent over-view: inclusion and exclusion criteria are appropriate- no missing articles. Well written and clinically relevant</p>	<p>None needed</p>

Commentator & Affiliation	Section	Comment	Response
American College of Surgeons	General	The American College of Surgeons Bariatric Surgery Center Network would like to congratulate the AHRQ for their initiative, diligence and timeliness in addressing this topic. It is appropriate that the indication for bariatric surgery be re-evaluated given the strong prevalence of type 2 diabetes (T2DM) in the BMI of 30 to 35kg/m ² group and the observational evidence to date suggesting the effectiveness of these procedures in treating T2DM in patients with BMI over 35 kg/m ² . It is important to recognize that the NIH Consensus Development Statement in 1991 assessed benefit and risk for severely obese patients in an era when perioperative management and operative approaches were markedly different than what is practiced commonly today.	None needed.
American College of Surgeons	General	The AHRQ has compiled an exhaustive review of the existing literature evaluating the comparative effectiveness of bariatric surgical interventions in patients with a lower BMI than those addressed by the 1991 Consensus Statement. In short, 28 publications were identified. The conclusions were that bariatric surgery in patients with a BMI in the 30-35kg/m ² range has a moderate level of evidence indicating effectiveness and safety and that long-term studies of bariatric surgery in this patient population are needed to assess the overall safety and effectiveness compared to non-surgical interventions.	None needed.
American College of Surgeons	General	With regard to endpoints, the major focus of diabetes treatment in this analysis was glycosylated hemoglobin. We would call attention to the standing recommendation from the American Diabetes Association in using several therapeutic endpoints to determine success in the management of diabetes (i.e. HbA1c <7%, LDL <100 mg/dl, SBP <130 mmHg). Achieving these individual targets as a composite endpoint is an important basis of community wide comparisons of success in the surgical or medical treatment of diabetes. As such we would point out a potentially relevant set of manuscripts [References: Leslie et al Obesity Surgery 2011, Serrot et al. Surgery 2011]. Remission or resolution of diabetes (HbA1c <5.7-6.4) is somewhat of arbitrary target.	We agree that cholesterol and blood pressure outcomes are extremely important in evaluating efficacy of diabetes treatment. We report on these outcomes and emphasize in our Discussion section.

Commentator & Affiliation	Section	Comment	Response
American College of Surgeons	General	<p>Further, aggressive medical management targeting HbA1c < 6.0 has been shown to increase mortality. Additionally, microvascular and macrovascular endpoints are meaningful endpoints that would potentially increase the validity and applicability of studies evaluating the impact of medical and surgical treatment of diabetes in the aforementioned population.</p> <p>We, therefore, appreciate your input in order to identify the important endpoints of a long-term clinical study that would produce valid conclusions upon which policy could be based. Since there is an approximately 1% annual mortality associated with diabetes, this study demands adequate funding and our urgent attention. We call on your organization to exert whatever influence necessary to effect federal funding of studies that will address this important topic.</p>	This comment is targeted towards funders, rather than the authors of the report.
American College of Surgeons	General	<p>Finally, let us once again express our appreciation for this timely review and for the opportunity to comment of its findings. Clearly, this is a major national health issue that deserves the attention of multiple medical and surgical specialties in order to achieve the desired improvement in the health of our patients. It is our sincere hope that this review will result in a well-planned, well-funded, and well-conducted clinical trial that can fill the knowledge gap that is obvious in our understanding and treatment of diabetes in the obese population.</p>	None needed
American Dietetic Association	General	<p>The American Dietetic Association (ADA) appreciates the opportunity to submit comments to the Agency for Healthcare Research and Quality (AHRQ) at the United States Department of Health and Human Services (HHS) related to key questions of the research topic “Comparative Effectiveness of Bariatric Surgery and Nonsurgical Therapy in Adults With Metabolic Conditions and a Body Mass Index of 30.0 to 34.9 kg/m².” With over 72,000 members, ADA is the largest association of food and nutrition professionals in the United States and is committed to improving the nation’s health through food and nutrition. ADA supports the conclusions reached by the AHRQ based on the current evidence and acknowledges the limitations in the bariatric literature regarding this patient population.</p>	None needed

Commentator & Affiliation	Section	Comment	Response
American Dietetic Association	General	ADA associates itself with comments from the American Society for Metabolic & Bariatric Surgery and the Obesity Action Coalition. Like the ASMBS, ADA “recognizes Class 1 obesity as disease that deserves treatment. The morbidity and mortality risks of obesity have been subject to multiple systematic reviews and from these data we conclude that Class 1 obesity is a disease that leads to additional serious co-morbidities and a shortened life expectancy. The current AHRQ review summarizes well the data supporting the short-term benefits of bariatric surgery for metabolic disease in Class I obese patients. These data are supported and reinforced by a large body of literature in higher BMI populations. Therefore, in selected patients with inadequately controlled diabetes or other metabolic conditions and a BMI of 30.0 – 34.9 kg/m ² , the benefits of bariatric surgery likely outweigh the risks.”	None needed
American Dietetic Association	General	Comprehensive nutrition assessments are paramount during the pre-surgical screening to evaluate weight history, efforts to lose weight, food preferences and food-related behaviors (i.e., binge eating) to assist in electing the optimal procedure for the beneficiary.	We agree. We have mentioned this in the Introduction in the section describing the bariatric surgery procedures.
American Dietetic Association	General	The beneficiary must be motivated to make lifestyle changes needed to decrease postoperative complications and maintain weight loss. Weight loss surgery is most effective when accompanied by pre-and postoperative comprehensive therapy to alter behaviors such as eating, smoking and exercise. In addition, post-surgery and long-term, intensive behavioral counseling for obesity with regards to nutrition is vital in promoting lasting behavioral changes in dietary and supplementary requirements. This therapy augments the probability of long-term success and is a standard component of surgical weight management. ¹ Of note, all procedures require lifelong medical follow-up and monitoring to avoid and manage possible complications leading to more severe damage to the beneficiary’s health. In particular, patients with type 2 diabetes who have undergone bariatric surgery need life-long lifestyle support and medical monitoring.	We discuss these issues in the results for Key Question 4. The results are based on findings in higher BMI populations. We understand that long-term counseling and medical monitoring are important to good results. However, there is little published on this particular target population (lower BMI).
American Society for Metabolic & Bariatric Surgery	General	The ASMBS supports the conclusions reached by the AHRQ based on the current evidence and acknowledges the limitations in the bariatric literature regarding this patient population.	No response needed.
American Society for Metabolic & Bariatric Surgery	General	The ASMBS believes that Class 1 obesity is a disease that leads to additional serious co-morbidities and a shortened life expectancy. Therefore Class 1 obesity deserves treatment.	No response needed.

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Commentator & Affiliation	Section	Comment	Response
American Society for Metabolic & Bariatric Surgery	General	There is a large body of high quality literature (including several large matched cohort studies and systematic reviews) demonstrating decreased all-cause mortality, decreased cardiovascular mortality, and decreased diabetes-related mortality compared to nonsurgical therapy in the long term. ¹⁵⁻²⁰	In the report, we state this is the case for the higher BMI (>35) population.
American Society for Metabolic & Bariatric Surgery	General	The IDF statement also recommends that diabetic patients with BMI 30-35 kg/m ² be conditionally eligible for bariatric surgery if they have a HbA1c level > 7.5%	We were aware of the IDF statement when developing the report. We have added mention in the Introduction, under "Bariatric Surgery in Lower Weight Patients."
American Society for Metabolic & Bariatric Surgery	General	However, it is becoming widely accepted that there are particular gut hormone changes after both RYGB and SG that specifically impact insulin secretion and improve glycemic control. In fact, the rate of diabetes resolution in the higher BMI diabetic patients after surgery is greater with RYGB and SG than LAGB.	These peptide outcomes were not a focus of this review.
American Society for Metabolic & Bariatric Surgery	General	It has been clearly demonstrated that RYGB and SG result in rapid nutrient transport to the distal bowel. This results in stimulation of L cells in the distal bowel, which then produce incretin peptides such as GLP-1 and satiety peptides such as PYY	These peptide outcomes were not a focus of this review.
American Society for Metabolic & Bariatric Surgery	General	The relative complexity of RYGB and SG compared to LAGB leads to higher short term complication and reoperation rates. LAGB has a low short term complication rate, but does have a risk of long term reoperation for mechanical problems or failed weight loss.	No response needed.
American Society for Metabolic & Bariatric Surgery	General	Review of the clinicaltrials.gov website reveals 8 ongoing trials (including well controlled randomized trials) evaluating the effects of bariatric surgery in diabetic patients with BMI < 35.	We have added mention in Discussion section.
Novo Nordisk Inc.	General	To Achieve a Consistent Methodology, Studies of Non-Surgical Therapies for the Treatment of Diabetes with Less than One Year Follow-up should be Considered	This was considered during the development of our research protocol. Our protocol was posted for public comment for one month, at this point we can not change the methodology.
Novo Nordisk Inc.	General	Long-Term Data on Victoza [®] as Treatment for Type 2 Diabetes is Available and Must be Included for a Comprehensive and Accurate Review	We have added a systematic review on the safety and efficacy of GLP-1R agonists.
Novo Nordisk Inc.	General	The Review Must be Revised to Recognize that Victoza [®] causes Statistically Significant Weight Loss	Our report states that liraglutide is associated with statistically significant weight loss.
Novo Nordisk Inc.	General	GLP-1 Receptor Agonists and DPP-4 Inhibitors Should be Differentiated.	We believe we have made this differentiation in our Introduction and Results sections.
Novo Nordisk Inc.	General	Liraglutide for Obesity Data Should be Included in the Review	We have included in our review. Liraglutide is mentioned in the introduction under Nonsurgical Interventions and data are presented in the Results section, under medications.

Source: <http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1482>

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OAC	General	On behalf of the 33,000 members of the Obesity Action Coalition (OAC), I am pleased to provide comments on the comparative review compiled by the Agency for Healthcare Research and Quality (AHRQ) on the effectiveness of bariatric surgery and medical therapy for metabolic disease in patients with BMI between 30.0 and 34.9 kg/m ² . As the national non-profit organization dedicated to giving a voice to individuals affected by obesity through education, advocacy and support, the OAC applauds AHRQ for examining this issue.	None needed
OAC	General	The OAC supports the conclusions reached by AHRQ based on the current evidence and acknowledges the limitations in the bariatric literature regarding this patient population. We recognize Class 1 obesity as a disease that deserves treatment. The morbidity and mortality risks of obesity have been subject to multiple systematic reviews and from these data we conclude that Class 1 obesity is a disease that leads to additional serious co-morbidities and a shortened life expectancy. The current AHRQ review summarizes well the data supporting the short-term benefits of bariatric surgery for metabolic disease in Class I obese patients. These data are supported and reinforced by a large body of literature in higher BMI populations.	None needed
OAC	General	Therefore, in selected patients with inadequately controlled diabetes or other metabolic conditions and a BMI of 30.0 – 34.9 kg/m ² , the benefits of bariatric surgery likely outweigh the risks. Treating or addressing obesity among those already affected by obesity is difficult. This is clearly demonstrated by the more than 34% of Americans who are currently affected by obesity. However challenging though, efforts must be made to both prevent and treat obesity at all stages and in all age groups. Surprisingly, given the terrible toll obesity takes on our country's public health, we currently have very few clinical options available to treat this condition and reduce its damage. For these reasons, we applaud the agency for examining the benefits associated with bariatric surgery for those in the early stages of obesity. Expanding access to evidence-based obesity treatments is essential if our country is truly going to address the obesity epidemic.	None needed