

Technology Assessment Program

Short and Long Term Outcomes after Bariatric Surgery in the Medicare Population

Draft

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Short and Long Term Outcomes after Bariatric Surgery in the Medicare Population

Prepared for:

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Purpose and Key Messages:

Purpose

- To examine outcomes in Medicare eligible patients undergoing bariatric therapy

Key Messages

Among Medicare eligible patients:

- There are no randomized trials evaluating the effectiveness and safety of bariatric surgical or endoscopic procedures; there are few direct (head-to-head) comparisons between different surgical procedures with sufficient evidence in non-randomized studies but none for endoscopic procedures.
- Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric banding leads to improvements in weight loss and non-weight loss outcomes, particularly mortality, metabolic, cardiovascular, respiratory, and musculoskeletal outcomes, and polypharmacy up to 12 months.
- Roux-en-Y gastric bypass performs better compared to sleeve gastrectomy or adjustable gastric banding for metabolic and cardiovascular outcomes and for post-operative complications; Roux-en-Y gastric bypass may also perform better for weight loss outcomes.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The Centers for Medicare and Medicaid Services requested this report from the Evidence-based Practice Center (EPC) Program at the Agency for Healthcare Research and Quality (AHRQ). AHRQ assigned this report to the following EPC: (To be inserted in final report) Evidence-based Practice Center (Contract Number: HHSA290201500005I).

The reports and assessments provide organizations with comprehensive, evidence-based information on common medical conditions and new health care technologies and strategies. They also identify research gaps in the selected scientific area, identify methodological and scientific weaknesses, suggest research needs, and move the field forward through an unbiased, evidence-based assessment of the available literature. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review and public comment prior to their release as a final report.

AHRQ expects that the EPC evidence reports and technology assessments, when appropriate, will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

If you have comments on this evidence report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov

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This report is based on research conducted by the (name provided in final report) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. HHS A2902015000051). The findings and conclusions in this document are those of the authors who are responsible for its contents. The findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of the Agency for Healthcare Research and Quality or of the U.S. Department of Health and Human Services.

None of the investigators has any affiliations or financial involvement related to the material presented in this report.

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Acknowledgments

To be added to final report

Key Informants

In designing the study questions, the Evidence-based Practice Center (EPC) consulted a panel of Key Informants who represent subject experts and end-users of research. Key Informant input can inform key issues related to the topic of the technical brief. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The Task Order Officer and the EPC work to balance, manage, or mitigate any conflicts of interest.

The list of Key Informants who provided input to this report follows:

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To be added after peer review.

Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential non-financial conflicts may be retained. The Task Order Officer and the EPC work to balance, manage, or mitigate any potential non-financial conflicts of interest identified.

The list of Peer Reviewers will be added to the final report.

Short and Long Term Outcomes after Bariatric Therapies in the Medicare Population

Structured Abstract

Introduction. We conducted a technology assessment to summarize and appraise current evidence regarding the effectiveness and safety of bariatric surgery in the Medicare eligible population.

Data Sources. We searched six bibliographic databases and reference lists of published clinical practice guidelines, relevant narrative and systematic reviews, and Scientific Information Packages from manufacturers or other stakeholders on the outcomes and prediction models of different bariatric procedures studied in the Medicare eligible population.

Results. Of 94 eligible studies, 70 described outcomes after bariatric therapy and 24 described predictors of body weight loss or absolute body weight after bariatric therapy. We did not identify any randomized clinical trials in the Medicare eligible population. Studies examined surgical modalities. There were no studies on endoscopically-performed bariatric procedures. Only 13 studies had a design and/or analytical approach that allowed inferences for causal treatment effects on weight loss outcomes, adverse events/complications, or other non-weight loss outcomes. Bariatric surgery in the Medicare eligible population leads to improvements in weight loss and non-weight loss outcomes, particularly mortality, metabolic, cardiovascular, respiratory, and musculoskeletal outcomes, and polypharmacy but the strength of evidence is low to moderate. There is also low to moderate evidence that Roux-en-Y gastric bypass performs better compared to sleeve gastrectomy or adjustable gastric banding for metabolic and cardiovascular outcomes and for post-operative complications. Finally, no models to predict weight loss have undergone internal or external validation.

Conclusions. Relatively few non-randomized studies examine the effectiveness and safety of bariatric therapies in the Medicare population. Large gaps remain in regards to comparisons of individual bariatric surgical procedures to each other, and very limited evidence exists in regards to patient-centered outcomes such as quality of life after surgery.

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Executive Summary

Introduction

Treatments for severe obesity include lifestyle modifications (exercise, diet), use of medications (e.g., orlistat, sibutramine), endoscopically-placed devices (e.g. gastric balloons), and bariatric surgery. Most non-surgical treatments fail to achieve long-term weight control.¹ In contrast, bariatric surgery is perceived to be an effective obesity treatment, especially long-term, and probably reduces morbidities.²⁻⁴ It has become the preferred therapy for severely obese patients refractory to medical therapy.⁵ According to a National Institutes of Health (NIH) Panel, bariatric surgery is indicated for patients with BMI ≥ 40 Kg/m² (obesity grade 3), or BMI ≥ 35 Kg/m² (obesity grades 2 or 3) with an obesity-related comorbidity who have not responded to lifestyle modification therapy.⁶ Bariatric surgery has also been evaluated in moderately obese adults (obesity grade 1, BMI 30-34.9 Kg/m²).⁷

Bariatric surgical procedures result in anatomic manipulations of the gastrointestinal tract; and more recently similar anatomic modifications can be achieved through the use of endoscopic technologies. Many adults age 65 and older meet indications for bariatric treatment. Based on the U.S. National Health and Nutrition Examination Survey (NHANES), in 2012 people 60 years and older commonly had BMI ≥ 30 (prevalence 35 percent), ≥ 35 (14 percent), and ≥ 40 (6 percent) Kg/m².⁸ Thus, a large number of Medicare eligible people in the U.S. likely meet NIH indications for bariatric therapy either surgical or endoscopic. Therefore, the comparative effectiveness and safety of bariatric therapies (both surgical and endoscopic) is of great interest to the Centers for Medicare and Medicaid Services (CMS), the primary health insurer of elderly in the U.S.

We conducted a technology assessment to objectively summarize and appraise current evidence regarding the effectiveness and safety of bariatric therapies in the Medicare eligible population.

The Key Questions

We developed the following Key Questions (KQ) and study eligibility criteria:¹

KQ 1: What are the theorized mechanisms of action of bariatric procedures on weight loss and on type 2 diabetes in the Medicare population?

KQ 2: In studies that are applicable to the Medicare population and enroll patients who have undergone bariatric therapy, what are

- a) the characteristics and indications of patients receiving bariatric therapy
- b) the characteristics of the interventions
- c) the outcomes that have been measured?

KQ 3: In Medicare eligible patients:

- a) What are the effects of different bariatric therapies on weight outcomes?
- b) What patient- (KQ2a) and intervention-level characteristics (KQ2b) modify the effect of bariatric therapies on weight outcomes?

¹ These KQs are logically equivalent to preliminary Key Questions proposed by the Centers for Medicare and Medicaid Services (CMS), AHRQs sponsoring partner on this project.

- c) What is the frequency and the predictors of failing to achieve at least minimal weight loss?
- d) What is the effect of revisional bariatric therapies (contrasted between them or vs. non-bariatric therapies) on weight outcomes?

KQ 4: In Medicare eligible patients:

- a) What is the comparative effectiveness of different bariatric therapies with respect to the non-weight loss outcomes in KQ2c and what is the comparative safety of these therapies?
- b) What patient- (KQ2a) and intervention-level (KQ2b) characteristics modify the effects of the bariatric therapies on the outcomes other than weight loss in KQ2c?

KQ 5: In Medicare eligible patients:

- a) What is the association between weight outcomes and eligible short- and long-term outcomes (other than weight outcomes)?
- b) What proportion of the bariatric treatment effect on eligible short- and long-term outcomes (other than weight outcomes) is accounted for by changes in weight outcomes?

Methods

We conducted the technology assessment based on a systematic review of the published scientific literature using established methodologies as outlined in the Agency for Healthcare Research and Quality's (AHRQ) Methods Guide for Comparative Effectiveness Reviews.⁹ The PROSPERO registration number is CRD42017065285.

Eligibility Criteria

Because the interest is in Medicare eligible individuals, eligible studies were those whose population resembled Medicare beneficiaries. Medicare beneficiaries are people age 65 years and older as well as people younger than 65 who are disabled or have a diagnosis of end-stage renal disease. Therefore, we excluded studies in pediatric populations (ages 0-18 years) as well as studies on pregnant women. Because studies that are conducted exclusively in adults age 65 years and older are uncommon,¹⁰ eligible for inclusion in our systematic review were studies with a mean and/or median age of 55 years or above. Additionally, we included studies in disabled patients, and studies in patients with end-stage renal disease. We also included any study that used claims data from people already enrolled in and receiving benefits from Medicare. For all Key Questions, we included studies of bariatric therapies, defined as any surgical (open or laparoscopic) or endoscopic procedure that results in anatomic and/or functional alteration of the gastrointestinal system and that may or may not involve device placement. All reported clinical outcomes were considered eligible.

Estimates of treatment effects reported in non-randomized comparative studies were considered to represent causal associations between bariatric procedures and outcomes if the respective studies explicitly aimed to achieve a minimal balance between treatment groups in regards to confounders and other prognostic factors associated with the outcome. In studies that report data on multiple procedures but do not provide sufficient information on causal relationships, we considered each arm as a single-arm cohort and describe treatment effects by comparing outcome values before vs. after surgery or by providing descriptive statistics. This way, we aim to minimize unreliable inferences about causal treatment effects while at the same maximize the utilization of the evidence base to provide estimates that may still be useful to stakeholders for purposes other than causal treatment effects.

Searching for the Evidence

We searched six bibliographic databases from January 1, 2000 to October 20, 2016, as well as the reference lists of published clinical practice guidelines, relevant narrative and systematic reviews, and Scientific Information Packages (SIP) from manufacturers or other stakeholders on the outcomes and prediction models of different bariatric procedures studied in the Medicare eligible population.

Data Synthesis

All included studies have been summarized in narrative form and in summary tables that tabulate the important features of the study populations, design, intervention, outcomes, and results.

Due to sparsity of available data reported in the existing evidence base, a statistical synthesis (either through pairwise meta-analysis or network meta-analysis) was not feasible. In addition, clinical heterogeneity in regards to interventions, outcomes, and populations did not allow for a synthesis the findings of which would be informative of treatment effects.

All analyses pertain to qualitative synthesis of the available studies. We generated evidence maps that provide stakeholders with information about the type and amount of research available, the characteristics of that research, and the topics where a sufficient amount of evidence has accumulated for synthesis.

Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes

Following the standard AHRQ approach, for each intervention and comparison of intervention, and for each conclusion, we assessed the number of studies, their study designs, the study limitations, the directness of the evidence to the KQs, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, and the overall findings across studies. Based on these assessments, we assigned a strength of evidence rating as being either high, moderate, low, or insufficient.

Results

A total of 94 studies met the eligibility criteria, of which 24 reported models to predict body weight loss or absolute body weight after bariatric surgery and the remaining 70 studies pertained to the effectiveness and safety of bariatric procedures.

Seven studies¹¹⁻¹⁷ used claims data from beneficiaries enrolled in Medicare, 3 studies reported overall or subgroup analyses on patients with end-stage renal disease/dialysis-dependent renal failure; 3 studies were on disabled patients; and 57 studies were on patients with a mean or median age of 55 or older.

We did not identify any randomized trials on the effectiveness and safety of bariatric surgery conducted in patients aged 55 years or older, or in patients with other Medicare-eligibility criteria. A total of 28 non-randomized studies reported data on more than one procedures but only 13 of those had a design and/or analytical approach that explicitly attempted to address confounding bias. Treatment effects reported in these studies, where confounding was accounted for, approximate causal associations between bariatric procedures and weight loss outcomes, adverse events/complications, or other non-weight related health outcomes. The remaining

studies reported weight changes in outcomes before vs. after bariatric surgery or provided descriptive statistics such incidence or prevalence of outcomes among patients undergoing bariatric surgery without a comparison to an independent or paired group.

The 24 prediction studies reported a total of 40 distinct models predicting body weight loss or absolute body weight after bariatric surgery. None of these models was internally and/or externally validated. Few studies were conducted in US settings. The majority of studies were conducted recently, mainly after 2010.

Theorized Mechanisms

Bariatric surgery defines a group of procedures that alter gastrointestinal anatomy in order to produce long-term weight loss. Because food intake and absorption are central in weight gain, the anatomical changes occurring during bariatric surgery aim to disrupt these processes. One mechanism to achieve this is by restricting the diameter of the stomach's esophageal orifice, or restricting the stomach's effective volume, thereby reducing the volume and speed of food intake. Another approach involves diverting the physiological route of ingested food to more distal segments of the gastrointestinal tract, leading to malabsorption and reduced absorption of ingested food. These mechanisms seem to be dominant in the early weight loss period after surgery.¹⁸ In the long term, additional mechanisms appear to be responsible for maintaining weight loss. First, these mechanisms involve secondary changes to food intake due to the anatomical changes occurring during bariatric surgery. In particular, patients develop aversive conditioning food restriction to avoid experiencing gastrointestinal disturbances (e.g., dumping syndrome, dysphagia, vomiting, flatus), due to surgery-induced changes of the anatomy and function of the gastrointestinal tract.¹⁹ Second, current evidence suggests that the anatomical alterations of the gastrointestinal tract affect a complex array of gut hormones which can mediate many of the metabolic changes seen post-operatively by affecting insulin secretion and sensitivity, reducing appetite, increasing satiety, and also increasing energy expenditure.²⁰

Patient Characteristics, Interventions, and Outcomes in the Medicare eligible Population

The patient characteristics in studies of bariatric surgical procedures are as follows:

- Mean or median BMI at baseline ranged from 34.3 percent to 56.8 percent.
- Two studies^{21, 22} included only female patients undergoing bariatric surgery
- One study²³ included only male patients.
- In the remaining 53 studies, the percentage that were women ranged from 51.4 to 89.6.

The frequency of diabetes was as follows:

- Three studies were conducted in patients who all had type 2 diabetes,²⁴⁻²⁶
- In another 27 studies at least 50 percent of patients had type 2 diabetes.
- Prevalence of hypertension at baseline ranged from 35.2 percent to 97.7 percent.
- One study was exclusively conducted on patients who were on chronic dialysis.²⁷
- Prevalence of pulmonary comorbidities ranged from 2 percent to 44.3 percent.
- Five studies reported the prevalence of chronic obstructive pulmonary disease.
- Psychiatric comorbidities were reported in nine studies with the most commonly reported psychiatric comorbid condition being depression (n=5 studies).

- Percentage of bariatric patients with hypercholesterolemia and other lipid disorders ranged from 11.9 percent to 95 percent.
- Prevalence of gastroesophageal reflux disease ranged from 1.35 percent to 64.8 percent.
- Thirteen studies reported musculoskeletal comorbidities, mainly osteoarthritis and other degenerative joint disorders.
- Prevalence of congestive heart failure ranged from 11.1 percent to 32.4 percent, while one study examined bariatric surgery in patients with congestive heart failure exclusively.²⁸

We did not identify any studies in the Medicare eligible population reporting on endoscopically-performed bariatric procedures. In particular, there are no studies in the Medicare eligible population in regards to intragastric balloons or other nonballoon space-occupying endoscopic bariatric devices, aspiration therapy, endoscopic sleeve gastropasty, endoscopic duodenojejunal or gastroduodenojejunal bypass sleeve, duodenal mucosal resurfacing, and self-assembling magnets for endoscopy. Overall, evidence on bariatric therapies in the Medicare eligible population pertains exclusively to bariatric surgery and thus all bariatric procedures in the current technology assessment represent surgical procedures. Table A shows the different types of bariatric surgical procedures that have been evaluated in the Medicare eligible population for the treatment of obesity.

Table A. Method of surgery by bariatric procedure studied in the Medicare eligible population

| Bariatric Procedure | Method of surgery | | | |
|---------------------|-------------------|-------------------|-----------------------------|--------------|
| | Open only | Laparoscopic only | Either open or laparoscopic | Not reported |
| AGB | | 23 | | 1 |
| MGB | | 1 | | |
| Multiple surgeries | 1 | 6 | 7 | 10 |
| RYGB | 3 | 26 | 7 | 5 |
| SADS | | 1 | | |
| SG | | 22 | 2 | |
| VBG | | 1 | | |
| BPD-DS | 1 | 1 | 1 | |

The numbers correspond to the study arms across all eligible studies. Not shown are the concurrent performance of bariatric surgery and hernia repair (laparoscopic) and bariatric surgery before total knee arthroplasty (the mode of operation was not reported). Blank cells correspond to no studies. AGB: adjustable gastric banding; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; VBG: vertical band gastroplasty; BPD-DS: biliopancreatic diversion with duodenal switch

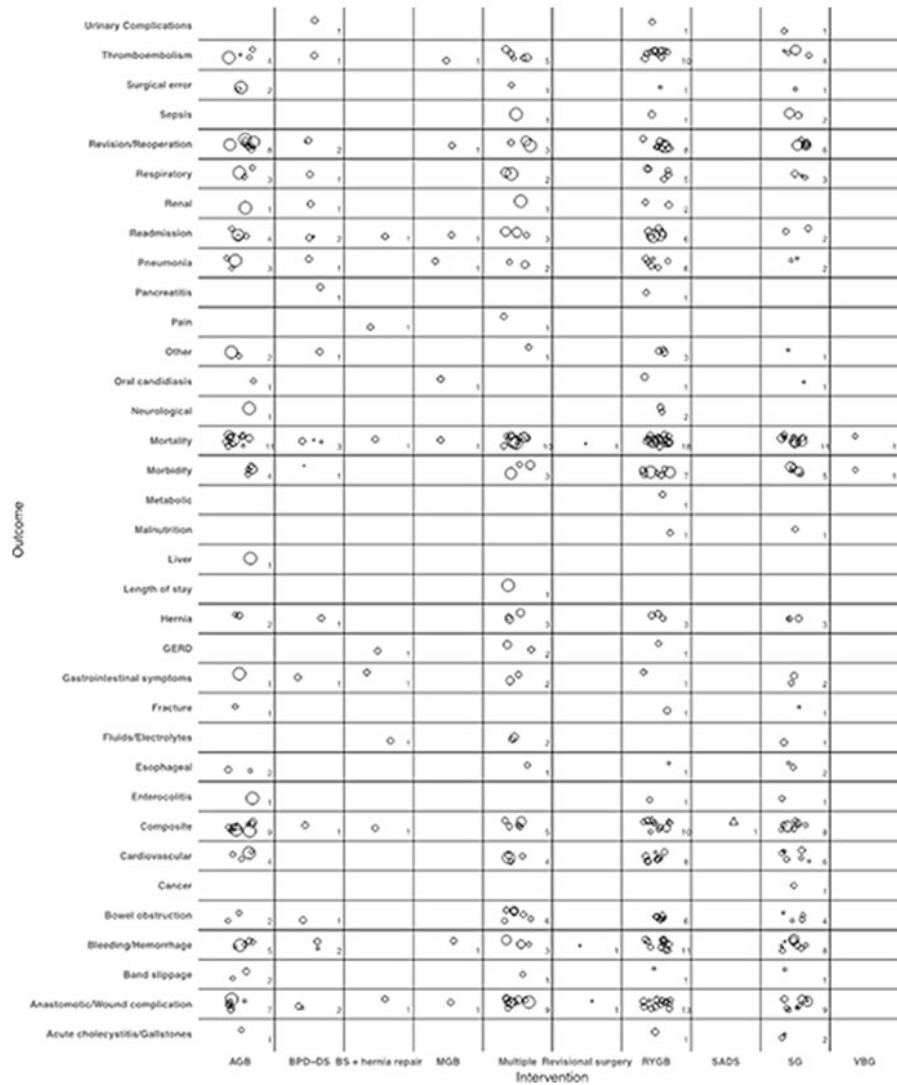
We did not identify any studies in the Medicare eligible population on gastric plication, vagal blockade, omentum removal (omentectomy), gastric stimulation, and mucosal ablation.

Weight loss outcomes measured in the Medicare eligible population include percent excess weight loss (EWL), percent weight loss (WL), percent excess BMI loss (EBMIL), absolute body weight loss, absolute BMI loss, while a few studies reported the mean body weight and BMI in patients undergoing bariatric surgery. Percent EWL and percent WL have been examined as outcomes for most bariatric surgical procedures, while absolute changes in weight and BMI have been studied less commonly. Of note, there are no studies about weight loss outcomes after VBG, while there is limited evidence regarding mini-gastric bypass and SADS. Most outcomes pertained to laparoscopically conducted surgeries while only five outcomes had been examined after open surgeries. These are percent excess BMI loss (EBMIL) and changes in BMI after open RYGB²⁹; and percent EWL, percent WL, and changes in BMI after open BPD-DS.³⁰

Studied adverse events and/or surgical complications in the 90-day post-operative period after bariatric surgical procedures is shown in Figure B. The sample sizes for these outcomes vary across procedures. The largest sample sizes have been used for AGB, RYGB, and SG, while evidence for BPD-DS, MGB, SADS, and VBG comes from smaller sample sizes.

Figure A. Post-operative (0 to 90 days after surgery) adverse events and surgical complications studied in the Medicare eligible population according to bariatric procedure.

Each circle represents a procedure-outcome pair within each eligible study; the diameter of each circle is proportional of the logarithm of the sample size of the arm for the largest applicable arm in each study

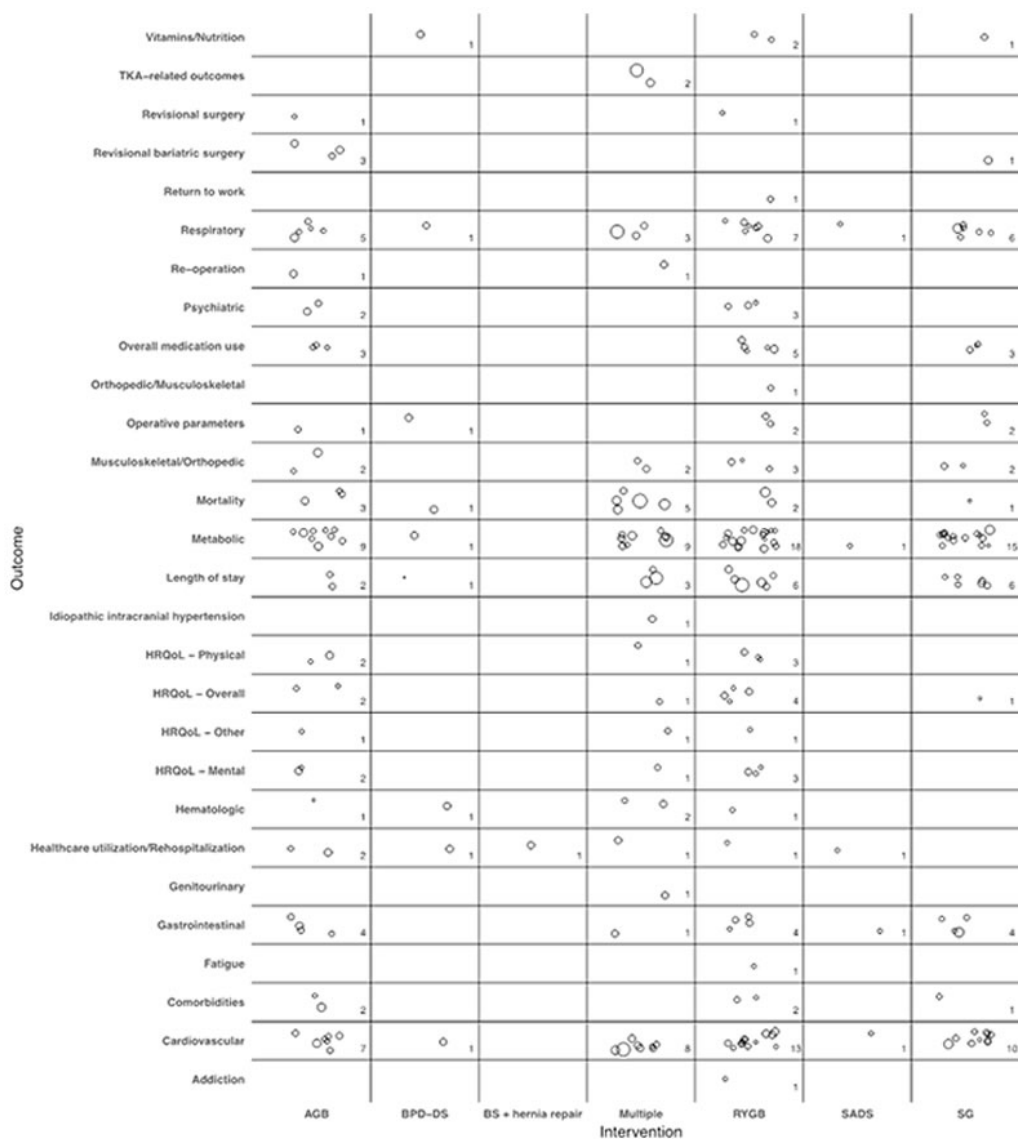


AGB: adjustable gastric banding; BS: bariatric surgery; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; VBG: vertical band gastroplasty; BPD-DS: biliopancreatic diversion with duodenal switch; GERD: gastroesophageal reflux disease

Health outcomes other than weight loss outcomes and adverse events/surgical complications examined in the Medicare eligible population are shown in Figure C. Most common were respiratory outcomes (n=23), metabolic/diabetes-related outcomes (n=53), and cardiovascular outcomes (n=40). Health-related quality of life, whether physical, mental, or overall, has not been extensively studied in Medicare eligible patients; in addition, the respective studies are relatively small.

Figure B. Short term and long term health outcomes other than weight loss outcomes and adverse events/surgical complications studied in the Medicare eligible population according to bariatric procedure.

Each circle represents a procedure-outcome pair within each eligible study; the diameter of each circle is proportional of the logarithm of the sample size of the arm for the largest applicable arm in each study



AGB: adjustable gastric banding; BS: bariatric surgery; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; BPD-DS: biliopancreatic diversion with duodenal switch; TKA: total knee arthroplasty; HRQoL: health-related quality of life

Weight Loss Outcomes

Three studies reported on the comparative effects of different approaches to bariatric surgeries on weight change.^{25, 31, 32} RYGB resulted in greater improvements for all four weight outcomes compared to either SG or LAGB. Similarly, the effect of SG on the four weight outcomes was greater than that of LAGB.³¹ In a second study, 71 percent of patients undergoing LSG experienced weight loss compared to only 2.8 percent in the conventional therapy group including pharmaceutical agents and lifestyle modifications (diet and physical activity) at 18 months after surgery. In the same study, the mean BMI loss in the LSG group 13.5 kg/m² compared to a mean 0.17 kg/m² increase in the conventional treatment group.²⁵ Finally, at a third study, weight loss at 1 year after surgery was higher for RYGB and SG compared to LAGB for patients 60 years of age or older. The percent of initial weight lost was 9.2 percentage points higher for those undergoing RYGB and 5.5 percentage higher for those undergoing SG compared to patients receiving LAGB.³²

Strength of Evidence

The strength of evidence for the effectiveness of different bariatric surgical procedures on weight loss outcomes in Medicare eligible patients is low to moderate (Table B).

Table B. Strength of evidence for weight loss outcomes in the Medicare eligible population.

| Conclusion statement | RoB (evidence base) | Consistency | Precision | Directness and Applicability | Overall Rating | Comments |
|--|---|-------------|----------------------------|------------------------------|---|--|
| RYGB results in greater improvements in weight outcomes compared to SG at 6 months after surgery (1) Mean weight loss (2) Mean BMI loss (3) Mean percent weight loss (4) Mean percent excess weight loss | Low for (1), (2), (3), (4) | [Not rated] | Low for (1), (2), (3), (4) | High for (1), (2), (3), (4) | Low SoE for (1), (2), (3), (4) | Only 1 non-randomized study addresses this question (N=162). <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| SG results in greater improvements in weight outcomes compared to LAGB at 6 or 12 months after surgery (1) Mean weight loss (2) Mean BMI loss (3) Mean percent weight loss (4) Mean percent excess weight loss | Low for (1), (2), (4) Moderate for (3) | [Not rated] | Low for (1), (2), (3), (4) | High for (1), (2), (3), (4) | Low SoE for (1), (2), (4) Moderate SoE for (3) | - Only 1 non-randomized study compares weight changes for all four outcomes at 6 months (N=162). - Only 1 non-randomized study compares weight changes for (1), (2), and (4) at 12 months (N=162). - Only two non-randomized studies (N=316) compare weight changes at 12 months for (3). <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| RYGB results in greater improvements in weight outcomes compared to LAGB at 6 or 12 months after surgery (1) Mean weight loss (2) Mean BMI loss (3) Mean percent weight loss | Low for (1), (2), (4) Moderate for (3) | [Not rated] | Low for (1), (2), (3), (4) | High for (1), (2), (3), (4) | Low SoE for (1), (2), (4) Moderate SoE for (3) | - Only 1 non-randomized study compares weight changes for all four outcomes at 6 months (N=162). - Only 1 non-randomized study compares weight changes for (1), (2), and (4) at 12 months (N=162). - Only two non-randomized studies (N=316) compare weight changes at 12 months for (3). |

| Conclusion statement | RoB (evidence base) | Consistency | Precision | Directness and Applicability | Overall Rating | Comments |
|---|---------------------|-------------|-----------|------------------------------|----------------|---|
| (4) Mean percent excess weight loss | | | | | | <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| LSG results in greater weight loss than conventional treatment at 18 months after surgery | Low | [Not rated] | Low | High | Low SoE | Only 1 study address this question (N=60). <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy; LAGB: laparoscopic gastric banding; LSG: laparoscopic sleeve gastrectomy; SoE: strength of evidence | | | | | | |

A total of 40 different models were reported in the eligible studies. Outcome definition was rarely consistent across models. There was no global agreement in regards to the definition of “minimal weight loss” and no model explicitly used this outcome definition. Fifteen models directly predict the probability of successful/failed weight loss. The area under the receiver operating characteristic curve (AUC) ranged from 0.58 for 3-year weight change to 0.85 for percent EWL >50 percent (good outcome/successful weight loss). Values of the R^2 metric for model fit ranged from 2 percent³³ to 99.7 percent.³⁴ Finally, a model³⁵ consisting of postsurgical global dietary adherence rating, postsurgical grazing frequency, highest lifetime BMI prior to surgery, and regular attendance at postsurgical bariatric support groups had a sensitivity of 0.62, a specificity of 0.92, an efficiency of 0.84, a positive predictive value of 0.72, and a negative predictive value of 0.88.

Outcomes other than Weight Loss

We identified 27 studies which contrasted bariatric surgical procedures to each other, to non-bariatric treatments, or to conventional or no treatment. No randomized trials in the Medicare eligible population were found.

Appropriate study design and/or analytical approaches that allowed credible estimation of treatment effects by achieving some degree of balance in confounders and prognostic factors between the compared procedures³⁶ were used in 12 studies.

Below we summarize the outcomes that were reported in these 12 studies. For the remaining studies, we considered each arm as a cohort of patients exposed to a specific intervention (either one or more bariatric surgical procedures) and we present the relevant outcome statistics in the Appendix for the interested reader.

Mortality

A total of four non-randomized comparative studies examined the effects of bariatric surgical procedures on mortality.

In one study, RYGB resulted in lower all-cause mortality rates (hazard ratio, HR, 0.50; 95% CI 0.31, 0.79; $P < 0.003$) compared to a non-surgical control group and in lower rates (HR 0.46; 95% CI 0.28-0.75; $P = 0.002$) of death due to any cause except for externally caused deaths (unintentional injury unrelated to drugs, poisoning of undetermined intent, suicide, and other

externally caused deaths). However, there was no association between RYGB and all externally caused deaths, cardiovascular mortality, or cancer mortality.³⁷

In a second study, patients 50 to 69 years of age receiving gastric bypass or AGB had lower risks for all-cause mortality (HR 0.68; 95% CI 0.38, 1.23; P=0.201), cardiovascular mortality (HR 0.83; 95% CI 0.36, 1.93; P=0.658), and for non-cardiovascular mortality (HR 0.60; 95% CI 0.26, 1.39; P=0.233) compared to morbidly obese patients undergoing orthopedic or gastrointestinal surgeries.³⁸

A third study found that bariatric surgery resulted in lower risk of all-cause mortality compared to gastrointestinal surgical procedures (HR 0.45, 95% CI 0.33, 0.60) but there was no evidence of difference in all-cause mortality compared to orthopedic surgeries (HR 0.81, 95% CI 0.60, 1.10).³⁹

Finally, bariatric surgery was associated with lower mortality rates at 2 years after surgery in morbidly obese Medicare beneficiaries 65 years and older compared to non-surgical controls (8 percent vs. 12.2 percent, P<0.001). However, mortality rate was increased in the 30-day post-operative period (1.55 percent vs. 0.53 percent; P<0.001).¹⁶

Because of heterogeneity in bariatric surgical procedures across studies, we deemed that a statistical synthesis would not result in a clinically meaningful estimate of an overall treatment effect.

Postoperative Complications

Two non-randomized comparative studies examined post-operative complications of different bariatric surgical procedures. Both found that complication rates were not significantly different in the bariatric groups compared to the control groups.^{40, 41}

Diabetes and Metabolic-Related Outcomes

Four non-randomized comparative studies evaluated the effect of bariatric surgery on diabetes and other metabolic-related outcomes.

In the first study, RYGB was more effective than LAGB in reducing insulin treatment among diabetic patients at 3 months after surgery (37.1 percent vs. 26.3 percent; P=0.03). In addition, the rates of clinical remission of type 2 diabetes for RYGB versus LAGB were 14.4 percent versus 7 percent (P=0.02) at 1 month; 28.0 percent versus 12.9 percent (P=0.001) at 3 months; 30.7 percent versus 19.3 percent (P=0.01) at 6 months; and 35.7 percent versus 24.4 percent (P=0.01) at 12 months.²⁴

In another study, there was no evidence in the improvement of diabetes among patients receiving bariatric surgery compared to non-surgical controls in 6 months and in 1 year after surgery; however, there was an improvement at 2 years.¹⁶

In a third study, There was no evidence that 6 or 12 months after surgery levels of HbA1c were lower for any of RYGB, SG, or LAGB surgery compared to the other. There was also no evidence of lower glucose levels, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein-cholesterol, total cholesterol or triglycerides for any surgery at either 6 or 12 months.³¹

Finally, LSG was associated with statistically significant larger decreases in triglycerides and HDL compared to conventional therapy consisting of pharmaceutical agents and lifestyle modifications (diet and physical activity) at 18 months after treatment. Higher decreases were also found for glucose and HbA1c levels but only among patients with duration of type 2

diabetes over 10 years. There was no evidence that LSG resulted in higher changes in the levels of LDL-cholesterol or total-cholesterol.²⁵

Cardiovascular Outcomes

Patients undergoing bariatric surgery had a lower risk of myocardial infarction (MI) compared to control patients undergoing orthopedic surgery (HR 0.59, 95% CI 0.44, 0.79) as well as compared to patients undergoing gastrointestinal surgery (HR 0.49; 95% CI 0.36, 0.68).³⁹ Bariatric surgery was associated with lower risk of MI, stroke, or all-cause mortality (HR 0.72, 95% CI 0.58-0.89 for bariatric surgery compared to orthopedic surgery; HR 0.48, 95% CI 0.39-0.61 for bariatric surgery compared to gastrointestinal surgery).³⁹

A second study found evidence of improvement in coronary artery disease in the 6-month period after surgery, which was maintained in 1 and 2 years after surgery. There is also evidence of improved lipid profile and improved in the 1 and 2 years after surgery, but no evidence of improvement in the immediate 6 months. The difference in outcomes between bariatric patients and non-surgical controls increased between 6 months, 1 year, and 2 years.¹⁶

Another study found no evidence that either systolic or diastolic blood pressure were lower at 6 or 12 months after surgery after any of RYGB, SG or LAGB compared to each other.³¹

A fourth study found that, compared to conventional therapy including pharmaceutical agents and lifestyle modifications (diet and physical activity), LSG was not associated with prevalence difference in hypertension at 18 months after treatment.²⁵

Finally, there was evidence of lower risk of stroke in bariatric patients compared to a control group of patients undergoing gastrointestinal surgery (HR 0.49; 95% CI 0.24, 0.98) but not compared to patients undergoing orthopedic surgery (HR 0.69; 95% CI 0.40, 1.30).³⁹

Respiratory Disease

Perry et al. found evidence of improvement in sleep apnea in the 6-month period after surgery but there was no evidence of long-term improvement at 1 and 2 years.¹⁶

Orthopedic/Musculoskeletal Outcomes

There was no evidence that RYGB 1 to 5 years prior to the time of outcome measurements affected BMI, body fat, calcium intake, vitamin D intake, caloric intake, serum calcium, phosphorus, albumin creatinine, thyroid stimulating hormone, 25-hydroxy vitamin D, vitamin D deficiency, alkaline phosphatase, femoral bone mineral density or lumbar spine bone mineral density. However, RYGB was associated with the prevalence of hyperparathyroidism.²²

In a second study, compared to patients with high BMI undergoing only total knee arthroplasty (TKA) without prior bariatric surgery, patients receiving bariatric surgery before TKA were more likely to be re-operated (HR 2.5; 95% CI 1.2 to 6.2; P = 0.02). However, there was no evidence of differences in the rates of complications, revision surgery, or periprosthetic joint infection. Compared to patients with low BMI undergoing only TKA without prior bariatric surgery, patients receiving bariatric surgery prior to TKA were more likely to be re-operated (HR 2.4; 95% CI 1.2 to 3.3; P = 0.02) as well as undergo revisional surgery (HR 2.2; 95% CI 1.1 to 6.5, P = 0.04).⁴²

Polypharmacy

Patients undergoing RYGB had experienced a higher reduction in the number of medications at 6 and 12 months after surgery compared to patients undergoing SG or LAGB.³¹

In another study, there was a statistically significant reduction in the mean number of antihypertensive drugs (from 1.5 to 0.83 pills) at 18 months after surgery and in the mean number of hypolipemic drugs reduced (from 0.4 to 0.2).²⁵

In a third study, the weekly median warfarin dose in the first 8 weeks as well the median dose between 2 and 3 months and between 3 and 6 months after bariatric surgery was lower than in the pre-surgical period for bariatric patients, while there was no difference over time for patients undergoing endoscopic retrograde cholangiopancreatography. For each time point, the decrease in warfarin dose in bariatric patients was significantly lower.⁴³ Bariatric surgery resulted in: (1) more patients achieving 20 percent or more decrease in preoperative warfarin dose at any time during follow-up; (2) lower percentage time in therapeutic INR range; (3) less bleeding during the 180-day period after surgery.⁴³

Strength of Evidence

There is at low to moderate strength of evidence regarding the comparative effectiveness and safety of different bariatric surgical procedures in the Medicare eligible population (Table C).

Table C. Strength of evidence for non-weight loss outcomes in the Medicare eligible population.

| Conclusion statement | RoB (evidence-base) | Consistency | Precision | Directness and Applicability | Overall Rating | Comments |
|---|---------------------------------------|-------------|---|---|---|--|
| Bariatric surgery results in favorable outcomes compared to no surgery/other non-bariatric surgery/conventional treatment in regards to: (1) Mortality (2) Metabolic outcomes (3) Cardiovascular outcomes (4) Musculoskeletal outcomes (5) Warfarin dose after surgery (6) Respiratory outcomes | High for (1), (2), (3), (4), (5), (6) | [Not rated] | Low for (4), (5) Moderate for (1), (2), (3), (6) | Moderate for (1), (2), (3), (4), (5), (6) | Low SoE for (4), (5) Moderate SoE for (1), (2), (3), (6) | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. Use of inappropriate control groups limits applicability/generalizability. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| RYGB results in favorable outcomes compared to SG in regards to: (1) Post-operative complications (2) Metabolic outcomes (3) Polypharmacy (4) Cardiovascular outcomes | Moderate for (1), (2), (3), (4) | [Not rated] | Low for (1), (2), (3), (4) | High for (1), (2), (3), (4) | Moderate SoE for (1), (2), (3), (4) | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| Concomitant bariatric surgery and hiatal hernia repair does not result in higher complication rates compared to bariatric surgery alone | High | [Not rated] | Low | Moderate | Low SoE | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. Only one study addressed this question. Technical aspects of the surgical procedures may limit the feasibility of these surgeries across surgeons. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE</i> |

| Conclusion statement | RoB (evidence-base) | Consistency | Precision | Directness and Applicability | Overall Rating | Comments |
|---|----------------------------|-------------|-----------------------|------------------------------|--------------------------------|--|
| RYGB results in favorable outcomes compared to LAGB in regards to: (1) Metabolic outcomes (2) Polypharmacy (3) Cardiovascular outcomes | Moderate for (1), (2), (3) | [Not rated] | Low for (1), (2), (3) | High for (1), (2), (3) | Moderate SoE for (1), (2), (3) | assessments. There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| SG results in favorable outcomes compared to LAGB in regards to: (1) Metabolic outcomes (2) Cardiovascular outcomes (3) Polypharmacy | Moderate for (1), (2), (3) | [Not rated] | Low for (1), (2), (3) | High for (1), (2), (3) | Moderate SoE for (1), (2), (3) | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |

RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy; LAGB: laparoscopic gastric banding; SoE: strength of evidence

Discussion

Evidence Summary

In the Medicare eligible population, we did not identify any studies in patients undergoing bariatric endoscopic procedures. However, multiple studies have been conducted in regards to one or more bariatric surgical procedures. Yet, limited comparative evidence exists about the effects of different bariatric surgical procedures on weight loss and non-weight loss outcomes in the Medicare eligible population. The overwhelming majority of evidence is comprised of studies reporting changes in weight loss and/or non-weight loss outcomes after one or more bariatric surgical procedures using pre-post designs.

It should be acknowledged that comparative evidence in younger patients strongly suggests that bariatric surgery overall as well as certain procedures are effective in regards to achieving weight loss and reducing the risk of other non-weight loss outcomes. Nevertheless, evidence from studies in younger populations may not be directly generalizable to the Medicare eligible population. Although statistical methods for the transportability of treatment effects exist, a formal generalization of evidence from younger patients to the Medicare eligible population was beyond the scope of this technology assessment.

Both weight loss and non-weight loss outcomes appear to be reduced after bariatric surgery compared to their pre-surgery values. However, because of the non-randomized nature of the available studies and the lack of a control group in most studies, the strength of the available evidence is at best moderate. Based on the evidence from studies reporting changes in weight outcomes before and after bariatric surgery, it is likely that bariatric surgery overall has a sustaining effect on both BMI and body weight loss over time. Although the follow-up rarely exceeded 1 year, in those studies with follow-up as long as 8 years, patients maintained their weight and/or BMI loss over time.

Although many models are available to predict body weight loss or absolute body weight after bariatric surgery, they have not undergone the processes of internal and external validation.

Moreover, very few models explicitly aim to predict “minimal weight loss”. Even among these models, there is considerable lack of standardized outcome definition as to how “minimal weight loss” is measured.

Evidence Limitations and Future Research Recommendations

Very few studies on health outcomes of bariatric surgical procedures in the Medicare eligible population utilize an appropriate design and/or analytical approach that can yield unbiased estimates of treatment effect by balancing prognostic factors between treatment groups. Even among those studies, the majority were deemed to have at most moderate risk of confounding, selection, or measurement biases.

The major drawback of pre-post study designs is because of the absence of a control comparison group that would capture changes in the outcome of interest when the studied procedure is not performed.⁴⁴ Still, their findings can be indicative of potential treatment effects and should be interpreted as hypothesis-generating evidence for future controlled trials. Finally, the lack of internally and/or externally predictive models for body weight loss or absolute body weight after bariatric surgery limits the clinical utility of the existing which have not passed the initial phase of development.

Since no randomized evidence is available for the effectiveness of different bariatric surgeries in Medicare eligible obese patients, generating such evidence is important for identifying both effective and safe surgeries. Nevertheless, large, well-powered randomized trials are rarely conducted in patients age 65 and older or with multiple comorbidities.⁴⁵ Hence, evidence may be generated by using Medicare claims data and electronic health records can be used to design non-randomized comparative studies to contrast bariatric surgeries to each other.⁴⁶⁻⁴⁸

Furthermore, routinely collected health data, such as registry data and electronic health records data from hospital and clinical practices, can also be used to externally validate existing models⁴⁹ and overcome issues related to number of event and granularity of clinical predictors.⁵⁰ Towards this end, it will be important for all relevant stakeholders to identify a core of clinically meaningful and standardized definitions of the outcomes that these models should predict, particularly what should be considered “minimal weight loss” and how it should be measured.

Conclusions

Very few studies address clinically relevant outcomes in Medicare eligible patients who undergo surgical or endoscopic bariatric procedures. Based on such sparse evidence, Medicare eligible patients undergoing bariatric surgery achieve sustained weight loss for most types of bariatric surgical procedures but the strength of the evidence is low to moderate. Large gaps remain in the literature regarding the comparison of individual procedures for both weight loss and non-weight loss outcomes. Very little or no information exists on the extent to which the effects of bariatric surgery on non-weight outcomes are mediated through weight loss. Evidence from new randomized trials or high-quality comparative observational studies is needed.

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Introduction

Obesity, an accumulation of excessive fat tissue, has been associated with morbidity (e.g., sleep apnea, diabetes, cardiovascular disease, osteoarthritis, hypertension),¹⁻⁴ mortality,^{5,6} decreased quality of life,⁷ and increased healthcare costs,^{2,4,8} especially among adults age 65 and older in whom chronic conditions are more prevalent. Obesity carries a substantial health burden,⁹ and obesity-related conditions include preventable leading causes of death, such as type 2 diabetes, cardiovascular disease, and some cancers. There are indications that the risks of morbidity and mortality increase as obesity becomes more severe.¹⁻⁴ The estimated annual medical cost of obesity in the U.S. was \$147 billion in 2008, and the medical costs for people who have a body mass index (BMI) over 30 Kg/m² were approximately \$1,400 higher than those with a normal BMI (between 18.5 and 24.9 Kg/m²).⁸ This cost-of-care differential between people with high versus normal BMI is probably even higher for people with more severe obesity (BMI ≥ 35 kg/m²). Among employed Americans, the 3 percent who are severely obese account for 21 percent of the health care costs associated with obesity.⁸

Treatments for severe obesity include lifestyle modifications (exercise, diet), use of medications (e.g., orlistat, sibutramine), endoscopically-placed devices (e.g. gastric balloons), and bariatric surgery. Most non-surgical treatments for obesity fail to achieve long-term weight control.¹⁰ In contrast, bariatric surgery is perceived to be an effective obesity treatment, especially long-term, and probably reduces morbidities.¹¹⁻¹³ It has become the preferred therapy for severely obese patients refractory to medical therapy.¹⁴ According to a National Institutes of Health (NIH) Panel, bariatric surgery is indicated for patients with BMI ≥ 40 Kg/m² (obesity grade 3), or BMI ≥ 35 Kg/m² (obesity grades 2 or 3) with an obesity-related comorbidity who have not responded to lifestyle modification therapy.³ Bariatric surgery has also been evaluated in moderately obese adults (obesity grade 1, BMI 30-34.9 Kg/m²).¹⁵

Bariatric surgery procedures result in anatomic manipulations of the gastrointestinal (GI) tract and more recently similar anatomic modifications can be achieved through the use of endoscopic technologies. Depending on the exact procedure, bariatric procedures are thought to achieve weight control through one or more of the following mechanisms: (1) a restricting mechanism, by restricting the diameter of the stomach's esophageal orifice, or restricting the stomach's effective volume, thereby reducing the volume and speed of food intake; (2) endocrine or metabolic mechanisms (e.g., removal of the stomach's fundus decreases secretion of hunger-inducing hormones such as ghrelin); (3) a diversionary malabsorptive mechanism, by diverting the physiological route of ingested food to more distal segments of the gastrointestinal tract, leading to malabsorption of ingested food; and (4) conditioning mechanisms, food restriction to avoid experiencing gastrointestinal disturbances (e.g., dumping syndrome, dysphagia, vomiting, flatus) due to surgery-induced changes of the anatomy and function of the gastrointestinal tract.

Many adults age 65 and older meet indications for bariatric treatment. Based on the U.S. National Health and Nutrition Examination Survey (NHANES), in 2012 people 60 years and older commonly had BMI ≥ 30 (prevalence 35 percent), ≥ 35 (14 percent), and ≥ 40 (6 percent) Kg/m².¹⁶ In these people, obesity was more prevalent among women than men, and varied across ethnicities, being highest among non-Hispanic blacks (49 percent) and Hispanics (47 percent), and lowest among Asians (9 percent).¹⁶ Thus, a large number of Medicare eligible people likely meet NIH indications for bariatric therapy either surgical or endoscopic.

Therefore, the comparative effectiveness and safety of bariatric therapies (both surgical and endoscopic ones) is of great interest to the Centers for Medicare and Medicaid Services (CMS).

We conducted a technology assessment to objectively summarize and appraise current evidence regarding the effectiveness and safety of bariatric surgery in the Medicare eligible population.

The Key Questions

With input from clinical experts, we developed the following Key Questions (KQ) and study eligibility criteria for the systematic review:²

KQ 1: What are the theorized mechanisms of action of bariatric procedures on weight loss and on type 2 diabetes in the Medicare population?

KQ 2: In studies that are applicable to the Medicare population and enroll patients who have undergone bariatric therapy, what are

- a) the characteristics and indications of patients receiving bariatric therapy including descriptives of age, BMI, and comorbid conditions
- b) the characteristics of the interventions, including the bariatric procedures themselves as well as pre- and/or post-surgical surgical work-ups (e.g., psychiatric evaluations, behavioral and nutritional counseling)
- c) the outcomes that have been measured, including peri-operative (i.e., 90 days or less after bariatric surgery), short-term (2 years or less from surgery), mid-term (more than 2 but 5 or less years), and long-term (more than 5 years after surgery) outcomes?

KQ 3

- a) In Medicare eligible patients, what are the effects of different bariatric therapies (contrasted between them or vs. non-bariatric therapies) on weight outcomes (including failure to achieve at least minimal weight loss)?
- b) What patient- (KQ2a) and intervention-level characteristics (KQ2b) modify the effect of bariatric therapies on weight outcomes (including failure to achieve at least minimal weight loss)?
- c) In Medicare eligible patients who have undergone bariatric therapy, what is the frequency and the predictors of failing to achieve at least minimal weight loss?
- d) In Medicare eligible patients who do not achieve weight loss after primary bariatric treatment, what is the effect of revisional bariatric therapies (contrasted between them or vs. non-bariatric therapies) on weight outcomes?

KQ 4

- a) In Medicare eligible patients, what is the comparative effectiveness of different bariatric therapies (contrasted between them or vs. non-bariatric interventions) with respect to the non-weight loss outcomes in KQ2c and what is the comparative safety of these therapies?
- b) What patient- (KQ2a) and intervention-level (KQ2b) characteristics modify the effects of the bariatric therapies on the outcomes other than weight loss in KQ2c?

KQ 5

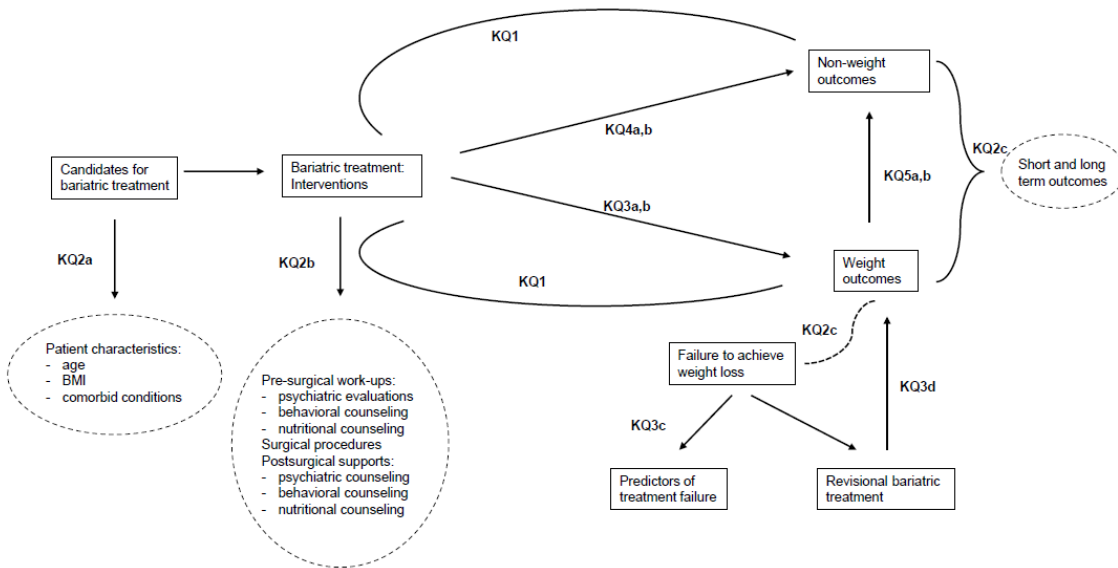
- a) In Medicare eligible patients who have undergone bariatric therapy, what is the association between weight outcomes and eligible short- and long-term outcomes (other than weight outcomes)?
- b) In Medicare eligible patients, what proportion of the bariatric treatment effect on eligible short- and long-term outcomes (other than weight outcomes) is accounted for by changes in weight outcomes?

² These KQs are logically equivalent to preliminary Key Questions proposed by the Centers for Medicare and Medicaid Services (CMS), AHRQs sponsoring partner on this project.

Analytic Framework

To guide the assessment of studies, the analytic framework maps the specific linkages associating the populations of interest, the interventions, and outcomes of interest. The analytic framework (Figure 1) depicts the chains of logic that evidence must support to link the studied interventions studied.

Figure 1. Analytic framework for short and long term outcomes after bariatric surgery in the Medicare eligible population



Methods

The Evidence-based Practice Center (EPC) has conducted the technology assessment based on a systematic review of the published scientific literature using established methodologies as outlined in the Agency for Healthcare Research and Quality's (AHRQ) Methods Guide for Comparative Effectiveness Reviews.¹⁷ We used a combination of a review of the published literature, interviews with key informants, a grey literature review, evidence mapping (i.e., a systematic description of the characteristics of the published studies), and quantitative methods to answer the key questions. The PROSPERO registration number is CRD42017065285.

Eligibility Criteria

For all KQs, the Eligibility Criteria are described based on the PICOTS formalism:

| | |
|----------------------|---|
| <u>Population</u> | Medicare eligible population to include those age 65 and older, the disabled, and those with end-stage renal disease. Also, patients receiving Medicare benefits regardless of reason. |
| <u>Interventions</u> | Bariatric treatments including anatomic alteration, FDA-approved device placements, open surgical procedures, as well as laparoscopic and endoscopic procedures |
| | <p>A. Surgical bariatric therapies</p> <ol style="list-style-type: none"> 1. Adjustable gastric banding (AGB) <ol style="list-style-type: none"> a. LAP-band, pars flaccida technique b. LAP-band, perigastric technique c. Swedish-band (also known as REALIZE-band), pars flaccida technique d. Swedish-band (also known as REALIZE-band), pars flaccida technique, single bolus filling 2. Gastroplasties <ol style="list-style-type: none"> a. Horizontal banded gastroplasty b. Vertical banded gastroplasty c. Endoluminal vertical gastroplasty 3. Sleeve gastrectomy 4. Gastric plication (also referred to as gastric greater curvature plication or gastric imbrication) 5. Jejunioileal bypass 6. Biliopancreatic diversion (BPD) <ol style="list-style-type: none"> a. Biliopancreatic diversion (BPD) with RYGB (BPD-RYGB) b. BPD with duodenal switch (BPD-DS) 7. Roux-en-Y Gastric Bypass (RYGB) 8. Mini-gastric bypass 9. Single Anastomosis Duodeno-Ileostomy (SADI) 10. Vagal blockade 11. Omentum removal (omentectomy) 12. Gastric stimulation (also referred to as gastric pacing) 13. Mucosal ablation |
| | <p>B. Endoscopic bariatric therapies</p> <ol style="list-style-type: none"> 1. Space-occupying endoscopic bariatric therapies <ol style="list-style-type: none"> a. Intra gastric balloons |

| | |
|--------------------|--|
| | <ul style="list-style-type: none"> b. Nonballoon devices 2. Aspiration therapy 3. Endoscopic sleeve gastropasty 4. Endoscopic gastrointestinal bypass devices <ul style="list-style-type: none"> a. Duodenojejunal bypass sleeve b. Gastroduodenojejunal bypass sleeve 5. Duodenal mucosal resurfacing 6. Self-assembling magnets for endoscopy |
| <u>Comparisons</u> | comparisons between different bariatric therapies, or between bariatric and non-bariatric therapies |
| <u>Outcomes</u> | were classified as peri-operative (i.e., 90 days or less after bariatric surgery), short-term (2 years or less from surgery), mid-term (more than 2 but 5 or less years), and long-term (more than 5 years after surgery). The following outcome categories are of interest: |
| | <ul style="list-style-type: none"> a. Mortality b. Weight loss c. Reoperations/need for revisional bariatric surgery d. Postoperative complications including mortality e. Metabolic/diabetes-related outcomes <ul style="list-style-type: none"> i. Correction of glucose tolerance, including elimination of all medications with Hemoglobin A1c (HbA1c) <6 ii. Diabetes: new onset diabetes; treatment of diabetes; diabetic complications (microvascular disease, kidney disease, retinopathy) iii. Hypoglycemic-like syndromes such as nesidioblastosis, post-gastric surgery hypoglycemia, and dumping syndrome iv. Non-alcoholic steatohepatitis (NASH) and/or non-alcoholic fatty liver disease (NAFLD) f. Reflux g. Cardiovascular outcomes <ul style="list-style-type: none"> i. Myocardial infarction ii. Stroke iii. Hypertension h. Respiratory disease <ul style="list-style-type: none"> i. Asthma ii. COPD iii. Sleep apnea including the discontinuation of CPAP or BiPAP i. Orthopedic/musculoskeletal outcomes <ul style="list-style-type: none"> i. Fractures ii. Falls iii. Osteoporosis/bone-mineral density (DEXA, DEEG) j. Incidence of specific cancers (breast, colorectal cancer, endometrial cancer, esophageal adenocarcinoma, gall bladder cancer, and renal cell cancer) k. Nutritional deficiencies including zinc, iron, thiamine, and vitamin D, and associated disorders such as neuropathy and bone disease l. Renal function as measured by creatinine clearance or urinary albumin excretion m. Compliance to follow-up |

| | |
|----------------|---|
| | <ul style="list-style-type: none"> n. Mental health outcomes <ul style="list-style-type: none"> i. Incidence of suicide and suicide attempts ii. Incidence of depression iii. Alcohol addiction after surgery/Substance abuse iv. Psychiatric hospitalizations v. Anxiety vi. Panic disorder vii. Borderline personality disorder viii. PTSD ix. Bipolar disorder o. Function and quality of life (validated measurements only), e.g., <ul style="list-style-type: none"> i. Cognitive functioning ii. Sexual functioning iii. Ability to participate in an exercise program iv. Ability to return to work v. Physical performance test pain (joint pain, joint aches) vi. Regular daily activities p. Polypharmacy q. Admission to a skilled-nurse facility r. Access to plastic surgery s. Readmissions/rehospitalizations |
| <u>Timing</u> | Studies published since 2000 |
| <u>Setting</u> | Any |

Comments About the Eligibility Criteria

Because the interest is in Medicare eligible individuals, eligible studies were those whose population resembled Medicare beneficiaries. Medicare beneficiaries are people age 65 years and older as well as people younger than 65 who are disabled or have a diagnosis of end-stage renal disease. Therefore, we excluded studies in pediatric populations (ages 0-18 years) as well as studies on pregnant women. Because studies that are conducted exclusively adults age 65 years and older are uncommon,¹⁸ eligible for inclusion in our systematic review were studies with a mean and/or median age of 55 years or above. We also included studies in disabled patients, and studies in patients with end-stage renal disease. We also included any study that used claims data from people already enrolled in and receiving benefits from Medicare.

For all Key Questions, we included studies of bariatric therapies, i.e. any surgical (open or laparoscopic) or endoscopic procedure that results in anatomic and/or functional alteration of the gastrointestinal system and that may or may not involve device placement. Studies that focus exclusively on non-bariatric therapies (i.e., pharmacological, behavioral, nutritional) were ineligible; as were studies in which subjects were not candidates for bariatric surgery or had not undergone bariatric surgery. We also excluded studies of the management of bariatric therapy complications (e.g. anastomosis leak, post-surgical hernias etc.) since these studies address clinical questions that are distinct from the effects of bariatric therapies. Studies reporting on hormonal, biochemical, and other molecular changes in relation to bariatric therapies are included only if these changes are related to health outcomes. Finally, we excluded cost-effectiveness analyses, case-control studies, case series, case reports, letters, comments, animal studies because they were not informative for the KQs. We also excluded data available only in

abstracts because they were not reported in enough detail to extract results or assess study design, conduct, or analysis.

Primary outcome categories are weight loss, mortality, type 2 diabetes, quality of life, and ability to perform daily activities. All other outcomes are secondary.

- For Key Question 1, we focused on biological, pathophysiological, and mechanistic studies.
- For Key Question 2, we included comparative and non-comparative studies (registries, cross-sectional studies, cohort studies).
- For Key Questions 3a, 3b, and 3d we included both comparative and non-comparative studies.
- For Key Question 3c, we included prospective cohort studies that report on predictive models for the success or failure of bariatric surgery in regards to weight outcomes.
- Because KQs 4a and 4b are about comparative effectiveness and/or safety, only comparative studies, including randomized controlled trials (RCTs) and nonrandomized comparative studies, are eligible.
- For Key Question 5a, we included both comparative and non-comparative studies, while for Key Question 5b we include randomized and non-randomized comparative studies.

Randomized trials are the preferred design to estimate causal effects of bariatric procedures, because randomization ensures that, on average, the compared groups are similar in terms of measured and unmeasured effect modifiers. In the absence of randomization, the compared groups are likely to differ in terms of important prognostic factors (including confounders) that are known to be associated with the outcome of interest. Not accounting for these differences between the compared treatment groups is likely to result in biased estimates of treatment effects.¹⁹ For example, the anatomical modifications involved in sleeve gastrectomy are likely to lead to gastric reflux but the reduction in the stomach pouch during Roux-en-Y gastric bypass does not have such an effect.^{20, 21} Thus, patients who are at increased risk of gastro-esophageal reflux disease are more likely to receive Roux-en-Y gastric bypass rather than sleeve.²² When comparing the rates of gastro-esophageal reflux disease as an adverse event between sleeve gastrectomy and Roux-en-Y gastric bypass without taking into account (e.g. through statistical modeling) the fact the certain patient characteristics (e.g. baseline risk of gastro-esophageal reflux disease) are related to treatment selection (i.e. patients with increased risk of GERD are more likely to receive Roux-en-Y gastric bypass) is not sufficient to attribute differences in adverse event rates between surgeries to surgeries themselves.

Moreover, non-randomized comparative studies ought to emulate (mimic) a target randomized trial in order to be maximally and reliably informative for policy actions based on the evidence base that they comprise.^{23, 24} By designing and/or analyzing observational data in a way that emulates a target randomized trial one can make inferences about causal treatment effects. This involves specification of the PICOTS elements as in the target trial and in addition emulation of the random treatment assignment to ensure that the groups being compared are similar. This can be achieved via matching using propensity score, stratification or regression, standardization or inverse probability weighting, and other more advanced methods such as g-estimation, or doubly robust methods.²⁵

Therefore, in the current technology assessment, estimates of treatment effects reported in non-randomized comparative studies were considered to represent causal associations between bariatric procedures and outcomes if the respective studies explicitly aimed to achieve a minimal balance between treatment groups in regards to confounders and other prognostic

factors associated with the outcome. Accounting for potential confounders and other prognostic factors is typically done either through design (e.g. matching) or analytical approach (e.g. statistical modeling).¹⁹ In studies that report data on multiple procedures but do not provide sufficient information on causal relationships, we considered each arm as a single-arm cohort and describe treatment effects by comparing outcome values before vs. after surgery or by providing descriptive statistics. This way, we aim to minimize unreliable inferences about causal treatment effects while at the same maximize the utilization of the evidence base to provide estimates that may still be useful to stakeholders for purposes other than causal treatment effects.

Searching for the Evidence

We conducted literature searches of studies in PubMed, EMBASE, CINAHL, PsycINFO, the Cochrane Central Trials Registry (CENTRAL), and the Cochrane Database of Systematic Reviews from January 1, 2010 to October 20, 2016, to identify primary research studies meeting our criteria. These databases should adequately cover the published literature on this topic. The search strategy is detailed in Appendix A, and was adapted as needed for each database. Additionally, we perused the reference lists of published clinical practice guidelines, relevant narrative and systematic reviews, and Scientific Information Packages (SIP) from manufacturers or other stakeholders. We searched ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) for ongoing studies and studies that are not published in the medical literature. In addition, we searched the FDA drugs and devices portals for unpublished data. We used existing systematic reviews primarily as sources of studies; we extracted and incorporated all studies *de novo* and did not summarize or incorporate existing systematic reviews, per se. Peer-review will provide an additional opportunity for the TEP and other experts in the field to ensure that no key publications have been missed. The search will be updated upon submission of the draft report for peer and public review.

All citations were independently screened by two researchers. At the start of abstract screening, we implemented a training session, in which all researchers screened the same articles and conflicts were discussed. During double-screening, we resolved conflicts as a group. All screening was done in the open-source, online software Abstrackr (<http://abstrackr.cebm.brown.edu/>).^{26, 27} All potentially relevant studies were rescreened in full text to ensure eligibility.

Data Extraction and Data Management

Each study was extracted by one methodologist. The extraction has been reviewed and confirmed by at least one other experienced methodologist. Any disagreements were resolved by discussion among the team. Data was extracted into a customized form in Systematic Review Data Repository (SRDR) online system (<https://srdr.ahrq.gov>) designed to capture all elements relevant to the Key Questions. Upon completion of the review, the SRDR database will be made accessible to the general public (with capacity to read, download, and comment on data). The basic elements and design of the extraction form are similar to those used for other AHRQ comparative effectiveness reviews and include elements that address population characteristics, including characteristics of pre- and post-surgical work-ups, descriptions of patients, descriptions of the interventions, exposures, outcomes, and comparators analyzed, outcome definitions, effect modifiers, enrolled and analyzed sample sizes, study design features, funding source, and results.

Assessment of Methodological Risk of Bias of Individual Studies

We assessed the methodological quality of each study based on predefined criteria. For RCTs, we would have used the Cochrane risk of bias tool,¹⁷ which asks about risk of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential biases. For observational studies, we used domains included in the Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool.²⁴ Quality/risk of bias issues pertinent to specific outcomes within a study were noted and considered when determining the overall strength of evidence for conclusions related to those outcomes.

Data Synthesis

All included studies have been summarized in narrative form and in summary tables that tabulate the important features of the study populations, design, intervention, outcomes, and results. These included descriptions of the study design, sample size, populations, interventions, follow-up duration, outcomes, results, funding source, and study quality. We did not find any relevant information in the FDA Web site, ClinicalTrials.gov, the ICTRP registry, or through the scientific information packet requests.

For KQ 1, we conducted a narrative review by searching editorials, published narrative and systematic reviews in specialty journals, and textbooks in relevant medical specialties. We employed a systematic and replicable, but non-exhaustive, methodology to efficiently appraise the available evidence as well as to identify major knowledge gaps.²⁸ Descriptive analyses for KQ2 were done at the outcome-category level, and not for each individual outcome. For example, we describe studies reporting “orthopedic outcomes” together, instead of separately describing studies reporting outcomes such as fractures (e.g., of the knee, hip, spine), need for joint replacement surgery (knee or hip), or falls. The goal was to generate evidence maps that provide stakeholders with information about the type and amount of research available, the characteristics of that research, and the topics where a sufficient amount of evidence has accumulated for synthesis. Evidence mapping can inform users of the current state of research findings that could be used to generate hypotheses, inform ongoing research, and identify research gaps.

To address KQ 3a, 3d, and 4a, we would have conducted quantitative syntheses for all primary outcome categories and for those secondary outcome categories for which at least 4 studies were available based on the evidence map. However, due to sparsity of available data reported in the existing evidence base, a statistical synthesis (either through pairwise meta-analysis or network meta-analysis) was not feasible. In addition, clinical heterogeneity in regards to interventions, outcomes, and populations did not allow for a synthesis the findings of which would be informative of treatment effects. is that estimates of treatment effects reported in pre- vs. post-surgery studies that do not include a comparison control group are subject to confounding bias and thus do not represent unbiased estimates of causal treatment effects. For the same reasons, no meta-regression was performed for probing statistical between-study heterogeneity in treatment effect estimates.

Because all procedures identified have been approved by the FDA and are currently used in the U.S. clinical practice, we did not conduct subgroup analysis by excluding non-FDA approved procedures or surgeries not practiced in the U.S.

For Key Question 3b and 4b, we examined heterogeneity of treatment effects for the patient- and intervention-level characteristics in Key Questions 2a and 2b by summarizing and appraising the findings reported in the eligible studies. No meta-regression and subgroup analyses were feasible due to the lack of data across studies.

For Key Question 3c, we identified studies that develop and/or validate predictive models for the change in weight outcomes before and after bariatric surgery. We summarized the variables used as predictors of treatment effects, the populations in which the models have been developed, whether any validation attempts have been undertaken, and metrics of model performance (e.g. calibration, discrimination etc.).

For Key Question 5a, we qualitatively synthesize the metrics of association between weight loss and short- or long-term outcomes. Because associations were reported in only very few studies using diverse metrics to quantify it, we did not perform a meta-analysis of the relevant metrics.

For Key Question 5b, we summarized whether the eligible studies reported mediation analyses to estimate the proportion of the bariatric surgical effect on outcomes other than weight loss that is accounted for by weight loss (indirect treatment effect).²⁹

Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes

We graded the strength of the body of evidence as per the AHRQ methods guide on assessing the strength of evidence.³⁰ We assessed the strength of evidence for each outcome. Following the standard AHRQ approach, for each intervention and comparison of intervention, and for each outcome, we assessed the number of studies, their study designs, the study limitations (i.e., risk of bias and overall methodological quality), the directness of the evidence to the KQs, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, and the overall findings across studies. Based on these assessments, we assigned a strength of evidence rating as being either high, moderate, or low, or there being insufficient evidence to estimate an effect.

Assessing Applicability

We assessed the applicability within and across studies with reference to demographics of enrolled participants (e.g. age and sex distributions), the degree of obesity, and the availability of treatments (e.g. contemporary treatments; availability/FDA approval of devices; established clinical practices in the U.S.).

Results

Summary of Studies

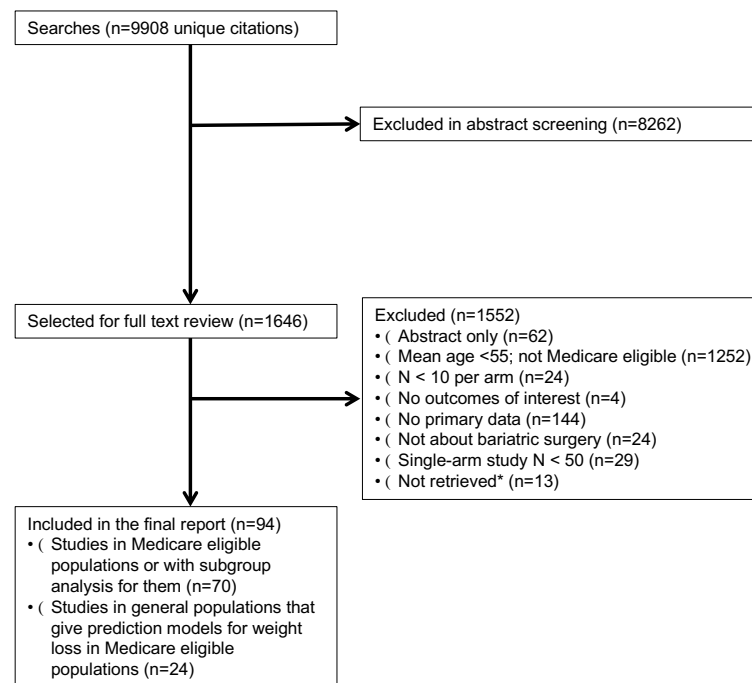
The literature search yielded 9,908 citations (Figure 2) that were screened for eligibility. Of those, 8,262 were excluded in abstract screening. A total of 94 studies met the eligibility criteria, of which 24 reported models to predict weight loss or absolute body weight after bariatric treatment and the remaining 70 studies pertained to the effectiveness and safety of bariatric procedures. Appendix A presents the literature search strategies for each searched database. Appendix B lists the articles that were reviewed in full text that were excluded along with reasons of exclusion.

Appendix E describes in detail the patient characteristics in the studies reporting effectiveness or safety data in the Medicare eligible population. Of the 70 studies, 7 studies³¹⁻³⁷ used claims data from beneficiaries enrolled in Medicare. Of the 63 remaining studies, 3 reported overall or subgroup analyses on patients with end-stage renal disease/dialysis-dependent renal failure; 3 on disabled patients; and 57 on patients with a mean or median age of 55 or older.

We did not identify any randomized trials on the effectiveness and safety of bariatric surgery conducted in patients aged 55 years or older or in patients with other Medicare-eligibility criteria. A total of 28 non-randomized studies reported data on more than one bariatric procedures but only 13 of those had a design and/or analytical approach that explicitly attempted to address confounding bias. Treatment effects reported in these studies where confounding was accounted for approximate causal associations between bariatric procedures and weight loss outcomes, adverse events/complications, or health outcomes other weight loss (non-weight loss outcomes). The remaining studies reported weight changes in outcomes before vs. after bariatric surgery or provided descriptive statistics such incidence or prevalence of outcomes among patients undergoing bariatric surgery without a comparison to an independent or paired group. Details about study design, baselines, and treatments are given in Appendix C, D, and E, respectively.

Appendix F and G describe in detail the characteristics of the 24 studies reporting a total of 40 distinct prediction models of weight loss outcomes. There was no study with internal or external model validation. Few studies were conducted in US settings. The majority of studies were conducted recently, mainly after 2010.

Figure 2. Flow diagram for eligible studies



Key Question 1

What are the theorized mechanisms of action of bariatric procedures on weight loss and on type 2 diabetes in the Medicare population?

Bariatric surgery defines a group of procedures that alter gastrointestinal anatomy in order to produce long-term weight loss. Because food intake and absorption are central in weight gain, the anatomical changes occurring during bariatric surgery aim to disrupt these processes. One mechanism to achieve this is by restricting the diameter of the stomach's esophageal orifice, or restricting the stomach's effective volume, thereby reducing the volume and speed of food intake. Another approach involves diverting the physiological route of ingested food to more distal segments of the gastrointestinal tract, leading to malabsorption and reduced absorption of ingested food. These mechanisms seem to be dominant in the early weight loss period after surgery.³⁸ In the long term, additional mechanisms appear to be responsible for maintaining weight loss. First, these mechanisms involve secondary changes to food intake due to the anatomical changes occurring during bariatric surgery. In particular, patients develop aversive conditioning food restriction to avoid experiencing gastrointestinal disturbances (e.g., dumping syndrome, dysphagia, vomiting, flatus), due to surgery-induced changes of the anatomy and function of the gastrointestinal tract.³⁹ Second, current evidence suggests that the anatomical alterations of the gastrointestinal tract affect a complex array of gut hormones which can mediate

many of the metabolic changes seen post-operatively by affecting insulin secretion and sensitivity, reducing appetite, increasing satiety, and also increasing energy expenditure.⁴⁰

The operations classically defined as “restrictive” are the laparoscopic gastric band (LAGB) and the laparoscopic sleeve gastrectomy (LSG). The LAGB is an implanted device that is passed around the upper stomach during surgery. It has an associated balloon attached to a subcutaneous port. By injecting fluid, the balloon can be inflated to narrow the stomach, creating a tiny pouch. This physical barrier to food limits intake, reduces emptying of the esophagus, and increases pressure on the vagal fibers, leading to satiety.⁴¹

The LSG procedure laterally resects the stomach, leaving a narrow tube of tissue based off of the lesser curvature of the stomach. The lateral portion of upper stomach (the fundus) is removed during the procedure; the bottom portion of the stomach (the antrum) is left intact. This makes the stomach unable to expand and limits intake. Controversy exists over whether smaller LSG post-operative volume relates to improved weight loss, suggesting mechanisms other than pure restriction are at work. These may include reduction in intestinal transit time, possibly due to increased pressure within the gastric lumen, vagal effects, and changes in gut hormone levels associated with increased satiety.⁴¹ Ghrelin, a hormone involved in appetite stimulation produced in the gastric fundus, is reduced after LSG.⁴²

The operation classically defined as “restrictive/malabsorptive” is the Roux-en-Y gastric bypass (RYGB). The RYGB procedure creates a small pouch at the top of the stomach, excluding the remainder of the stomach (including the fundus) from contact with ingested food. This reduces the amount of food ingested. The small intestine is then divided. The distal end of the divided bowel is pulled up and attached to the small stomach pouch, creating the new passage for food to enter the gut, or alimentary limb. The proximal end of the divided bowel, which now carries important digestive enzymes produced by the stomach, liver, and pancreas, is reattached to the alimentary limb at a distance downstream. At this point, the digestive enzymes and the food will meet to begin digestion downstream from where this would begin in a patient with unaltered anatomy, which is classically explained as the malabsorptive portion of the procedure. More recent study has debunked this theory, with little evidence for true malabsorption (increased fecal fat, decreased albumin, diarrhea) when patients follow a recommended low-fat diet.

It is increasingly likely that metabolic effects are responsible for the sustained weight loss seen after RYGB. The altered pathway of food, which avoids the gastric fundus and reaches the distal small intestine more rapidly, changes levels of the gut hormones that regulate satiety.⁴³⁻⁴⁵ Similarly to what is seen after LSG, ghrelin levels are decreased post-operatively, leading to decreased appetite. In the distal small intestine, increased levels of glucagon-like-peptide-1 (GLP-1), peptide YY (PYY), and oxyntomodulin (OXM) are secreted, promoting satiety. In addition, GLP-1 improves pancreatic beta cell function, with better control of diabetes seen in advance of weight loss (hindgut theory). Changes in the gut microbiome and increases in circulating bile acids also appear to improve glucose tolerance.⁴⁶ Increased pressure on vagal fibers from the small gastric pouch likely also plays a role in appetite regulation.

Much attention has been given to improvement seen in type 2 diabetes following weight loss surgery, especially following RYGB.⁴⁷ This is typically seen within the first few days to weeks after surgery, which is in advance of significant weight loss. There are several possible mechanisms for this besides increased levels of GLP-1. Exclusion of food from the duodenum may cause downregulation of a hypothetical molecule that decreases incretin levels, allowing for more appropriate insulin responses to meals and thus improving post-prandial glucose levels

(foregut theory). Intestinal adaptation, with increased expression of glucose transporters seen in the RYGB alimentary limb likely improves glycemic control, as do changes in the gut microbiome and increased circulating bile acids.^{46, 47}

Food preferences also change after RYGB.^{41, 48} Patients self-report less interest in eating calorie-dense foods, with a lower preference for high-sugar and high-fat foods than before surgery.⁴⁹ This may relate to GLP-1 and PYY effects on the brainstem, as both hormones activate areas of the brainstem and may contribute to conditioned taste aversion. Researchers using functional MRI have also demonstrated reduced reward-center activation for post-RYGB patients when presented with calorie-dense foods.

Key Question 2

In studies that are applicable to the Medicare population and enroll patients who have undergone bariatric therapy, what are

- a) the characteristics and indications of patients receiving bariatric therapy including descriptives of age, body mass index (BMI), and comorbid conditions**
- b) the characteristics of the interventions, including the bariatric procedures themselves as well as pre- and/or post-surgical surgical work-ups (e.g., psychiatric evaluations, behavioral and nutritional counseling)**
- c) the outcomes that have been measured, including peri-operative (i.e., 90 days or less after bariatric surgery), short-term (2 years or less from surgery), mid-term (more than 2 but 5 or less years), and long-term (more than 5 years after surgery) outcomes?**

Patient characteristics and indications for bariatric surgery

For the population eligible for Medicare benefits, regardless of eligibility criteria, the mean or median BMI at baseline was reported in 53 studies and ranged from 34.3 percent to 56.8 percent. Sixty studies reported the ratio between male and female patients. Two studies^{50, 51} included only female patients undergoing bariatric surgery, while one⁵² included only male patients. In the remaining 53 studies, 51.4 to 89.6 percent of the study population was female.

Appendix E describes the comorbid conditions in the eligible studies. Three studies were conducted in patients who all had type 2 diabetes,⁵³⁻⁵⁵ while in another 27 studies at least 50 percent of patients had type 2 diabetes. One study compared outcomes in patients with type 1 and type 2 diabetes.⁵⁶ The prevalence of hypertension at baseline ranged from 35.2 percent to 97.7 percent. One study was exclusively conducted on patients who were on chronic dialysis.⁵⁷ The prevalence of pulmonary comorbidities ranged from 2 percent to 44.3 percent. Five studies reported the prevalence of chronic obstructive pulmonary disease. Psychiatric comorbidities were reported in nine studies with the most commonly reported psychiatric comorbid condition being depression (n=5 studies). Hypercholesterolemia and other lipid disorders were reported as comorbidities in 25 studies; the percentage of bariatric patients with these comorbidities ranged from 11.9 percent to 95 percent. Gastroesophageal reflux disease was reported in 12 studies and its prevalence ranged from 1.35 percent to 64.8 percent. Thirteen studies reported musculoskeletal comorbidities, mainly osteoarthritis and other degenerative joint disorders. The prevalence of congestive heart failure was reported in six studies and ranged from 11.1 percent to 32.4 percent, while one study examined bariatric surgery in patients with congestive heart failure

exclusively.⁵⁸ Less commonly reported comorbidities include hypothyroidism (n=2 studies), neurological disorders (n=6), and alcohol abuse (n=2 studies).

Interventions

We did not identify any studies in the Medicare eligible population reporting on endoscopically-performed bariatric procedures. In particular, there are no studies in the Medicare eligible population in regards to intragastric balloons or other nonballoon space-occupying endoscopic bariatric devices, aspiration therapy, endoscopic sleeve gastropasty, endoscopic duodenojejunal or gastroduodenojejunal bypass sleeve, duodenal mucosal resurfacing, and self-assembling magnets for endoscopy. Overall, evidence on bariatric therapies in the Medicare eligible population pertains exclusively to bariatric surgery and thus all bariatric procedures in the current technology assessment represent surgical procedures.

Table 1 shows the different types of bariatric surgical procedures that have been evaluated in the Medicare eligible population for the treatment of obesity. The most commonly studied surgery was RYGB (n=41), followed by sleeve gastrectomy (SG; n=24) and adjustable gastric banding (AGB; n=24). Twenty-four studies used a combined treatment group that consisting of two or more bariatric surgical procedures. The pertinent data were reported in only four studies and included RYGB and SG⁵²; RYGB, AGB, vertical banded gastropasty (VBG), and biliopancreatic diversion with duodenal switch (BPD-DS)⁵⁹; gastric bypass and AGB⁶⁰; AGB, SG, RYGB, and revisional surgery.³² We found a small number of studies on mini-gastric bypass (MGB) alone, (n=1), revisional surgery alone (n=1), single-anastomosis duodenal switch (SADS) alone (n=1), VBG alone (n=1), and biliopancreatic diversion alone (n=3). One study evaluated outcomes in patients who concurrently received bariatric surgery and hiatal hernia repair.⁶¹ We did not identify any studies in the Medicare eligible population on gastric plication, vagal blockade, omentum removal (omentectomy), gastric stimulation, and mucosal ablation.

Table 1 also shows how many bariatric surgeries were performed through laparotomy (open) and/or laparoscopically according to the specific procedure. The majority of bariatric surgeries had been performed laparoscopically, while only RYGB and BPD-DS had also been performed through laparotomy. Ten studies reported data for patients who received the same surgery either performed either open or laparoscopically (RYGB, n=7; SG, n=2; BPD-DS, n=1).

Table 1. Method of surgery by bariatric procedure studied in the Medicare eligible population

| Bariatric Procedure | Method of surgery | | | |
|---------------------|-------------------|-------------------|-----------------------------|--------------|
| | Open only | Laparoscopic only | Either open or laparoscopic | Not reported |
| AGB | | 23 | | 1 |
| MGB | | 1 | | |
| Multiple surgeries | 1 | 6 | 7 | 10 |
| RYGB | 3 | 26 | 7 | 5 |
| SADS | | 1 | | |
| SG | | 22 | 2 | |
| VBG | | 1 | | |
| BPD-DS | 1 | 1 | 1 | |

The numbers correspond to the study arms across all eligible studies. Not shown are the concurrent performance of bariatric surgery and hernia repair (laparoscopic) and bariatric surgery before total knee arthroplasty (the mode of operation was not reported). Blank cells correspond to no studies. AGB: adjustable gastric banding; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; VBG: vertical band gastropasty; BPD-DS: biliopancreatic diversion with duodenal switch

Appendix D shows the pre- and/or post-surgical surgical work-ups (e.g., psychiatric evaluations, behavioral and nutritional counseling) that were reported in the eligible studies.

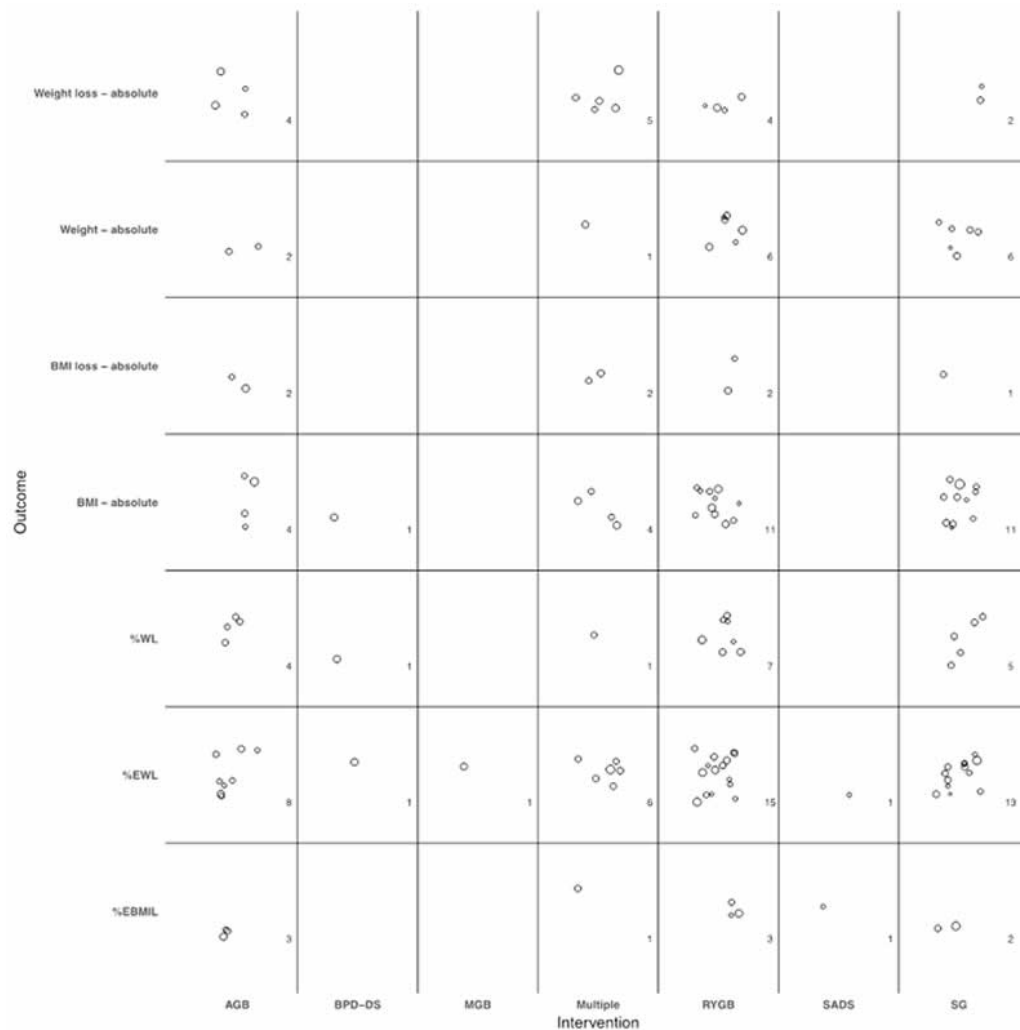
Outcomes

Because of the wide variety of outcome definitions, we classified outcomes in hierarchical categories based on their clinical importance for the management of bariatric patients (see Methods).

Figure 3 shows the weight loss outcomes measured in Medicare eligible patients undergoing bariatric surgery. Percent excess weight loss (EWL) and percent weight loss (WL) have been examined as outcomes for the vast majority bariatric surgical procedures, while absolute changes in weight and BMI have been studied less commonly. Of note, there are no studies about weight outcomes after VBG, while there are is limited evidence regarding MGB and SADS. Most outcomes pertained to laparoscopically conducted surgeries while only five outcomes had been examined after open surgeries (Table 2). These are percent excess BMI loss (EBMIL) and changes in BMI after open RYGB⁶²; and percent EWL, percent WL, and changes in BMI after open BPD-DS.⁶³

Figure 3. Weight loss outcomes reported in studies in the Medicare eligible population according to bariatric procedure.

Each circle represents a procedure-outcome pair within each eligible study; the diameter of each circle is proportional of the logarithm sample size of the arm for the largest applicable arm in each study

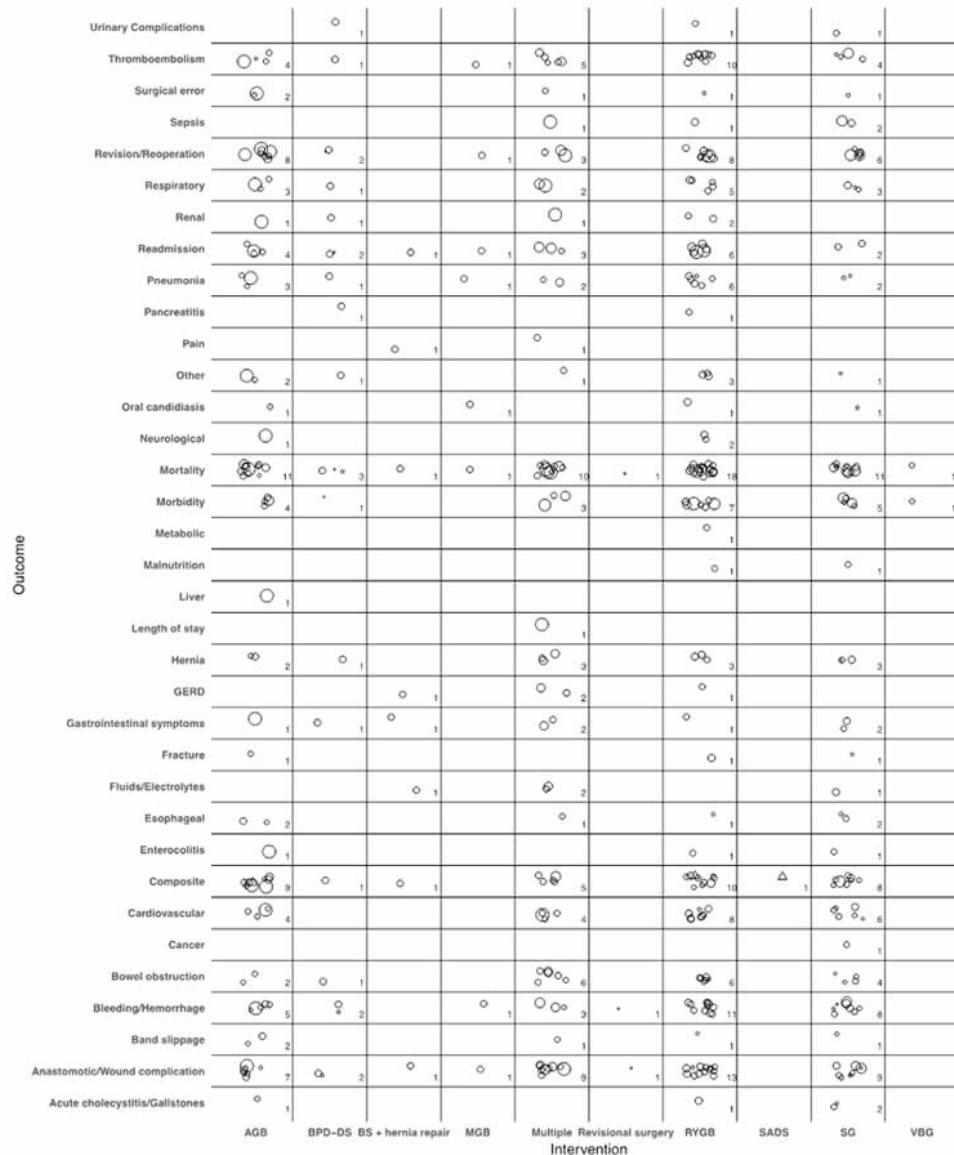


AGB: adjustable gastric banding; BS: bariatric surgery; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; BPD-DS: biliopancreatic diversion with duodenal switch; BMI: body mass index; EBMIL: excess BMI loss; EWL: excess weight loss; WL: weight loss

The incidence of a wide variety of adverse events and/or surgical complications in the 90-day post-operative period after bariatric surgical procedures is shown in Figure 4. The sample sizes for these outcomes vary across procedures. The largest sample sizes have been used for AGB, RYGB, and SG, while evidence for BPD-DS, MGB, SADS, and VBG comes from smaller sample sizes.

Only 17 adverse events/surgical complications were reported for patients undergoing open surgery (Table 2). These include post-operative mortality after open RYGB³⁷ and the following 16 outcomes after open BPD-DS⁶³: anastomotic/wound complications, bleeding/hemorrhage, bowel obstruction, gastrointestinal symptoms, hernia, mortality, pancreatitis, pneumonia, readmission, renal, respiratory, revision/reoperation, thromboembolism, urinary complications, other complications, as well as a composite endpoint of multiple adverse events/complications.

Figure 4. Post-operative (0 to 90 days after bariatric surgery) adverse events and surgical complications studied in the Medicare eligible population according to bariatric procedure.
Each circle represents a procedure-outcome pair within each eligible study; the diameter of each circle is proportional of the logarithm of sample size of the arm for the largest applicable arm in each study



AGB: adjustable gastric banding; BS: bariatric surgery; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; VBG: vertical band gastroplasty; BPD-DS: biliopancreatic diversion with duodenal switch; GERD: gastroesophageal reflux disease

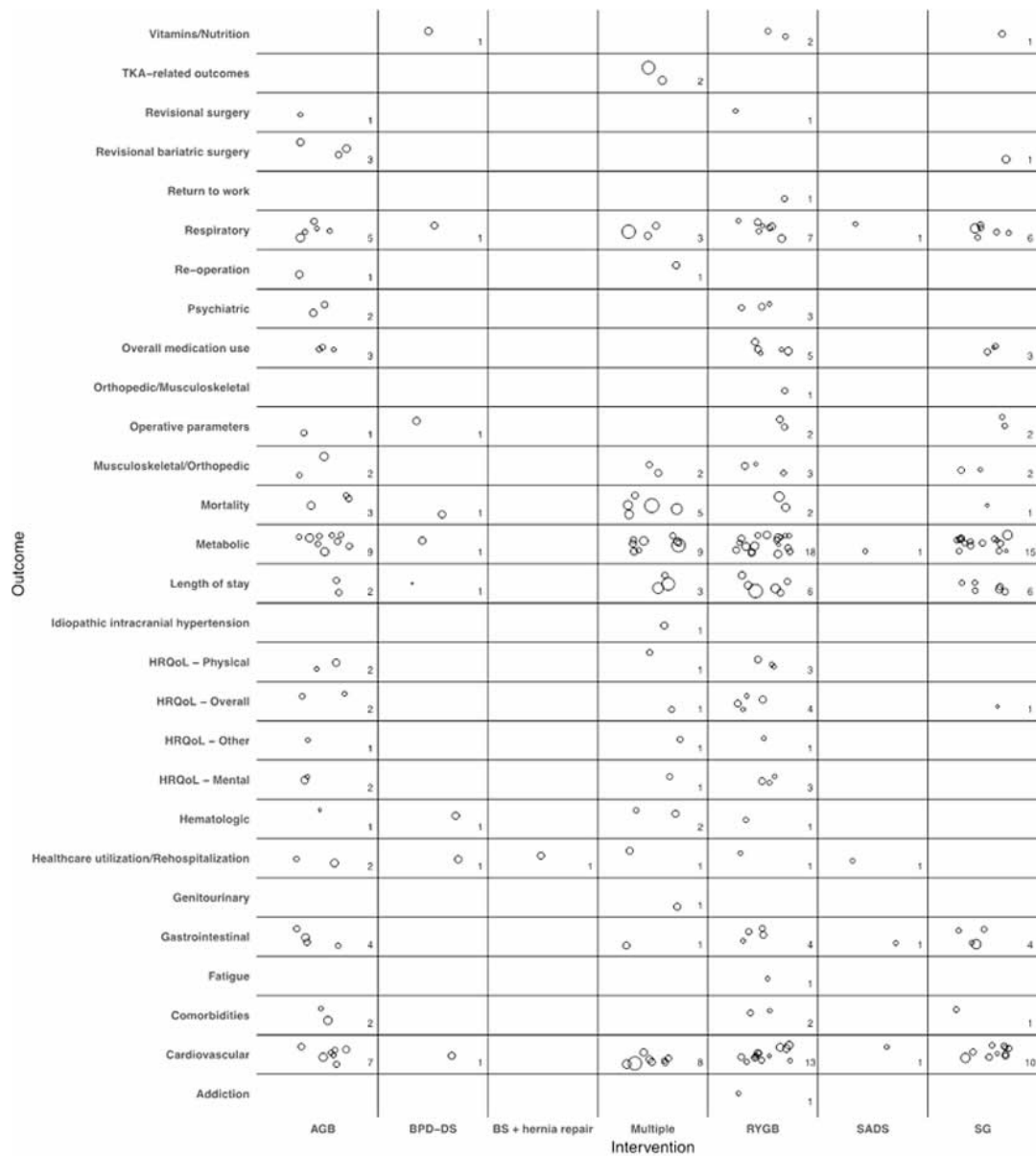
Other outcomes that have been studied in patients undergoing bariatric surgery are shown in Figure 5. Commonly examined are respiratory outcomes (n=23), metabolic/diabetes-related outcomes (n=53), and cardiovascular outcomes (n=40). Health-related quality of life, whether physical, mental, or overall, has not been extensively studied in Medicare eligible patients. The majority of evidence pertains to RYGB but limited evidence exists in regards to other procedures.

The sample sizes of the study arms vary substantially. Mortality, metabolic, cardiovascular, and respiratory outcomes have relatively large sample sizes, while for most health-related quality of life outcomes smaller sample sizes have been utilized.

As with weight outcomes and adverse events/surgical complications, all but 28 outcomes pertain to laparoscopic surgeries (Table 2). Evidence about open surgery refers to open RYGB (cardiovascular outcomes, comorbid conditions, gastrointestinal outcomes, mental and physical health-related quality of life, metabolic outcomes, orthopedic outcomes, psychiatric outcomes, respiratory outcomes, and return to work), and BPD-DS (cardiovascular outcomes, healthcare utilization/rehospitalization, hematological outcomes, metabolic outcomes, mortality, perioperative outcomes, respiratory outcomes, and vitamins/nutrition-related outcomes).

Figure 5. Short term and long term health outcomes other than weight loss outcomes and adverse events/surgical complications studied in the Medicare eligible population according to bariatric procedure.

Each circle represents a procedure-outcome pair within each eligible study; the diameter of each circle is proportional of the logarithm of the sample size of the arm for the largest applicable arm in each study



AGB: adjustable gastric banding; BS: bariatric surgery; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; BPD-DS: biliopancreatic diversion with duodenal switch; TKA: total knee arthroplasty; HRQoL: health-related quality of life

Table 2. Summary of outcomes after bariatric surgery by procedure and method of surgery (open versus laparoscopic) in the Medicare eligible population

| Bariatric Procedure | Adverse Events, N | | Weight/BMI, N | | Other Outcomes, N | |
|---------------------|-------------------|--------------|---------------|--------------|-------------------|--------------|
| | Open | Laparoscopic | Open | Laparoscopic | Open | Laparoscopic |
| AGB | | 81 | | 27 | | 54 |
| MGB | | 8 | | 1 | | |
| Multiple surgeries | | 26 | | 10 | | 15 |
| RYGB | 1 | 97 | 2 | 34 | 10 | 53 |
| SADS | | 1 | | 2 | | 5 |
| SG | | 76 | | 36 | | 47 |
| VBG | | 2 | | | | |
| BPD-DS | 16 | 3 | 3 | | 8 | |

AGB: adjustable gastric banding; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; VBG: vertical band gastroplasty; BPD-DS: biliopancreatic diversion with duodenal switch

Key Question 3

- In Medicare eligible patients, what are the effects of different bariatric therapies (contrasted between them or vs. non-bariatric therapies) on weight outcomes (including failure to achieve at least minimal weight loss)?
- What patient- (KQ2a) and intervention-level characteristics (KQ2b) modify the effect of bariatric therapies on weight outcomes (including failure to achieve at least minimal weight loss)?
- In Medicare eligible patients who have undergone bariatric therapy, what is the frequency and the predictors of failing to achieve at least minimal weight loss?
- In Medicare eligible patients who do not achieve weight loss after primary bariatric treatment, what is the effect of revisional bariatric therapies (contrasted between them or vs. non-bariatric therapies) on weight outcomes?

KQ 3.a. Comparative studies

Three studies reported on the comparative effects of bariatric surgeries on weight change.^{54, 64, 65}

Lee et al. compared mean weight loss, mean BMI loss, percent weight loss, and percent excess weight loss at 6 and 12 months after surgery in RYGB versus SG, RYGB versus LAGB, and SG versus LAGB. As shown in Table 3, RYGB resulted in greater improvements for all four weight outcomes compared to either SG or LAGB. Similarly, the effect of SG on the four weight outcomes was greater than this of LAGB.⁶⁴

Table 3. Changes in weight outcomes at 6 months and 12 months after RYGB, SG, and LAGB in the Medicare eligible population

| | Mean (SD) | | | Difference in outcome measure (P-value) | | |
|---|-------------|-------------|-------------|---|----------------|----------------|
| | RYGB (n=84) | SG (n=48) | LAGB (n=30) | RYGB vs. SG | RYGB vs. LAGB | SG vs. LAGB |
| Weight lost (kg) | | | | | | |
| 6 months post-surgery | 34.0 (12.9) | 23.5 (17.9) | 14.0 (14.1) | 10.5 (P<0.001) | 20 (P<0.001) | 9.5 (P<0.001) |
| 12 months post-surgery | 40.7 (14.5) | 24.4 (22.1) | 15.3 (15.7) | 16.3 (P<0.001) | 25.4 (P<0.001) | 9.1 (P=0.001) |
| BMI reduction (kg/m²) | | | | | | |
| 6 months post-surgery | 11.1 (4.0) | 7.8 (6.1) | 4.4 (4.5) | 3.3 (P<0.001) | 6.7 (P<0.001) | 3.4 (P<0.001) |
| 12 months post-surgery | 13.4 (4.1) | 7.9 (7.3) | 5.0 (5.0) | 5.5 (P<0.001) | 8.4 (P<0.001) | 2.9 (P=0.001) |
| Percent weight loss | | | | | | |
| 6 months post-surgery | 26.0 (7.2) | 18.5 (13.7) | 10.3 (10.4) | 7.5 (P<0.001) | 15.7 (P<0.001) | 8.2 (P<0.001) |
| 12 months post-surgery | 31.5 (8.5) | 20.2 (21.5) | 12.0 (11.7) | 11.3 (P<0.001) | 19.5 (P<0.001) | 8.2 (P<0.001) |
| Percent excess weight loss | | | | | | |
| 6 months post-surgery | 34.2 (9.4) | 24.6 (18.2) | 13.9 (14.3) | 9.6 (P<0.001) | 20.3 (P<0.001) | 12.5 (P<0.001) |
| 12 months post-surgery | 41.4 (11.6) | 26.7 (27.6) | 16.1 (15.9) | 14.7 (P<0.001) | 25.3 (P<0.001) | 25.3 (P<0.001) |

LAGB: laparoscopic adjustable gastric banding; RYGB: Roux-en-Y gastric bypass; SD: standard deviation

Leonetti et al. found that, compared to conventional treatment including pharmaceutical agents and lifestyle modifications (diet and physical activity), a higher proportion of patients undergoing LSG achieved better weight outcomes at 18 months of follow-up. Seventy-one percent of patients in the LSG group experienced weight loss compared to 2.8 percent in the conventional therapy group. Similarly, the mean BMI loss in the LSG group 13.5 kg/m² compared to a mean 0.17 kg/m² increase in the conventional treatment group.⁵⁴

Finally, Ritz et al. found that, 1 year after surgery, weight loss was higher for RYGB and SG compared to LAGB for patients 60 years of age or older. The percent of initial weight lost was 9.2 percentage points higher for those undergoing RYGB and 5.5 percentage higher for those undergoing SG compared to patients receiving LAGB.⁶⁵

Although 2 studies (Lee et al. and Ritz et al.) reported estimates of weight changes at 12 months after surgery for SG versus LAGB and for RYGB versus LAGB, the different modeling strategies (linear mixed models for longitudinal data in Ritz et al.; inverse-probability treatment weighted propensity score in Lee et al.) used to account for confounders and other prognostic factors associated with weight loss as well as the differences in the modelled covariates (e.g. Ritz et al. do not account for comorbid conditions as does the study by Lee et al.) do not allow for a meaningful statistical synthesis of the results.

KQ 3.b. Pre- versus post-surgery studies

A total of 42 studies reported the effect of bariatric surgeries by estimating the differences in weight outcomes between baseline and at different time points during follow-up.

Adjustable gastric banding

AGB was evaluated in 12 studies. The outcomes assessed included percent EBML (n=3 studies), percent EWL (n=8 studies), percent WL (n=4 studies), BMI loss (n=2 studies), weight loss (n=1 study). In addition, three studies reported mean BMI at baseline and at different points

during follow-up, and five studies reported mean weight at baseline and at different points during follow-up.

Table 4 shows the changes over time in different weight outcomes by study. All studies evaluated changes in weight outcomes at one year after surgery. Eight studies reported weight changes at 2 years and only 6 studies provided data on follow-up longer than 2 years.

Across all studies, the mean percent EBMI ranged from 35.5 percent to 43.3 percent at 1 year. The mean percent EWL at 1 year ranged from 16 percent to 50 percent and the percent WL from 12 percent to 13.7 percent. Finally, the mean BMI reduction at 1 year ranged from 5 to 8.4 kg/m² and the mean weight reduction ranged from 40.7 kg to 93.8 kg.

Because the standard deviation of weight change was not consistently reported across studies, a meta-analysis was not conducted. Another reason for not conducting a meta-analysis is that these results are based on crude pre- vs. post-surgery comparisons and cannot account for temporal trends that are not due to bariatric surgery. Thus, a description of their range values rather than averaging them was performed.

Moon et al., in addition to mean percent EWL (Table 4), also evaluated the effect of LAGB on weight failure defined as percent EWL less than 30. At the time of last follow-up, 40/68 patients (58.8 percent) failed to achieve weight loss, while 3 patients (4.4 percent) gained weight.⁶⁶

O'Keefe et al. reported that the average percent EWL among patients undergoing any of RYGB, LAGB or VSG was 44.5 percent (range, 11.1–77.0 percent) at 6 months and 55.1 percent (range, 8.73–94.9 percent) at 1 year. Percent EWL by surgery type was not reported and could not be estimated with the available data.⁶⁷

Ritz et al. graphically present the percent WL at 3, 6, 9 and 12 months after AGB surgery, which consistently increased at each time point of follow-up.⁶⁵

Loy et al. graphically present the trajectory of percent EWL up to 5 years after surgery. Percent EWL increased up to >40 percent at 2 years after surgery, then remained stable between years 2 and 3, and increased again in years 4 and 5. However, the number of patients followed over time declined from 55 at baseline to nine at 5 years.⁶⁸

Table 4. Changes in weight outcomes in patients undergoing adjustable gastric banding in the Medicare eligible population.

Data are presented as mean (SD) for each outcome.

| Author Year PMID | 0 mo | 3 mo | 6 mo | 9 mo | 12 mo | 15 mo | 18 mo | 24 mo | 3 y | 4 y | 5 y | 6 y | 7 y | 8 y |
|---------------------------------|------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|----------------------|-----|-----|-----|--------------|-----|-----|
| percent EBMIL | | | | | | | | | | | | | | |
| Clough 2011 20490708 | | | | | 43.3 (NR) | | | | | | | 44.1 (NR) | | |
| Moon 2016 26220238 | | | 29.8 (NR) | | 35.5 (NR) | | 37 (NR) | 35.6 (NR) | | | | | | |
| Zaveri 2016 27795883 | | 25.6 (8.1) ^f | 32.4 (6.9) ^f | 35.3 (5.8) ^f | 36.6 (7.2) ^f | 37 (8.4) ^f | 37.2 (8.9) ^f | | | | | | | |
| percent EWL | | | | | | | | | | | | | | |
| Quebbema nn 2005 16925254 | | | | | 32 (NR) | | | 35 (NR) | | | | | | |
| Ramirez 2012 22551574 | | | | | 32.8 (17) | | | | | | | | | |
| Wise 2016 26091994 | | | 27.2 (12.6) | | 30.2 (19.2) | | | | | | | | | |
| Moon 2016 26220238 | | | 26.1 (NR) | | 30.9 (NR) | | 32.8 (NR) | 31.5 (NR) | | | | | | |
| Lee 2016 27220823 | | | 13.9 (14.3) | | 16.1 (15.9) | | | | | | | | | |
| Ochner 2013 23700235 | | | | | 50 (NR) ^g | | | 53 (NR) ^g | | | | | | |
| Zaveri 2016 27795883 | | 22.5 (7.4) ^f | 28.4 (4.7) ^f | 29.9 (5.4) ^f | 30.3 (4.4) ^f | 30.4 (6.3) ^f | 30.4 (6.2) ^f | | | | | | | |
| percent WL | | | | | | | | | | | | | | |
| Moon 2016 26220238 | | | 11.8 (NR) | | 13.7 (NR) | | 15 (NR) | 14.3 (NR) | | | | | | |

| Author Year PMID | 0 mo | 3 mo | 6 mo | 9 mo | 12 mo | 15 mo | 18 mo | 24 mo | 3 y | 4 y | 5 y | 6 y | 7 y | 8 y |
|----------------------------------|-------------------------|------|--------------------------|------|--------------------------|-------|------------------------|------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| Lee 2016 27220823 | | | 10.3 (10.4) | | 12 (11.7) | | | | | | | | | |
| BMI (kg/m ²) | | | | | | | | | | | | | | |
| Ramirez 2012 22551574 | 44 (NR) ^a | | | | 35.8 (4.5) | | | | | | | | | |
| BMI loss (kg/m ²) | | | | | | | | | | | | | | |
| Mittermair 2008 18830777 | | | | | 8.4 (NR) | | | 11.0 (NR) | 12.3 (NR) | 12.4 (NR) | 11.8 (NR) | 12.5 (NR) | 10.2 (NR) | |
| Lee 2016 27220823 | | | 4.4 (4.5) | | 5 (5) | | | | | | | | | |
| O'Keefe 2010 20532834 | | | 8.1 (6.1) ^e | | 6.5 (7) ^e | | | | | | | | | |
| Loy 2014 24582414 | | | 6 (5.9) ^e | | 8 (5.9) ^e | | 9 (6.1) ^e | | 10 (5.9) ^e | 13 (5.6) ^e | 14 (5.4) ^e | 14 (6) ^e | 13 (7.1) ^e | 13 (5.4) ^e |
| Weight (kg) | | | | | | | | | | | | | | |
| Ramirez 2012 22551574 | 124.5 (NR) ^a | | | | 96.1 (14.1) | | | | | | | | | |
| Weight loss (kg) | | | | | | | | | | | | | | |
| Lee 2016 27220823 | | | 14 (14.1) | | 15.3 (15.7) | | | | | | | | | |
| Clough 2011 20490708 | | | | | | | | | | | | 23.2 (NR) | | |
| O'Keefe 2010 20532834 | | | 21.3 (22.6) ^e | | 17.3 (24.1) ^e | | | | | | | | | |
| Loy 2014 24582414 | | | 16 (21.1) ^e | | 20 (21.5) ^e | | 24 (22.5) ^e | 25 (23.6) ^e | 29 (21.1) ^e | 34 (19.7) ^e | 41 (20) ^e | 41 (20) ^e | 41 (19.7) ^e | 41 (19.2) ^e |
| Mittermair 2008 18830777 | | | | | 23.5 (NR) ^b | | | 29.5 (NR) ^a | 29.5 (NR) ^a | 27.5 (NR) ^a | 28.5 (NR) ^a | 32.5(N R) ^a | 19.5 (NR) ^a | |

| Author Year PMID | 0 mo | 3 mo | 6 mo | 9 mo | 12 mo | 15 mo | 18 mo | 24 mo | 3 y | 4 y | 5 y | 6 y | 7 y | 8 y |
|--------------------------------|------|------|------|------|----------------------|-------|-------|------------------------|-------------------------|---------------------------|---------------------------|-------------------------|---------------------------|-----|
| Mittermair 2008 18830777 | | | | | 24 (NR) ^c | | | 30 (NR) ^b | 29 (NR) ^b | 28 (NR) ^b | 29 (NR) ^b | 33 (NR) ^b | 19 (NR) ^b | |
| Mittermair 2008 18830777 | | | | | 26 (NR) ^d | | | 26.5 (NR) ^c | 35 (NR) ^c | 29.5 (NR) ^c | 30.5 (NR) ^c | 35 (NR) ^c | 25.5 (NR) ^c | |

NR: not reported; EBML: excess BMI loss; EWL: excess weight loss; WL: weight loss; mo: months after surgery; y: years after surgery; PMID: PubMed ID

^a Numbers correspond to median weight and BMI for all patients undergoing any of AGB, LSG, or LRYG are reported. Baseline weight and BMI were not reported separately by procedure.

^b All patients (mean age 55.6 years)

^c Patients 50-60 years old

^d Patients older than 60 years

^e Estimated based on the reported mean and standard deviation of BMI or weight at baseline and the respective time point at follow-up. We assumed a correlation coefficient of 0.5.

^f Standard deviations were computed based on reported 95% confidence intervals and assuming a t-distribution because of small sample sizes

^g Outcome values were reported graphically in the primary study. Values presented in the table are approximated based on the original graph.

Biliopancreatic Diversion with Duodenal Switch

Michaud et al. graphically presented the trajectory of percent EWL at 6, 12, 24, 36, 48, and 60 months after BPD-DS for patients 60 years or older. Percent EWL increased between surgery and 24 months and then remained stable until 60 months. Over a mean follow-up of 7.1 years, the mean percent EWL was 72.2 (SD, 20.7). In addition, 82.9 percent of patients lost more than 50 percent of their initial excess weight (successful weight loss) and only one patient (0.9 percent) had lost less than 25 percent of their initial excess weight.⁶³

Mini-Gastric Bypass

MGB was evaluated in one study. Peraglie et al. reported that patients undergoing laparoscopic MGB achieved sustained percent EWL during the 5 years of post-surgery follow-up. In particular, percent EWL at 1, 6, 12, 24, 36, 48, 60, and 72 months after surgery was 18, 52, 67, 70, 68, 66, 67, and 72. It should be noted that the number of patients followed over time decreased from 95 percent at 1 month to 42 percent at 72 months.⁶⁹

Roux En Y Gastric Bypass

RYGB was evaluated in 21 studies. The outcomes assessed included percent EBML (n=3 studies), percent EWL (n=16 studies), percent WL (n=7 studies), BMI loss (n=2 studies), weight loss (n=3 studies). In addition, 11 studies reported mean BMI at baseline and at different points during follow-up, and seven studies reported mean weight at baseline and at different points during follow-up.

Table 5 shows the changes over time in different weight outcomes by study. 15 studies evaluated changes in weight outcomes at one year after surgery. Three studies reported weight changes at 2 years and only two studies provided data on follow-up longer than 2 years.

Across all studies, the mean percent EBML ranged from 73.1 percent to 80.6 percent at 1 year. The mean percent EWL at 1 year ranged from 41.4 percent to 82.8 percent, and the percent WL from 25 percent to 31.8 percent. Finally, the mean BMI reduction at 1 year ranged from 16.5 to 13.4 kg/m², and the mean weight reduction ranged from 40.7 kg to 93.8 kg. Because the standard deviation of weight change was not consistently reported across studies, we deemed that a meta-analysis of the subset of studies reporting relevant data would not be informative.

O'Keefe et al. reported that the average percent EWL among patients undergoing any of RYGB, LAGB or VSG was 44.5 percent (range, 11.1-77.0 percent) at 6 months and 55.1 percent (range, 8.73-94.9 percent) at 1 year. Specifically for RYGB, the percent EWL was 48.3 percent at 6 months and 59.8 percent at 1 year after surgery.⁶⁷

Miranda et al. evaluated the changes in weight among patient with heart failure undergoing bariatric surgery. During a median follow-up of 4.3 years, mean BMI was reduced from 55 kg/m² to 35 kg/m², and weight was reduced from 146 kg to 99 kg. The mean percent weight loss was 42.⁵⁸

Moon et al., in addition to mean percent EWL (Table 5), also evaluated the effect of RYGB on weight failure defined as percent EWL less than 30. At the time of last follow-up, 29/210 patients (14 percent) failed to achieve weight loss.⁶⁶

Dunkle-Blatter et al. found that, over a mean follow-up of 13.8 months, patients 60 years or older undergoing open or laparoscopic RYGB lost on average 54.9 percent (SD, 16.6) of their excess weight.⁷⁰

Table 5. Changes in weight outcomes in patients undergoing Roux-en-Y gastric bypass in the Medicare eligible population.

Data are presented as mean (SD) for each outcome.

| Outcome | Author Year PMID | 0 mo | 3 mo | 6 mo | 9 mo | 12 mo | 15 mo | 18 mo | 24 mo | 3.5 y |
|--------------|-----------------------------|------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------|--------------------------|
| percent EBML | Wagner 2007 17938305 | . | . | . | . | . | . | . | . | 62.6 (26.4) ^g |
| | Moon 2016 26220238 | . | . | 64.9 (NR) | . | 73.1 (NR) | . | 78.5 (NR) | 76.1 (NR) | . |
| | Zaveri 2016 27795883 | . | 41.0 (6.1) ^h | 60.2 (7.9) ^h | 72.5 (7.2) ^h | 80.6 (6.6) ^h | 85.2 (7.9) ^h | 88.4 (9.5) ^h | . | . |
| | | | | | | | | | | |
| percent EWL | Quebbemann 2005 16925254 | . | . | . | . | 71.0 (NR) | . | . | . | . |
| | Trieu 2007 17400516 | . | 38.4 (NR) | . | 55 (NR) | . | . | 68.3 (NR) | . | . |
| | Willkomm 2010 20870182 | . | . | . | . | 74.8 (NR) | . | . | 83.4 (NR) | . |
| | Serrot 2011 22000180 | . | . | . | . | 70.0 (21.0) | . | . | . | . |
| | Ramirez 2012 22551574 | . | . | . | . | 63.6 (32.2) | . | . | . | . |
| | Giordano 2014 24318411 | . | . | 51.2 (38.4) | . | 62.6 (41.8) | . | . | 64.5 (18.4) | . |
| | Huang 2015 25859266 | . | . | . | . | 65.1 (NR) ^a | . | . | . | . |
| | Huang 2015 25859266 | . | . | . | . | 49.5 (NR) ^b | . | . | . | . |
| | Huang 2015 25859266 | . | . | . | . | 69.8 (NR) ^c | . | . | . | . |
| | Huang 2015 25859266 | . | . | . | . | 63.5 (NR) ^d | . | . | . | . |
| | Moon 2016 26220238 | . | . | 57.4 (NR) | . | 64.8 (NR) | . | 69.4 (NR) | 67.5 (NR) | . |
| | Boules 2015 26243345 | . | . | . | . | 59.7 (42.3) | . | . | . | . |
| | Lee 2016 27220823 | . | . | 34.2 (9.4) | . | 41.4 (11.6) | . | . | . | . |
| | Praveenraj 2016 27279392 | . | . | . | . | 82.8 (34.3) | . | . | . | . |
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| Outcome | Author Year PMID | 0 mo | 3 mo | 6 mo | 9 mo | 12 mo | 15 mo | 18 mo | 24 mo | 3.5 y |
|----------------------------------|-----------------------------|----------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|------------------------|----------------------------|
| | Zaveri 2016 27795883 | . | 35.2 (5.9) ^h | 53.5 (5.7) ^h | 63.6 (5.3) ^h | 69.1 (6) ^h | 71.7 (7.1) ^h | 73.2 (7.8) ^h | . | . |
| | Sosa 2004 15603658 | . | . | . | . | 65 (NR) | . | . | . | . |
| | Ochner 2013 23700235 | . | . | . | . | 69.0 (NR) ^h | . | . | 71.0 (NR) ^h | . |
| | Soto 2013 23733390 | . | . | . | . | . | . | 68.2 (NR) | . | . |
| percent WL | Serrot 2011 22000180 | . | . | . | . | 25.0 (6.0) | . | . | . | . |
| | Ritz 2014 24708912 | . | . | . | . | 9.2 (2.0) | . | . | . | . |
| | Moon 2016 26220238 | . | . | 27.4 (NR) | . | 31.8 (NR) | . | 34.0 (NR) | 33.9 (NR) | . |
| | Lee 2016 27220823 | . | . | 26.0 (7.2) | . | 31.5 (8.5) | . | . | . | . |
| | Praveenraj 2016 27279392 | . | . | . | . | 28.0 (7.2) | . | . | . | . |
| BMI (kg/m ²) | Trieu 2007 17400516 | 48.5 (NR) | 38.4 (NR) | . | 39.0 (NR) | . | . | 30.9 (NR) | . | . |
| | Ramirez 2012 22551574 | 44 (NR) ^e | . | . | . | 34.0 (9.1) | . | . | . | . |
| BMI loss (kg/m ²) | Sosa 2004 15603658 | . | . | . | . | 16.5 (NR) | . | . | . | . |
| | Lee 2016 27220823 | . | . | 11.1 (4.0) | . | 13.4 (14.1) | . | . | . | . |
| | Wicklund 2015 | . | . | . | . | . | . | 13.5 (5.5) ^f | . | . |
| | Wagner 2007 17938305 | . | . | . | . | . | . | . | . | 21.8 (14.5) ^{f,g} |
| | Valderas 2009 19517199 | . | . | . | . | . | . | . | . | 14.1 (4.9) ^f |
| | O'Keefe 2010 20532834 | . | . | 12.4 (6.5) ^f | . | 15.8 (6.3) ^f | . | . | . | . |
| | Serrot 2011 22000180 | . | . | . | . | 8.8 (2.2) ^f | . | . | . | . |
| | Giordano 2014 24318411 | . | . | 7 (8.5) ^f | . | 12.9 (7.8) ^f | . | . | 31.9(8.4) ^f | . |

| Outcome | Author Year PMID | 0 mo | 3 mo | 6 mo | 9 mo | 12 mo | 15 mo | 18 mo | 24 mo | 3.5 y |
|---------------------|---------------------------|----------------------------|------------|--------------------------|------------|--------------------------|-------|--------------------------|-------------|-------|
| | Huang 2015 25859266 | . | . | . | . | 11.7 (6.5) ^f | . | . | . | . |
| Weight (kg) | Trieu 2007 17400516 | 136.6 (NR) | 109.3 (NR) | . | 105.0 (NR) | . | . | 87.6 (NR) | . | . |
| | Ramirez 2012 22551574 | 124.5 (NR) ^e | . | . | . | 93.8 (14.7) | . | . | . | . |
| Weight loss (kg) | Sosa 2004 15603658 | . | . | . | . | 43.2 (NR) | . | . | . | . |
| | Giordano 2014 24318411 | . | . | 28.2 (22.1) | . | 40.8 (22.1) | . | . | 41.5 (17.5) | . |
| | Lee 2016 27220823 | . | . | 34.0 (12.9) | . | 40.7 (14.5) | . | . | . | . |
| | Wiklund 2015 | . | . | . | . | . | . | 40.6 (22.1) ^f | . | . |
| | O'Keefe 2010 20532834 | . | . | 34.8 (20.4) ^f | . | 43.6 (20.4) ^f | . | . | . | . |
| | Serrot 2011 22000180 | . | . | . | . | 57 (22.8) ^f | . | . | . | . |
| | Huang 2015 25859266 | . | . | . | . | 29.9 (15.7) ^f | . | . | . | . |

EBMIL: excess BMI loss; EWL: excess weight loss; WL: weight loss; mo: months after surgery; y: years after surgery; PMID: PubMed ID (not reported for articles not indexed in PubMed but retrieved through other databases)

^a All patients

^b Diabetic patients

^c Patients with diabetes remission

^d Patients with no diabetes remission

^e Numbers correspond to median weight and BMI for all patients undergoing any of AGB, LSG, or LRYG are reported. Baseline weight and BMI were not reported separately by procedure.

^f Estimated based on the reported mean and standard deviation of BMI or weight at baseline and the respective time point at follow-up. We assumed a correlation coefficient of 0.5.

^g Results were reported for a mean follow-up of 44 months (3.7 years).

^h Outcome values were reported graphically in the primary study. Values presented in the table are approximated based on the original graph.

Single Anastomosis Duodenal Switch

Only one study reported on the effect on weight change of SADS. Zaveri et al. found that the percent EBMI at 3, 6, 9, 12, 15, and 18 months after SADS was 49.1 (95% CI 41.8, 56.5), 63.4 (95% CI 57.6, 69.2), 75.2 (95% CI 69.8, 80.7), 85.5 (95% CI 79.6, 91.4), 94.1 (95% CI 88, 100.2), and 100.6 (95% CI 94, 107.3), respectively. Similarly, the percent EWL at 3, 6, 9, 12, 15, and 18 months was 40.4 (95% CI 34.5, 46.3), 50.6 (95% CI 45.7, 55.5), 59.3 (95% CI 55, 63.7), 67.4 (95% CI 62.6, 72.2), 74.2 (95% CI 69.1, 79.4), 80.3 (95% CI 74.7, 86.2).⁷¹

Sleeve gastrectomy

Sleeve gastrectomy was evaluated in 16 studies. The outcomes assessed included percent EBMI (n=2 studies), percent EWL (n=13 studies), percent WL (n=5 studies), BMI loss (n=1 study), weight loss (n=1 study). In addition, 11 studies reported mean BMI at baseline and at different points during follow-up, and seven studies reported mean weight at baseline and at different points during follow-up.

Table 6 shows the changes over time in different weight outcomes by study. Changes in weight outcomes at 1 year after surgery or 2 years after surgery were evaluated in 16 studies. Only two studies reported outcomes for longer follow-up periods.

Across all studies, the mean percent EBMI ranged between 60 percent to 64.6 percent at 1 year. The mean percent EWL at 1 year ranged from 26 percent to 74.3 percent, and the percent WL from 5.5 percent to 26.5 percent. Finally, Lee et al. reported a mean BMI reduction at 1 year of 7.9 kg/m² and a mean weight reduction of 24.4 kg.⁶⁴ Because the standard deviation of weight change was not consistently reported across studies, we deemed that a meta-analysis of the subset of studies reporting relevant data would not be informative.

O'Keefe et al. reported that the average percent EWL among patients undergoing any of RYGB, LAGB or VSG was 44.5 percent (range, 11.1–77.0 percent) at 6 months and 55.1 percent (range, 8.73–94.9 percent) at 1 year. Specifically for RYGB, the percent EWL was 48.3 at 6 months and 59.8 at 1 year after surgery.⁶⁷

Moon et al., in addition to mean percent EWL (Table 6), also evaluated the effect of LSG on weight failure defined as percent EWL less than 30. At the time of last follow-up, 15/73 patients (20.5 percent) failed to achieve weight loss.⁶⁶

Leonetti et al. examined the effects LSG in patients with type 2 diabetes. They found that during a mean follow-up of 18 months, 71 percent of patients lost their excess weight.⁵⁴

Table 6. Changes in weight outcomes in patients undergoing sleeve gastrectomy in the Medicare eligible population.

Data are presented as mean (SD) for each outcome.

| Outcome | Author Year PMID | Prior to surgery | 3 mo | 6 mo | 12 mo | 18 mo | 2 y | After surgery | Last follow-up |
|---------------|-----------------------------|------------------|------|--------------------------|------------------------|-----------|-------------|---------------|--------------------------|
| percent EBMIL | Moon 2016 26220238 | . | . | 55.1 (NR) | 64.6 (NR) | 67.5 (NR) | 68.9 (NR) | . | . |
| | Lemaitre 2016 27063637 | . | . | . | 60.0 (19.2) | . | 64.6 (22.0) | . | . |
| percent EWL | Ramirez 2012 22551574 | . | . | . | 39.4 (15.4) | . | . | . | . |
| | van Rutte 2013 23344504 | . | . | 52.8 (16.1) ^a | . | . | . | . | 55.2 (17.8) ^a |
| | van Rutte 2013 23344504 | . | . | 49.9 (12.2) ^b | . | . | . | . | 52.2 (14.4) ^b |
| | van Rutte 2013 23344504 | . | . | 52.4 (10.7) ^c | . | . | . | . | 59.9 (14.9) ^c |
| | Soto 2013 23733390 | . | . | . | . | . | 43 | . | . |
| | Nagao 2014 24519024 | . | . | 48.0 (15.5) | 54.6 (15.3) | . | 54.4 (15.4) | . | . |
| | Huang 2015 25859266 | . | . | . | 68.5 (NR) ^g | . | . | . | . |
| | Huang 2015 25859266 | . | . | . | 68.1 (NR) ^h | . | . | . | . |
| | Huang 2015 25859266 | . | . | . | 65.0 (NR) ⁱ | . | . | . | . |
| | Huang 2015 25859266 | . | . | . | 74.3 (NR) ^j | . | . | . | . |
| | Moon 2016 26220238 | . | . | 48.8 (NR) | 56.6 (NR) | 59.8 (NR) | 60.8 (NR) | . | . |
| | Boules 2015 26243345 | . | . | . | 51.8 (39.8) | . | . | . | . |
| | Lemaitre 2016 27063637 | . | . | . | 64.8 (24.6) | . | 67.4 (24.0) | . | . |
| | Lee 2016 27220823 | . | . | 24.6 (18.2) | 26.7 (27.6) | . | . | . | . |
| | Praveenraj 2016 27279392 | . | . | . | 60.2 (17.5) | . | . | . | . |

| Outcome | Author Year PMID | Prior to surgery | 3 mo | 6 mo | 12 mo | 18 mo | 2 y | After surgery | Last follow-up |
|--------------------------|-----------------------------|-------------------------|------------|-------------------------|-------------|------------|------------|---------------|-------------------------|
| | Luppi 2015 25088486 | . | . | . | 49 (NR) | . | 45 (NR) | . | . |
| percent WL | van Rutte 2013 23344504 | . | . | 24.5 (6.5) ^a | . | . | . | . | 25.6 (7.6) ^a |
| | van Rutte 2013 23344504 | . | . | 23.3 (6.1) ^b | . | . | . | . | 23.4 (9.2) ^b |
| | van Rutte 2013 23344504 | . | . | 23.1 (4.3) ^c | . | . | . | . | 26.5 (6.9) ^c |
| | Ritz 2014 24708912 | . | . | . | 5.5 (2.5) | . | . | . | . |
| | Moon 2016 26220238 | . | . | 22.1 (NR) | 26.5 (NR) | 27.3 (NR) | 28.0 (NR) | . | . |
| | Lee 2016 27220823 | . | . | 18.5 (13.7) | 20.2 (21.5) | . | . | . | . |
| | Praveenraj 2016 27279392 | . | . | . | 25.0 (5.4) | . | . | . | . |
| BMI (kg/m ²) | O'Keefe 2010 20532834 | 50.0 (12.0) | . | 42.0 (8.1) | 42.0 (8.4) | . | . | . | . |
| | Leonetti 2012 22508671 | 41.3 (6.0) | 35.1 (3.8) | 31.6 (3.9) | 29.4 (4.9) | 28.3 (5.4) | . | . | . |
| | Ramirez 2012 22551574 | 44 (NR) ^k | . | . | 36.1 (4.3) | . | . | . | . |
| | van Rutte 2013 23344504 | 45.1 (6.9) ^a | . | 34.5 (5.7) ^a | . | . | . | . | 33.6 (6.2) ^a |
| | van Rutte 2013 23344504 | 45.4 (5.8) ^b | . | 34.5 (3.9) ^b | . | . | . | . | 35.0 (5.2) ^b |
| | van Rutte 2013 23344504 | 46.2 (8.9) ^c | . | 34.2 (5.9) ^c | . | . | . | . | 34.2 (5.0) ^c |
| | Mizrahi 2014 24442420 | 42.6 (0.7) | . | . | . | . | 31.8 (0.5) | . | . |
| | Nagao 2014 24519024 | 46.4 (6.0) | . | 36.1 (6.4) | 34.3 (6.0) | . | 34.8 (6.0) | . | . |
| | Luppi 2015 25088486 | 43.3 (NR) | . | . | 32.8 (NR) | . | 33.2 (NR) | . | . |
| | Freeman 2015 25708829 | 43.0 (5.4) | . | . | . | . | . | 36.3 (5.3) | . |
| | Huang 2015 25859266 | 37.6 (5.2) | . | . | 28.2 (4.9) | . | . | . | . |

| Outcome | Author Year PMID | Prior to surgery | 3 mo | 6 mo | 12 mo | 18 mo | 2 y | After surgery | Last follow-up |
|-------------------------------|---|-------------------------|------|--------------------------|--------------------------|-------|-------------------------|--------------------------|--------------------------|
| | Lemaitre 2016 27063637 | 46.2 (6.4) | . | . | 31.5 (5.8) | . | 31.3 (6.4) | . | . |
| | Praveenraj 2016 27279392 | 43.8 (9.7) | . | . | . | . | . | . | . |
| BMI loss (kg/m ²) | Lee 2016 27220823 | . | . | 7.8 (6.1) | 7.9 (7.3) | . | . | . | . |
| Weight (kg) | Luppi 2015 25088486 | 113.2 (NR) | . | . | 85.3 (NR) | . | 87.9 (NR) | . | . |
| | Ramirez 2012 22551574 | 124.5 (NR) ^k | . | . | 111.4 (18.1) | . | . | . | . |
| Weight loss (kg) | Lee 2016 27220823 | . | . | 23.5 (17.9) | 24.4 (22.1) | . | . | . | . |
| | O'Keefe 2010 20532834 | . | . | 25.2 (21.3) ⁱ | 26.7 (23.2) ⁱ | . | . | . | . |
| | van Rutte 2013 23344504 ^a | . | . | 30.6 (19.8) ⁱ | . | . | . | . | 31.9 (21.0) ⁱ |
| | van Rutte 2013 23344504 ^b | . | . | 29.3 (16.9) ⁱ | . | . | . | . | 29.8 (16.9) ⁱ |
| | van Rutte 2013 23344504 ^c | . | . | 36.2 (26.7) ⁱ | . | . | . | . | 34.3 (26.4) ⁱ |
| | Mizrahi 2014 24442420 | . | . | . | . | . | 30.1 (2.5) ⁱ | . | . |
| | Freeman 2015 25708829 | . | . | . | . | . | . | 19.9 (21.4) ⁱ | . |
| | Huang 2015 25859266 | . | . | . | 25.1 (18.8) ⁱ | . | . | . | . |

EBMIL: excess BMI loss; EWL: excess weight loss; WL: weight loss; PMID: PubMed ID

^a Patients 55-59 years of age

^b Patients 60-64 years of age

^c Patients older than 65 years

^g All patients

^h Diabetic patients

ⁱ Patients with no diabetes remission

^j Patients with diabetes remission

^k Numbers correspond to median weight and BMI for all patients undergoing any of AGB, LSG, or LRYG are reported. Baseline weight and BMI were not reported separately by procedure.

^l Estimated based on the reported mean and standard deviation of BMI or weight at baseline and the respective time point at follow-up. We assumed a correlation coefficient of 0.5.

Strength of the Evidence

Grades of strength of evidence for weight loss outcomes based on the three comparative studies are summarized in Table 7. The strength of evidence for weight changes in Medicare eligible patients after bariatric surgery is at best moderate. There are no randomized trials in the Medicare population that compare bariatric surgical procedures to each other, to non-surgical treatments, or to no treatment. Although enough non-randomized studies report data on more than one procedure, only three studies were designed and/or analyzed in order to compare treatment groups amongst each other. Even among these three studies, it is likely that unmeasured confounding may be substantial. In addition, many studies did not have a control group (uncontrolled before-after surgery studies) but reported changes in outcomes before vs. after surgery; the absence of a control group limits our confidence in establishing causal associations between bariatric surgical procedures and weight loss outcomes. Finally, use of percent change from baseline as an outcome measure is statistically problematic leading to inaccurate estimation of treatment effects. In conclusion, the available evidence base is likely subject to confounding, selection, or measurement biases.

Table 7. Strength of evidence for weight loss outcomes in the Medicare eligible population

| Conclusion statement | RoB (evidence-base) | Consistency | Precision | Directness and Applicability | Overall Rating | Comments |
|--|---|-------------|----------------------------|------------------------------|---|---|
| RYGB results in greater improvements in weight outcomes compared to SG at 6 months after surgery (1) Mean weight loss (2) Mean BMI loss (3) Mean percent weight loss (4) Mean percent excess weight loss | Low for (1), (2), (3), (4) | [Not rated] | Low for (1), (2), (3), (4) | High for (1), (2), (3), (4) | Low SoE for (1), (2), (3), (4) | Only 1 non-randomized study addresses this question (N=162). <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| SG results in greater improvements in weight outcomes compared to LAGB at 6 or 12 months after surgery (1) Mean weight loss (2) Mean BMI loss (3) Mean percent weight loss (4) Mean percent excess weight loss | Low for (1), (2), (4) Moderate for (3) | [Not rated] | Low for (1), (2), (3), (4) | High for (1), (2), (3), (4) | Low SoE for (1), (2), (4) Moderate SoE for (3) | - Only 1 non-randomized study compares weight changes for all four outcomes at 6 months (N=162). - Only 1 non-randomized study compares weight changes for (1), (2), and (4) at 12 months (N=162). - Only two non-randomized studies (N=316) compare weight changes at 12 months for (3). <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| RYGB results in greater improvements in weight outcomes compared to LAGB at 6 or 12 months after surgery (1) Mean weight loss (2) Mean BMI loss (3) Mean percent weight loss (4) Mean percent excess weight loss | Low for (1), (2), (4) Moderate for (3) | [Not rated] | Low for (1), (2), (3), (4) | High for (1), (2), (3), (4) | Low SoE for (1), (2), (4) Moderate SoE for (3) | - Only 1 non-randomized study compares weight changes for all four outcomes at 6 months (N=162). - Only 1 non-randomized study compares weight changes for (1), (2), and (4) at 12 months (N=162). - Only two non-randomized studies (N=316) compare weight changes at 12 months for (3). <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| LSG results in greater weight loss than conventional treatment at 18 months after surgery | Low | [Not rated] | Low | High | Low SoE | Only 1 study address this question (N=60). <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy; LAGB: laparoscopic gastric banding; LSG: laparoscopic sleeve gastrectomy; SoE: strength of evidence; RoB: risk of bias | | | | | | |

KQ 3.b.

None of the comparative studies reported on modifiers of the effect of bariatric surgery on weight outcomes. Of the studies reporting weight changes among people who received bariatric surgery, none conducted a formal evaluation of treatment effect heterogeneity by the means of statistical interaction between treatment and some patient or procedure characteristic. Two studies reported the effects on weight of bariatric treatments in subgroups defined by patients, and one study in subgroups defined by bariatric surgical procedure characteristics. Results of these subgroup analyses are summarized in Table 8. A third study examined the predictive value of pre-operative comorbidities related to obesity rather than conducting subgroup analyses.⁶²

Huang et al., in addition to their overall analysis, estimated the percent EWL among a subgroup of diabetic patients. They did not report results for the complementary subgroup of non-diabetic patients, and therefore heterogeneity of treatment effect cannot be formally explored. In addition, they conducted stratified analyses based on whether diabetic patients achieved disease remission or not after surgery. However, because these stratifications are based on the outcome rather than on a baseline covariate, they are indicative of effect modification.⁷²

Freeman et al. found that, compared to diabetic patients, non-diabetics had significantly higher percent EWL ($P=0.04$) and significantly higher BMI loss ($P=0.02$) at 6 months after LSG. They also found that time to achieve BMI $< 35 \text{ kg/m}^2$ was significantly shorter among patients with baseline BMI of 40 kg/m^2 or less compared to those with BMI $> 40 \text{ kg/m}^2$ at baseline ($P=0.02$).⁷³

van Rutte et al. report percent EWL and percent WL and 6 months and at an average of 14 months after SG in three subgroups based on age. The three age groups had on average similar outcomes at each time point, but the differences were not statistically evaluated.⁷⁴

The study by Soto et al. was the only study examining treatment effect heterogeneity according to bariatric surgical procedure characteristics, in particular based on the size of the bougie used in LSG. They found that the percent EWL was higher when a smaller bougie size was used.⁷⁵

Finally, Wagner et al. found no association between these comorbidities and return to work after RYGB. No relevant data were reported.⁶²

Table 8. Subgroup analyses of weight changes in the Medicare eligible population

| Outcome | Time point | Study | Surgery | Subgroup | Effect | P-value between |
|-------------|------------|-------|--------------|----------------|--------|-----------------|
| percent EWL | 12 mo | Huang | LRYGB | Diabetes | 63.5 | NA |
| | | | | No diabetes | NR | |
| | | | LSG | Diabetes | 68.1 | NA |
| | | | | No diabetes | NR | |
| | | | LRYGB or LSG | Diabetes | 66.8 | NA |
| | | | | No diabetes | NR | |
| | 3 mo | Soto | LSG | Bougie size 52 | 28 | NR |
| | | | | Bougie size 46 | 31 | |
| | | | | Bougie size 38 | 37 | |
| | 6 mo | Soto | LSG | Bougie size 52 | 34 | NR |
| | | | | Bougie size 46 | 57 | |
| | | | | Bougie size 38 | 50 | |
| | 12 mo | Soto | LSG | Bougie size 52 | 26 | NR |
| | | | | Bougie size 46 | 64 | |
| | | | | Bougie size 38 | 55 | |
| | 24 mo | Soto | LSG | Bougie size 52 | 18 | NR |

| Outcome | Time point | Study | Surgery | Subgroup | Effect | P-value between |
|---|------------|-----------|---------|------------------|--------------|-------------------|
| percent WL | 48 mo | Soto | LSG | Bougie size 46 | 62 | NR |
| | | | | Bougie size 38 | 56 | |
| | | | | Bougie size 52 | 27 | |
| | | | | Bougie size 46 | 82 | |
| | 6 mo | Freeman | LSG | Bougie size 38 | NA | 0.60 |
| | | | | Males | 30.0 (5.3) | |
| | | | | Females | 32.9 (21.1) | |
| | | | | Caucasian | 30.7 (20.5) | |
| | | | | African American | 32.6 (14.5) | |
| | | | | Diabetes | 26.6 (16.8) | |
| | | | | No diabetes | 36.5 (18.6) | |
| | | | | BMI > 40 | 32.2 (16.2) | |
| | | | | BMI ≤ 40 | 29.4 (23.6) | |
| | 6 mo | van Rutte | SG | Age 55-59 years | 52.8 (16.1) | NR |
| | | | | Age 60-64 years | 49.9 (12.2) | |
| | | | | Age 65+ years | 52.4 (10.7) | |
| | 14 mo | van Rutte | SG | Age 55-59 years | 55.2 (17.8) | NR |
| | | | | Age 60-64 years | 52.2 (14.4) | |
| | | | | Age 65+ years | 59.9 (14.9) | |
| | 6 mo | van Rutte | SG | Age 55-59 years | 24.5 (6.5) | NR |
| | | | | Age 60-64 years | 23.3 (6.1) | |
| | | | | Age 65+ years | 23.1 (4.3) | |
| | 14 mo | van Rutte | SG | Age 55-59 years | 25.6 (7.6) | NR |
| | | | | Age 60-64 years | 23.4 (9.2) | |
| | | | | Age 65+ years | 26.5 (6.9) | |
| BMI loss | 6 mo | Freeman | LSG | Males | 6.1 (3.7) | 0.34 |
| | | | | Females | 7.4 (4.9) | |
| | | | | Caucasian | 6.4 (4.0) | 0.72 |
| | | | | African American | 6.9 (4.9) | |
| | | | | Diabetes | 5.2 (3.8) | 0.02 ^b |
| | | | | No diabetes | 8.1 (4.8) | |
| | | | | BMI > 40 | 7.3 (4.3) | 0.12 |
| | | | | BMI ≤ 40 | 5.1 (4.1) | |
| Time to BMI < 35 kg/m ² | 6 mo | Freeman | | Males | 77.2 (52.2) | 0.82 |
| | | | | Females | 86 (122.5) | |
| | | | | Caucasian | 88 (118.2) | 0.72 |
| | | | | African American | 75 (51.6) | |
| | | | | Diabetes | 85.4 (105.8) | 0.82 |
| | | | | No diabetes | 76.3 (74.2) | |
| | | | | BMI > 40 | 122 (106.1) | 0.02 |
| | | | | BMI ≤ 40 | 33.8 (37.4) | |
| Change in anti-hypertensive medications | 6 mo | Freeman | | Males | 0.7 (0.8) | 0.64 |
| | | | | Females | 0.8 (1.4) | |
| | | | | Caucasian | 1.0 (.2) | 0.06 |
| | | | | African American | 0.3 (0.9) | |
| | | | | Diabetes | 0.9 (1.3) | 0.34 |
| | | | | No diabetes | 0.5 (1.0) | |
| | | | | BMI > 40 | 0.6 (1.1) | 0.36 |
| | | | | BMI ≤ 40 | 1.0 (1.2) | |
| Change in total insulin dose (unit/day) | 6 mo | Freeman | | Males | 75.1 (61.5) | 0.10 |
| | | | | Females | 27.4 (46.5) | |
| | | | | Caucasian | 73.6 (59.9) | 0.18 |

| Outcome | Time point | Study | Surgery | Subgroup | Effect | P-value between |
|---------|------------|-------|---------|------------------|-------------|-----------------|
| | | | | African American | 35.4 (56.1) | |
| | | | | Diabetes | NA | NA |
| | | | | No diabetes | NA | |
| | | | | BMI > 40 | 57.2 (64.7) | 0.97 |
| | | | | BMI ≤ 40 | 58.3 (53.8) | |

NR: not reported; NA: not applicable. Effects are presented as mean (SD) unless if otherwise specified; EWL: excess weight loss; WL: weight loss; LSG: laparoscopic sleeve gastropasty; LRYGB: laparoscopic Roux-en-Y gastric bypass

^a Primary study reported P=0.07. We recalculated the p-value using t-test based on sample size, mean, and SD reported in the primary study

^b Primary study reported P=0.03. We recalculated the p-value using t-test based on sample size, mean, and SD reported in the primary study

KQ 3.c.

Appendix F summarizes the characteristics of the eligible prediction studies. A total of 40 different (Appendix G and Table 9) models were reported in the eligible studies (some studies reported more than one model). Outcome definition was rarely consistent across models. There was no global agreement in regards to the definition of “minimal weight loss” and no model explicitly used this outcome definition. Table 10 shows in detail the 15 models that directly predict the probability of successful/failed weight loss, which is defined based on percent EWL achieved after surgery, and an additional model that predicts nadir weight. The models defined successful weight loss as percent EWL of 50 percent or more at 1 year after surgery^{76, 77} or at two years after surgery.⁷⁸⁻⁸⁰ Ortega et al. defined surgical success as percent EWL of 60 percent or more at 1 year. Fried defined suboptimal weight loss as residual BMI>35.9 at 6 months.⁸¹ Yanos et al. developed a model to predict regaining of ≥20 percent initial weight loss versus <20 percent initial weight loss.⁸² Two models (Manning et al.) predicted maximal percent WL (percent WL of 20% or more),⁸³ and one model (Yanos et al.) predicted nadir weight loss as the percentage of total weight lost at the patient’s lowest self-reported post-operative weight (percent TWL).⁸² Arterburn et al. developed 3 models, each one predicting >25 percent, >30 percent or >35 percent weight loss at 1 year after any bariatric surgery. The remaining models predicted percent EWL, percent WL, absolute weight loss, or absolute weight without defining a threshold for successful/failed weight loss but we are including them for completeness.⁸⁴

In each of two studies, a single set of predictors was used to predict multiple outcomes after the same bariatric surgical procedure⁸⁴ or a single outcome but after different bariatric surgical procedures.⁸⁵ Brown et al. sequentially assessed the performance of two different sets of predictors to predict the same outcome among patients receiving a single bariatric treatment.⁸⁶ Courcoulas et al. and Manning et al. identified that different sets of predictors predict the same outcome among patients who receive different types of surgery.^{83, 87} In the analyses by Lee et al, different predictors for the same outcome among patients receiving the same procedure were the result of different statistical techniques used for model derivation.⁷⁸⁻⁸⁰ Manning et al., Martin et al., Obeidat et al., and Yanos et al. each reported different sets of predictors for different outcomes among patients receiving the same bariatric surgical procedure.^{82, 83, 88, 89} Finally, in the analysis by Ortega et al. all patients received the same procedure but different sets of predictors are reported for the same outcome, while a model for a separate outcome and separate set of predictors was also assessed. None of the 40 models was internally or externally validated after their initial derivation.⁹⁰

Six models (models 7, 26, 28, 29, 31, 32) predicted weight outcomes after SG; eight models (models 6, 9, 10, 12, 16, 17, 21, 22) after AGB; one model (model 37) after BPD; 10 models

(models 2, 3, 4, 5, 11, 13, 27, 30, 39, 40) after RYBG; one model (model 15) after plication; and one after VBG. The remaining 13 models (models 1, 8, 14, 18, 19, 20, 23, 24, 25, 33, 34, 35, 36) predicted outcomes after any of multiple surgeries. Thirteen models included the type of bariatric surgery as one of the predictors (1 2 3 4 13 14 18 23 24 25 33 19 20).

The most common method used to derive the risk prediction model was stepwise logistic regression. Multiple logistic regression without variable selection (i.e. pre-specified predictors) was also performed for some models. Two models were constructed by applying the least absolute shrinkage and selection operator (LASSO) procedure. Other statistical techniques used for model derivation include artificial neural networks, discriminant analysis, classification and regression tree (CART), and signal detection analysis. Two models used the Akaike's Information Criterion and log-likelihood.

Of the 36 for which model performance was reported, this was assessed through the coefficient of determination (R^2) alone in 18 models; area under the curve (AUC) alone was reported for 5 models; both R^2 and AUC were reported for 2 models; AUC, Nagelkerke's R^2 , and Hosmer-Lemeshow statistic were reported for 2 models; sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported for one model. The performance of the remaining 8 models was assessed using other metrics such as predictive accuracy, or classification rate (Table 9).

Model discrimination using c-statistic (AUC) was reported for 7 models, while one model reported the AUC for only one predictor (1 month percent EWL) but not the full model.⁸⁹ The AUC ranged from 0.58 for 3-year weight change to 0.85 for percent EWL >50 percent (good outcome/successful weight loss) [model 1].⁸⁷ Model calibration was reported for only 2 models; for both, the Hosmer-Lemeshow test had a p-value greater than 0.05. Values of the R^2 metric for model fit ranged from 2 percent⁸⁶ to 99.7 percent.⁹¹

One model reported measures of clinical validity, namely sensitivity, specificity, positive predictive value, and negative predictive value. Using signal detection analysis, Robinson et al. found that the model consisting of postsurgical global dietary adherence rating, postsurgical grazing frequency, highest lifetime BMI prior to surgery, and regular attendance at postsurgical bariatric support groups had a sensitivity of 0.62, a specificity of 0.92, an efficiency of 0.84, a PPV of 0.72, and a NPV of 0.88.⁹²

Table 9. Summary of 40 models predicting weight loss

| Model Number | Author | Year | Modeling method | Metric of Model Performance | Model Performance |
|--------------|---------------|------|---|---|---|
| 1 | Agüera | 2015 | Stepwise logistic regression estimated the best predictive model for a good %EWL outcome | Hosmer-Lemeshow; Nagelkerke's R ² ; AUC | Hosmer and Lemeshow P =0.296 R ² =0.26 AUC= 0.85 (95% CI, 0.73-0.98) |
| 2 | Arterburn | 2013 | Multivariable logistic regression | AUC | 0.69 |
| 3 | | | Multivariable logistic regression | AUC | 0.68 |
| 4 | | | Multivariable logistic regression | AUC | 0.70 |
| 5 | Benoit | 2014 | Stepwise selection and multivariate linear regression | Coefficient of determination (R ²) | 0.5075 |
| 6 | | | Stepwise selection and multivariate linear regression | Coefficient of determination (R ²) | 0.1674 |
| 7 | | | Stepwise selection and multivariate linear regression | Coefficient of determination (R ²) | 0.5075 |
| 8 | Brandao | 2015 | Pearson's correlations to identify significant predictors. For variables significantly associated with outcomes, multiple linear regression was use | Adjusted R ² | 0.383 |
| 9 | Brown | 2013 | Stepwise selection and multivariate linear regression | Coefficient of determination (R ²), Adjusted R ² | R ² =0.02; Adjusted R ² =0.002 |
| 10 | | | Stepwise selection and multivariate linear regression | Coefficient of determination (R ²), Adjusted R ² | R ² =0.17; R ² =0.135 |
| 11 | Courcoulas | 2015 | Multivariable linear regression with LASSO procedure | Coefficient of determination (R ²); AUC | R ² = 0.14; AUC=0.65 |
| 12 | | | Multivariable linear regression with LASSO procedure | Coefficient of determination (R ²); AUC | AUC=0.58 |
| 13 | Dallal | 2009 | Mixed-model regression | Coefficient of determination (R ²); AIC | R ² =0.997 Nagelkerke R ² =0.208 |
| 14 | de Raaff | 2016 | Multivariable logistic regression analysis with backward selection | Nagelkerke R ² ; Hosmer and Lemeshow; AUC | Hosmer and Lemeshow p= 0.443, AUC=0.77 (95% CI 0.729-0.812) |
| 15 | Fried | 2012 | Multivariable logistic regression | Overall accuracy rate | 0.84 |
| 16 | Galtier | 2006 | Multiple linear regression with stepwise selection | Coefficient of determination (R ²) | R ² =0.725 |
| 17 | Gouillat | 2012 | Multilevel model | AIC, -2LL | -2LL= 11,633.5; AIC 11,647.5 |
| 18 | Gras-Miralles | 2014 | Linear regression after backward, forward, and mixed stepwise approaches; model selection based on adjusted R ² | Coefficient of determination (R ²) | 0.90 |

| Model Number | Author | Year | Modeling method | Metric of Model Performance | Model Performance |
|--------------|-------------|------|--|--|---|
| 19 | Lee | 2007 | Logistic regression | Classification rate | 0.887 |
| 20 | | | Artificial Neural Network Model | Classification rate | 0.94 |
| 21 | Lee | 2009 | Multivariate logistic regression | NR | NR |
| 22 | | | Artificial Neural Network Model | NR | NR |
| 23 | Lee | 2009 | Logistic regression | Classification rate | 0.849 |
| 24 | | | Discriminant analysis model | Classification rate | 0.857 |
| 25 | | | Classification and regression tree (| Classification rate | 0.861 |
| 26 | Manning | 2015 | Multiple regression analyses after backward selection | AUC | NR |
| 27 | | | Multiple regression analyses after backward selection | AUC | NR |
| 28 | Martin | 2015 | Backward stepwise selection followed; final predictors used in mixed models | Coefficient of determination (R^2) | $R^2=0.11$ |
| 29 | | | Backward stepwise selection followed; final predictors used in mixed models | Coefficient of determination (R^2) | $R^2=0.21$ |
| 30 | Melton | 2008 | Multiple logistic regression | NR | NA |
| 31 | Obeidat | 2016 | Multivariate analysis | Adjusted R^2 | Adjusted $R^2=0.321$ |
| 32 | | | Multivariate analysis | Adjusted R^2 | 0.292 |
| 33 | Ortega | 2012 | Stepwise linear regression analysis | Adjusted R^2 | 0.27 |
| 34 | | | Stepwise linear regression analysis | Adjusted R^2 | 0.30 |
| 35 | | | Binary logistic regression based on the predictors from the linear stepwise regression | NR | NA sensitivity = 0.62 specificity = 0.92 efficiency = 0.84 PVP = 0.72 PVN = 0.88 |
| 36 | Robinson | 2014 | Signal Detection Analysis | Sensitivity, specificity, PVP, PVN, efficiency | PVN = 0.88 |
| 37 | Valera-Mora | 2005 | Simple and multiple linear regression analyses were used to identify predictors of weight loss | Coefficient of determination (R^2) | $R^2=0.51$ |

| Model Number | Author | Year | Modeling method | Metric of Model Performance | Model Performance |
|--------------|----------|------|--|--|--|
| 38 | van Hout | 2009 | Hierarchical multiple regression analyses. Variable selection based on statistically significant Pearson correlation coefficients between predictors and outcome | Coefficient of determination (R^2) | Age explained 3.8% and 4.0% additional variance, respectively. |
| 39 | Yanos | 2015 | Stepwise linear and logistic regression analyses | Coefficient of determination (R^2) | $R^2=0.09$ |
| 40 | | | Stepwise linear and logistic regression analyses | Coefficient of determination (R^2) | $R^2=0.22$ |

AIC: Akaike's Information Criterion; LL: likelihood; PPV: predictive value positive; PVN: predictive value negative; NR: not reported; AUC: area under the curve; NA: not applicable

Table 10. Models predictive of successful or failed weight loss after bariatric surgery.

| | Arterburn, 2013 | Arterburn, 2013 | Arterburn, 2013 | Aguiera, 2015 | de Raaff, 2016 | Fried, 2012 | Lee, 2007 (M1) | Lee, 2007 (M2) | Lee, 2009a (M1) | Lee, 2009a (M1) | Lee, 2009b (M1) | Lee, 2009b (M2) | Lee, 2009b (M3) | Ortega, 2012 | Yanos, 2015 | Yanos, 2015 |
|--------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-------------------|--------------|-----------------|
| | percent WL ≥35 | percent WL ≥30 | percent WL ≥25 | percent EWL ≥50 | percent EWL ≤50 | BMI >35.9 | percent EWL ≥50 | percent EWL ≥50 | percent EWL ≥50 | percent EWL ≥50 | percent EWL ≥50 | percent EWL ≥50 | percent EWL ≥50 | percent EWL ≥60 | Nadir weight | Weight regain |
| Age | 2.18 | 3.92 | 1.57 | 0.88 | 1.035 | | | | | | | | | 1.40 ^a | | |
| Albumin | | | | | | | | | | | | | | NR ^a | | |
| Antidiabetic medications | | | | | | | | | | | | | | | | |
| Insulin+ | | | | | | | | | | | | | | | | |
| OHAS | 0.83 | 1.05 | 1.88 | | | | | | | | | | | | | |
| OHAS | 0.46 | 0.78 | 0.54 | | | | | | | | | | | | | |
| Anxiety | | | | 13.85 | | | | | | | | | | | | |
| Apneahypopnea index | | | | | 0.992 | | | | | | | | | | | |
| ASA class (3/4) | | | | | | | | | | | | | | | | |
| ASA class 3 | 1.4 | 0.79 | 0.69 | | | | | | | | | | | | | |
| ASA class 4 | 1.28 | 0.54 | 0.39 | | | | | | | | | | | | | |
| BMI | | | | | 1.148 | 1.90 | | | | | | | | 1.90 ^a | | |
| Depression | | | | 0.23 | | | | | | | | | | | | NR ^b |
| Diabetes | | | | | 1.921 | | | | | | | | | | | |
| DCG score | | | | | | | | | | | | | | | | |
| Score = 1-2 | 1.22 | 1.20 | 0.74 | | | | | | | | | | | | | |
| Score = 2+ | 1.85 | 1.52 | 1.98 | | | | | | | | | | | | | |

| | | Arterburn, 2013 | Arterburn, 2013 | Arterburn, 2013 | Aguiera, 2015 | de Raaff, 2016 | Fried, 2012 | Lee, 2007 (M1) | Lee, 2007 (M2) | Lee, 2009a (M1) | Lee, 2009a (M1) | Lee, 2009b (M1) | Lee, 2009b (M2) | Lee, 2009b (M3) | Ortega, 2012 | Yanos, 2015 | Yanos, 2015 |
|-----------------------|-----------------|-----------------|-----------------|-----------------|---------------|----------------|-------------|-----------------|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-------------------|-----------------|-----------------|
| Gender | | | | | | | | | | | NR ^a | | | | | | |
| | Male | | | | | | | | | | | | | | 1.60 ^b | | |
| | Female | 2.03 | 2.48 | 2.04 | | 1.645 | | | | | | | | | | | |
| HbA1c | | | | | | | | NR ^a | | | | NR ^b | NR ^b | | 1.20 ^b | | |
| Insulin | | | | | | | | | | NR ^a | | NR ^b | | | | | |
| Lipids | | | | | | | | NR ^a | | | | | | | 1.20 ^b | | |
| Liver function | | | | | | | | | | | | NR ^b | NR ^b | NR ^b | | | |
| Marital status | | | | | | | | | | | | | | | | | |
| | Married | 1.38 | 1.87 | 1.49 | 7.5 | | | | | | | | | | | | |
| | Never married | 2.81 | 2.65 | 1.18 | | | | | | | | | | | | | |
| Medical comorbidities | | | | | | | | | | | | | | | | NR ^b | |
| Obesity status | | 0.53 | 0.9 | 1.63 | | | | | | | | | | | | | |
| Personality traits | | | | | 1.05 | | | | | | | | | | | | |
| Race/ethnicity | | | | | | | | | | | | | | | | | |
| | Unknown/missing | 4.17 | 2.05 | 1.08 | | | | | | | | | | | | | |
| | Caucasian | 2.69 | 2.31 | 2.28 | | | | | | | | | | | | | |
| Smoking | | 1.83 | 1.39 | 0.51 | | | | | | | | | | | | | |
| SNPs | | | | | | | | | | | | | | | | | |
| | rs4684846 | | | | | | | | | NR ^a | | | | | | | |
| | rs660339 | | | | | | | | | NR ^a | | | | | | | |
| Sweets avoidance | | | | | | | | | | | | | | | | | NR ^b |

| | Arterburn, 2013 | Arterburn, 2013 | Arterburn, 2013 | Aguiera, 2015 | de Raaff, 2016 | Fried, 2012 | Lee, 2007 (M1) | Lee, 2007 (M2) | Lee, 2009a (M1) | Lee, 2009a (M1) | Lee, 2009b (M1) | Lee, 2009b (M2) | Lee, 2009b (M3) | Ortega, 2012 | Yanos, 2015 | Yanos, 2015 |
|---------------------------|-----------------|-----------------|-----------------|---------------|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-------------------|-------------|-------------|
| Type of bariatric surgery | | | | | 1.961 | NR ^a | NR ^b | NR ^b | NR ^b | NR ^b | NR ^b | NR ^b | NR ^b | | | |
| Laparoscopic | 1.32 | 1.24 | 0.77 | | | | | | | | | | | | | |
| Gastric bypass | | | | 22.14 | | | | | | | | | | 1.20 ^a | | |
| Duodenal switch | | | | 2.54 | | | | | | | | | | | | |
| VSG | | | | 9.45 | | | | | | | | | | | | |
| White blood cells count | | | | | | | NR ^b | NR ^b | NR ^b | NR ^b | NR ^b | NR ^b | | | | |
| Waist circumference | | | | | | | | | | | | | | 0.7 ^b | | |

^a Not statistically significant (P>0.05)

^b Statistically significant (P<0.05)

OHAS: oral hypoglycemic agents; VSG: vertical sleeve gastrectomy; SNPs: single-nucleotide polymorphisms; WL: weight loss; ASA: American Society of Anesthesiologists; DCG: diagnostic cost group

KQ 3.d.

We identified four studies (Altieri et al., Flum et al., Hazzan et al., Lemaître et al.) that examined outcomes after revisional bariatric surgery in the Medicare eligible population. Only one study (Altieri et al.) specifically focused on outcomes after revisional surgery; the remaining studies evaluated this procedure in stratified analyses by the type of surgery.

Altieri et al. used an administrative health database from the state of New York to identify 3,158 patients who underwent either removal or revision of a previously implemented AGB. Revisional procedures occurred within 3.11 (SD, 1.85) years from the primary surgery and included gastric bypass (12 percent), SG (5.6 percent), band removal (32.8 percent), band replacement (19.1 percent), and band revision (30.5 percent). Complication rates at the revision were significantly higher than that at initial band surgery; nevertheless, the presence of complication at primary surgery was not a risk factor for complication after revision. Among all revisional procedures, complication rates were higher for band revision and band removal. The most common complications at revision were digestive/intestinal complications (74.2 percent), surgical error (7.2 percent), and pneumonia (4.3 percent). Significant predictors of subsequent revision were age, race/ethnicity, admission status, and geographical region. In addition, chronic pulmonary disease, depression, hypothyroidism, neurological disorders, psychoses, and rheumatoid arthritis/collagen vascular disease were associated with increased risk of revisional surgery, while patients with hypertension were less likely to undergo revision. Finally, there was no difference in the complications during the original procedure among those who underwent subsequent revision and those who did not.⁹³

Flum et al. used Medicare fee-for-service claims data to evaluate mortality after bariatric surgery. A total of 1225 (7.6 percent) Medicare beneficiaries had undergone revision of gastric restrictive procedure. There was no evidence that early mortality rates for revisional surgery were statistically different from those after primary surgery (2.0 percent vs 1.5 percent, 2.8 percent vs 2.2 percent, and 4.6 percent vs 4.3 percent at 30 days, 90 days, and 1 year, respectively; $P > 0.10$ for all time points).³¹

In the cohort ($n=55$) studied by Hazzan et al., 3 patients (5.5 percent) had revisional surgery. None of them experienced any complications after surgery.⁹⁴

Lemaitre et al. evaluated weight loss after LSG performed as revisional bariatric surgery after a previously failed LAGB ($n=57$ patients), intragastric balloon ($n=46$) or LSG ($n=6$). When LSG was done as revisional surgery for LAGB, patients achieved a mean percent EWL of 61.5 (SD, 20.4) at 1 year and 68.9 (SD, 18.5) at 2 years; the percent EBMIL at the respective time points was 62.4 (SD, 25.4) and 84.4 (SD, 37). When LSG was done as revisional surgery for intragastric balloon, patients achieved a mean percent EWL of 63.8 (SD, 20.7) at 1 year and 71.9 (SD, 12.9) at 2 years; the percent EBMIL at the respective time points was 102.5 (SD, 37) and 129.4 (SD, 40.4). When LSG was done as revisional surgery for a previously failed LSG, patients achieved a mean percent EWL of 55.8 (SD, 3.7) at 1 year and 40.4 (SD, 3.8) at 2 years; the percent EBMIL at the respective time points was 59.4 (SD, 11.5) and 34.7 (SD, 9.9).³⁴

Revisional surgery was also assessed by Quirante et al. However, the authors report complications rates for patients who received any of multiple types of bariatric surgical procedures and not specifically for revisional surgery.⁹⁵

Key Question 4

4.a. In Medicare eligible patients, what is the comparative effectiveness of different bariatric interventions (contrasted between them or vs. non-bariatric interventions) with respect to the non-weight loss outcomes in KQ2c and what is the comparative safety of these interventions?

4.b. What patient- (KQ2a) and intervention-level (KQ2b) characteristics modify the effects of the bariatric therapies on the outcomes other than weight loss in KQ2c?

KQ 4.a.

We identified 27 studies which contrasted bariatric surgical procedures to each other, to non-bariatric treatments, or to conventional or no treatment. No randomized trials in the Medicare eligible population were found.

In the absence of randomization, failure to achieve balance in important confounders and other prognostic factors associated with the studied outcome is likely to result in biased estimates of treatment effects. Comparing the rates of adverse events between two different bariatric surgeries without taking into account (e.g. through statistical modeling) the fact the different patient characteristics are related to treatment selection is not sufficient to attribute differences in adverse event rates between surgeries to treatments themselves.

Appropriate study design and/or analytical approaches that allowed credible estimation of treatment effects by achieving some degree of balance in potential confounders and other prognostic factors associated with the outcome of interest (e.g. cardiovascular event, mortality, etc.) between the compared procedures¹⁹ were used in 12 studies. These factors included demographic characteristics (age,^{36, 51, 53, 54, 60, 61, 64, 96, 97} gender,^{36, 53, 54, 60, 61, 64} race^{60, 64}) comorbid conditions (hypertension,^{36, 60} dyslipidemia,^{36, 60} history of diabetes,^{36, 60} duration of diabetes,^{54, 98} obstructive sleep apnea,^{36, 60} tobacco abuse,⁶⁰ history of transient ischemic attack,⁶⁰ cardiovascular event history,^{36, 60} gallstones,³⁶ fatty liver disease,³⁶ venous stasis,³⁶ cellulitis,³⁶ deep vein thrombosis,³⁶ pulmonary embolisms,³⁶ arthritis,³⁶ gastro-esophageal reflux disease [GERD],³⁶ stress incontinence,³⁶ back pain,³⁶ disc disease,³⁶ Charlson comorbidity score⁶⁴); BMI,^{51, 53, 54, 61, 64, 96, 99} year of surgery,^{36, 97} international normalized ratio;⁹⁷ type of bariatric surgery for concomitant effects of bariatric and other surgeries;⁶¹ body weight;⁶⁴ glucose levels;⁶⁴ percent EWL;⁵³ and cholesterol levels.⁵⁴ One study did not report on potential confounders or other prognostic factors.¹⁰⁰

The potential confounders and other prognostic factors associated with the outcome of interest were accounted for through adjustment for these covariates in models based on multiple regression^{54, 60, 96-100}; through matching^{51, 53, 61}; or through construction of propensity scores which were subsequently used for estimating inverse probability of treatment weights⁶⁴ or for weighted propensity score analyses.³⁶

Below we summarize the outcomes that were reported in these 12 studies. For the remaining studies, we considered each arm as a cohort of patients exposed to a specific intervention (either one or more bariatric surgical procedures) and we present the relevant outcome statistics in the Appendix H.

Mortality

A total of four non-randomized comparative studies examined the effects of bariatric surgical procedures on mortality.

In Davidson et al., RYGB resulted in lower all-cause mortality rates compared to a non-surgical control group (hazard ratio, HR, 0.50; 95% CI 0.31, 0.79; $P<0.003$). In subgroup analyses by gender, the reduced risk of all-cause mortality after RYGB relatively to no surgery was seen only in men (HR 0.23; 95% CI 0.07, 0.94) but not in women (HR 0.61; 95% CI 0.36, 1.03). In regards to cause-specific mortality, RYGB resulted in statistically significant lower mortality (HR 0.46; 95% CI 0.28-0.75; $P=0.002$) from any cause other than externally caused deaths (unintentional injury unrelated to drugs, poisoning of undetermined intent, suicide, and other externally caused deaths). However, there was effect between RYGB and all externally caused deaths (HR 1.30; 95% CI 0.25, 6.86; $P=0.76$), cardiovascular mortality (HR 0.57; 95% CI 0.28, 1.15; $P=0.12$), or cancer mortality (HR 0.54; 95% CI 0.21, 1.35; $P=0.19$).⁹⁶

Johnson et al. compared all-cause, cardiovascular, and non-cardiovascular mortality in patients receiving gastric bypass or AGB versus morbidly obese patients undergoing orthopedic or gastrointestinal surgeries. They found no evidence that bariatric patients 50 to 59 years of age or 60 to 69 years of age had lower all-cause mortality risk. In the combined 50 to 69 age group, HRs for the effects of bariatric surgery on mortality outcomes were 0.68 (95% CI 0.38, 1.23; $P=0.201$) for all-cause mortality; 0.83 (95% CI 0.36, 1.93; $P=0.658$) for cardiovascular-mortality; and 0.60 (95% CI 0.26, 1.39; $P=0.233$) for non-cardiovascular mortality.⁶⁰

Scott et al. compared mortality outcomes in patients who received any bariatric surgery with two non-bariatric surgery control groups. The first control group consisted on patients undergoing orthopedic procedures and the second of patients undergoing gastrointestinal surgery. Bariatric surgery resulted in lower risk of all-cause mortality compared to the gastrointestinal surgical procedures (HR 0.45, 95% CI 0.33, 0.60) but there was no evidence of difference in all-cause mortality compared to orthopedic surgeries (HR 0.81, 95% CI 0.60, 1.10).¹⁰⁰

Perry et al. report lower mortality rates at 2 years after surgery in morbidly obese Medicare beneficiaries 65 years and older undergoing any bariatric surgery compared to non-surgical controls (8 percent vs. 12.2 percent, $P<0.001$) as well as in disabled Medicare beneficiaries younger than 65 years undergoing any bariatric surgery compared to non-surgical controls (4.5 percent versus 8.6 percent ($P<0.001$)). They also note of an increased mortality rate in the 30-day post-operative period for both patients aged 65 and over (1.55 percent vs. 0.53 percent; $P<0.001$) and disabled younger than 65 (1.27 percent vs. 0.49 percent; $P<0.001$). However, mortality rates did not differ between the surgical and non-surgical groups at 6 and 11 months after surgery for disabled Medicare beneficiaries below 65 years of age and for Medicare beneficiaries older than 65 years, respectively.³⁶

Because of heterogeneity in bariatric surgical procedures across studies, we deemed that a statistical synthesis would not result in a clinically meaningful estimate of an overall treatment effect.

Appendix H shows mortality rates at different time points of follow-up in any eligible studies which reported on mortality outcomes but without any design and/or analytical approaches that would account for confounders and other prognostic factors associated with the respective outcome. The table also shows the rates in studies that reported only on a single bariatric surgical procedure.

Weight loss

Weight loss outcomes are examined in detail in KQ3.

Reoperations/Need for Revisional Bariatric Surgery

We identified no studies that accounted for potential confounders or other prognostic factors associated with the reoperations or need for revisional bariatric surgery. The rates of revisional surgery by treatment arm in studies are shown in Appendix H. The table also shows the rates in studies that reported only on a single treatment arm consisting of one or more bariatric surgical procedures.

Postoperative Complications

Two non-randomized comparative studies examined post-operative complications of different bariatric surgical procedures.

Spaniolas et al. examined 30-day complications rates in patients undergoing RYGB compared to SG using models adjusted for history of diabetes. They found no evidence of an effect on overall mortality (OR 0.85 95% CI 0.1, 7.41) as well as overall (OR 1.0; 95% CI 0.55, 1.82) or serious (OR 1.10; 95% CI 0.51, 2.38) morbidity. Morbidity included post-operative bleeding, organ-specific infection, pulmonary embolism, reoperation, surgical site infection, and septic occurrences.⁹⁸

Boules et al. evaluated post-operative outcomes in patients undergoing concomitant bariatric surgery and hiatal hernia repair. They found that, compared to a control group receiving bariatric surgery only, the concomitant performance of hiatal hernia repair and bariatric surgery was not associated with operative time, intraoperative complication, duration of stay, postoperative early symptoms or late postoperative complications.⁶¹

The rates of post-operative complications in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest are shown in Appendix H. The table also shows the rates in studies that reported only on a single treatment arm consisting of one or more bariatric surgical procedures.

Diabetes and Metabolic-Related Outcomes

Four non-randomized comparative studies evaluated the effect of bariatric surgery on diabetes and other metabolic-related outcomes.

Ardestani et al. found that RYGB to be more effective than LAGB in reducing insulin treatment among diabetic patients. At 3 months after surgery, a higher percentage of RYGB patients successfully ceased insulin compared to LAGB patients (37.1 percent vs. 26.3 percent; $P=0.03$). In addition, the rates of clinical remission of type 2 diabetes for RYGB versus LAGB were 14.4 percent versus 7 percent ($P=0.02$) at 1 month; 28.0 percent versus 12.9 percent ($P=0.001$) at 3 months; 30.7 percent versus 19.3 percent ($P=0.01$) at 6 months; and 35.7 percent versus 24.4 percent ($P=0.01$) at 12 months.⁵³

Perry et al. found no evidence in the improvement of diabetes among patients receiving bariatric surgery compared to non-surgical controls in 6 months and in 1 year after surgery; however, there was an improvement at 2 years.³⁶

Lee et al. examined all pairwise comparisons between RYGB, SG, and LAGB using inverse-probability treatment weighting in regards to their effects on HbA1c levels. They found no evidence that 6 or 12 months after surgery levels of HbA1c were lower for any one surgery compared to the other. There was also no evidence of lower glucose levels for any surgery at either 6 or 12 months.⁶⁴

Lee et al. found no evidence that RYGB, LAGB or SG result to lower levels of low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein-cholesterol, total cholesterol or triglycerides at 6 or 12 months after surgery relatively to each other.⁶⁴

Leonetti et al. compared LSG versus conventional therapy including pharmaceutical agents and lifestyle modifications (diet and physical activity) in regards to the differences from baseline in levels of LDL-cholesterol, HDL-cholesterol, triglycerides at 18 months after treatment among type 2 diabetes patients. They found statistically significant larger decreases in triglycerides and HDL in the LSG group compared to the conventional therapy group. Higher decreases were also found for glucose and HbA1c levels but only among patients with duration of type 2 diabetes over 10 years. There was no evidence that LSG resulted in higher changes in the levels of LDL-cholesterol or total-cholesterol compared to conventional treatment.⁵⁴

Because of the heterogeneity in the bariatric surgical procedures and outcomes across studies, we deemed that a statistical synthesis would not result in a clinically meaningful estimate of an overall treatment effect.

Changes in diabetes and other metabolic outcomes in the post-surgical period compared to baseline/pre-surgical outcome values are shown in Appendix H. The table also shows the rates by treatment arm in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Reflux

We did not identify any studies achieving balance of potential confounders or other prognostic factors between treatment groups in regards to the effects of bariatric surgeries on reflux or GERD. Outcome incidence rates by treatment group in studies that did not account for confounders or other prognostic factors associated with reflux are shown in Appendix H. The table also shows the rates in studies that reported only on a single treatment arm consisting of one or more bariatric surgical procedures.

Cardiovascular Outcomes

In this section, we consider long-term cardiovascular outcomes occurring after 90 days from bariatric surgery. Short-term cardiovascular outcomes occurring within 90 days were considered as surgery-related post-operative complications/adverse events and are described earlier under “Postoperative Complications” and in Appendix H.

Scott et al. compared the effect on myocardial infarction of multiple bariatric surgical procedures combined into a single treatment arm. Compared to patients undergoing orthopedic surgery (controls), patients undergoing bariatric surgery had a lower risk (HR 0.59, 95% CI 0.44, 0.79) of myocardial infarction (MI). The same benefit was also observed when bariatric patients were compared to a control group of patients undergoing gastrointestinal surgery (HR 0.49; 95% CI 0.36, 0.68).¹⁰⁰

Scott et al. also reported on the composite endpoint of MI, stroke, or all-cause mortality. Bariatric surgery was associated with lower risk of MI, stroke, or all-cause mortality (HR 0.72, 95% CI 0.58-0.89 for bariatric surgery compared to orthopedic surgery; HR 0.48, 95% CI 0.39-0.61 for bariatric surgery compared to gastrointestinal surgery).¹⁰⁰

Perry et al. found that evidence of improvement in coronary artery disease in the 6-month period after surgery, which was maintained in 1 and 2 years after surgery. There was also evidence of improved lipid profile in 1 year and 2 years after surgery, but no evidence of

improvement in the immediate 6 months. The difference in outcomes between bariatric patients and non-surgical controls increased between 6 months, 1 year, and 2 years.³⁶

Lee et al. found no evidence that either systolic or diastolic blood pressure were lower at 6 or 12 months after surgery after any of RYGB, SG or LAGB compared to each other.⁶⁴

Leonetti et al. compared LSG versus conventional therapy consisting of pharmaceutical agents and lifestyle modifications (diet and physical activity) in regards to the prevalence of hypertension at 18 months after treatment. They found no evidence the prevalence was different between the two treatment groups.⁵⁴

Scott et al. also compared the effect on stroke of surgery single treatment arm, which comprised multiple bariatric surgical procedures. Compared to a control group of patients undergoing gastrointestinal surgery, there was evidence of lower risk of stroke in bariatric patients (HR 0.49; 95% CI 0.24, 0.98). Compared to patients undergoing orthopedic surgery (controls), patients undergoing bariatric surgery had a lower, though not statistically significant, risk of stroke (HR 0.69; 95% CI 0.40, 1.30).¹⁰⁰

Because of heterogeneous the bariatric surgical procedures and outcomes across studies, we deemed that a statistical synthesis would not result in a clinically meaningful estimate of an overall treatment effect.

Appendix H shows the changes the measures of relevant outcomes before versus after surgery without comparisons to a control group or other bariatric surgery, as well as in studies that did not control for confounders or other prognostic factors associated with the outcome of interest.

Respiratory Disease

Perry et al. found evidence of improvement in sleep apnea in the 6-month period after surgery but there was no evidence of long-term improvement at 1 and 2 years.³⁶

Appendix H shows the changes in respiratory outcomes before versus after surgery among patients who received bariatric surgery without comparing to a control group or another surgery as well as in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Orthopedic/Musculoskeletal Outcomes

Valderas et al. retrospectively compared bone-related parameters in post-menopausal women undergoing RYGB in BMI- and age-matched controls. They found no evidence that RYGB affected BMI, body fat, calcium intake, vitamin D intake, caloric intake, serum calcium, phosphorus, albumin creatinine, thyroid stimulating hormone, 25-hydroxy vitamin D, vitamin D deficiency, alkaline phosphatase, femoral bone mineral density or lumbar spine bone mineral density after 1 to 5 years. However, RYGB was associated with an increased prevalence of hyperparathyroidism.⁵¹

Martin et al. evaluated the effect of bariatric surgery on outcomes after total knee arthroplasty (TKA). They compared outcomes in TKA patients who had receive bariatric surgery prior to the TKA (TKA plus bariatric surgery) versus patients of high and low BMI undergoing TKA without prior bariatric surgery (TKA alone). The high BMI group had a mean BMI of 51.2 kg/m² at the time of TKA (i.e., similar to the pre-bariatric surgery BMI of the study group), while the low BMI group had a mean BMI of 37.2 kg/m² at the time of TKA (i.e., similar to the post-bariatric bariatric /pre-TKA BMI of the study group). Compared to patients with high BMI undergoing only TKA without prior bariatric surgery, patients receiving bariatric surgery before

TKA were more likely to be re-operated (HR 2.5; 95% CI 1.2 to 6.2; $P = 0.02$). However, there was no evidence of differences in the rates of complications, revision surgery, or periprosthetic joint infection. Compared to patients with low BMI undergoing only TKA without prior bariatric surgery, patients receiving bariatric surgery prior to TKA were more likely to be re-operated (HR 2.4; 95% CI 1.2 to 3.3; $P = 0.02$) as well as undergo revisional surgery (HR 2.2; 95% CI 1.1 to 6.5, $P = 0.04$). There was no evidence that rates of complications or periprosthetic joint infection were different.⁹⁹

Appendix H shows the changes in orthopedic and musculoskeletal outcomes before versus after surgery among patients who received bariatric surgery without comparing to a control group as well as in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Incidence of Specific Cancers

We did not identify any comparative studies on cancer incidence after bariatric surgery. Appendix H shows incidence of cancer outcomes after surgery among patients who received bariatric surgery without comparing to a control group as well as in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Nutritional Deficiencies

We did not identify any comparative studies on nutritional deficiencies or other malnutrition outcomes after bariatric surgery. Appendix H shows the incidence of such outcomes after surgery among patients who received bariatric surgery without comparing to a control group as well as in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Renal Function

We did not identify any studies comparing one or more bariatric surgeries to a control group and estimate treatment effects in regards to renal function outcomes. Studies reporting on changes of these outcomes before versus after surgery with no comparison to a control group are shown in Appendix H.

Compliance with Follow-Up

We did not identify any studies that compared bariatric surgeries in regards to compliance to follow-up. Follow-up times and relevant outcomes by surgery are shown in Appendix H.

Mental Health

We did not identify any studies whose design and/or analytical approach allowed for unbiased estimates of comparative treatment effects by balancing prognostic factors between treatment groups in regards to mental health outcomes. Changes in the prevalence and/incidence of such outcomes before versus after surgery are shown in Appendix H. The table also shows the rates of relevant outcomes in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Function and Quality of Life

We did not identify any studies whose design and/or analytical approach allowed for unbiased estimates of comparative treatment effects by balancing prognostic factors between

treatment groups in regards to health-related quality of life outcomes. Appendix H shows the changes in physical, mental, and overall health-related quality of life in studies that measured these outcomes before and after bariatric surgery. It also shows the rates of relevant outcomes in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Cognitive Functioning

We did not identify any studies with balanced potential confounders or other prognostic factors associated with cognition-related outcomes between treatment groups. Appendix H shows the changes in relevant outcomes in studies that measured these outcomes before and after bariatric surgery as well as in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Sexual Functioning

We did not identify any studies on sexual functioning.

Ability to Participate in an Exercise Program

We did not identify any studies with balanced prognostic factors between treatment groups reporting treatment effects on patients' ability to participate in an exercise program after bariatric surgery. Appendix H shows the changes in relevant outcomes in studies that measured these outcomes before and after bariatric surgery as well as in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest.

Ability to Return to Work

We did not identify any studies that achieved balance for prognostic risk factors that reported treatment effects between bariatric surgery and a control group in regards to patients' ability to return to work. Results for studies comparing relevant outcomes but without a proper design and/or analytical approach for estimating causal treatment effects are shown in Appendix H.

In one such study, Wagner et al. performed a non-parametric comparison between 38 medically disabled, morbidly obese patients receiving Medicaid benefits who had undergone open RYGB and 16 non-operative controls. They found that 37 percent of the bariatric group returned to work compared to 6 percent in the control group ($P=0.02$).⁶²

Physical Performance/Test Pain (joint pain, joint aches)

We did not identify any studies that achieved balance for prognostic risk factors that reported treatment effects between bariatric surgery and a control group in regards to pain tests. Results for studies comparing relevant outcomes but without a proper design and/or analytical approach are shown in Appendix H. This table also shows studies that reported changes in the outcomes measured before versus after surgery but with no comparison to a control group.

Regular Daily Activities

We did not identify any studies that achieved balance in potential confounders or other prognostic risk factors that reported treatment effects between bariatric surgery and a control group in regards to patients' ability to perform regular daily activities. Results for studies comparing relevant outcomes but without a proper design and/or analytical approach are shown

in Appendix H. This table also shows studies that reported changes in the outcomes measured before versus after surgery but with no comparison to a control group.

Polypharmacy

Lee et al. found that at 6 and 12 months after surgery, patients undergoing RYGB had experienced a greater reduction in the number of medications from baseline compared to patients undergoing SG or LAGB. However, there was no difference between SG and LAGB.⁶⁴

In the study of diabetics by Leonetti et al., medication use decreased at 18 months after surgery. The mean number of antihypertensive drugs decreased from 1.5 to 0.83 pills and the mean number of hypolipemic drugs reduced from 0.4 to 0.2. Reductions for both drug classes were statistically significant at $P=0.05$.⁵⁴

Irwin et al. compared post-surgical differences in warfarin doses in reference to the pre-surgical period between bariatric patients receiving RYGB or gastric banding and a control group of patients undergoing cholecystectomy or endoscopic retrograde cholangiopancreatography (ERCP). The weekly median warfarin dose in the first 8 weeks as well the median dose between 2 and 3 months and between 3 and 6 months after bariatric surgery was lower than in the pre-surgical period for bariatric patients, while there was no difference over time for non-bariatric patients. For each time point, the decrease in warfarin dose in bariatric patients was significantly lower than in the non-bariatric patients.⁹⁷

Irwin et al. also found that bariatric surgery resulted in: (1) more patients achieving 20 percent or more decrease in preoperative warfarin dose at any time during follow-up; (2) lower percentage time in therapeutic INR range; (3) less bleeding during the 180-day period after surgery. Results are shown in Appendix H.⁹⁷

Admission to a Skilled-Nursing Facility

We did not identify any studies reporting on risk of admission to skilled nursing facilities after bariatric surgery.

Access to Plastic Surgery

We did not identify any studies comparing access to surgery among patients undergoing different bariatric procedures.

Readmissions/Rehospitalizations

We did not identify any studies with balanced potential confounders or other prognostic factors reporting on treatment effects of different bariatric surgeries on the risk of hospital readmission after surgery. Appendix H shows the incidence rates within treatment arms for eligible studies that did not compare between different treatments or they did not account for confounders or other prognostic factors associated with the outcomes of interest.

Strength of the Evidence

There is at most moderate strength of evidence regarding the comparative effectiveness and safety of bariatric surgery in Medicare eligible populations (Table 11). There are no randomized trials in the Medicare eligible population that compare bariatric surgical procedures amongst them, to non-surgical treatments or procedures, or to no treatment at all. The evidence base consists of non-randomized studies. Many of these studies report data on more than one bariatric surgical intervention but only a relatively small fraction of them allows causal inferences about

whether the changes in the outcomes are because of bariatric surgery. This is because few studies were designed and/or analyzed with a comparative and/or causal inference aim. Among the comparative studies, we cannot exclude the possibility that unmeasured confounding may result in inaccurate estimates of treatment effect.

Table 11. Strength of evidence for non-weight loss outcomes in the Medicare eligible population

| Conclusion statement | RoB (evidence-base) | Consistency | Precision | Directness and Applicability | Overall Rating | Comments |
|---|---------------------------------------|-------------|---|---|---|--|
| Bariatric surgery results in favorable outcomes compared to no surgery/other non-bariatric surgery/conventional treatment in regards to: (1) Mortality (2) Metabolic outcomes (3) Cardiovascular outcomes (4) Musculoskeletal outcomes (5) Warfarin dose after surgery (6) Respiratory outcomes | High for (1), (2), (3), (4), (5), (6) | [Not rated] | Low for (4), (5) Moderate for (1), (2), (3), (6) | Moderate for (1), (2), (3), (4), (5), (6) | Low SoE for (4), (5) Moderate SoE for (1), (2), (3), (6) | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. Use of inappropriate control groups limits applicability/generalizability. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| RYGB results in favorable outcomes compared to SG in regards to: (1) Post-operative complications (2) Metabolic outcomes (3) Polypharmacy (4) Cardiovascular outcomes | Moderate for (1), (2), (3), (4) | [Not rated] | Low for (1), (2), (3), (4) | High for (1), (2), (3), (4) | Moderate SoE for (1), (2), (3), (4) | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| Concomitant bariatric surgery and hiatal hernia repair does not result in higher complication rates compared to bariatric surgery alone | High | [Not rated] | Low | Moderate | Low SoE | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. Only one study addressed this question. Technical aspects of the surgical procedures may limit the feasibility of these surgeries across surgeons. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| RYGB results in favorable outcomes compared to LAGB in regards to: (1) Metabolic outcomes (2) Polypharmacy | Moderate for (1), (2), (3) | [Not rated] | Low for (1), (2), (3) | High for (1), (2), (3) | Moderate SoE for (1), (2), (3) | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. |

| Conclusion statement | RoB (evidence-base) | Consistency | Precision | Directness and Applicability | Overall Rating | Comments |
|--|----------------------------|-------------|-----------------------|------------------------------|--------------------------------|--|
| (3) Cardiovascular outcomes | | | | | | |
| <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> | | | | | | |
| SG results in favorable outcomes compared to LAGB in regards to: (1) Metabolic outcomes (2) Cardiovascular outcomes (3) Polypharmacy | Moderate for (1), (2), (3) | [Not rated] | Low for (1), (2), (3) | High for (1), (2), (3) | Moderate SoE for (1), (2), (3) | There are no randomized studies available in the Medicare eligible population. The evidence-base consists of non-randomized comparative studies. <i>Studies that were deemed as insufficient to make causal inferences about treatment effects do not contribute to SoE assessments.</i> |
| RYGB: Roux-en-Y gastric bypass; SG: sleeve gastrectomy; LAGB: laparoscopic gastric banding; SoE: strength of evidence; RoB: risk of bias | | | | | | |

KQ 4.b.

Two studies examined potential modifiers of the comparative effect of bariatric surgery on weight loss outcomes.^{54, 96}

Davidson et al. performed subgroup analyses on the effects on all-cause mortality of RYGB based on gender. For patients 55 years or older, risk of all-cause mortality was lower in the treatment group relative to the control in men (HR 0.23; 95% CI 0.07, 0.74) but not in women (HR 0.61; 95% CI 0.36, 1.03).⁹⁶

Leonetti et al. examined whether the effects on glucose levels and Hb1Ac of LSG relative to conventional surgery consisting of pharmaceutical agents and lifestyle modifications (diet and physical activity) were different based on the duration of diabetes history. They found that glucose levels reduced by 80.1 mg/dl among patients with diabetes for more than 10 years versus 14.6 mg/dl among patients with diabetes for less than 10 years. Similarly, Hb1Ac was reduced by 2.59 percentage points in patients with more than 10 years of diabetes undergoing bariatric surgery compared to conventional therapy, but for those with less than 10 years of diabetes Hb1Ac was increased by 0.01 percentage points between the two treatment groups.⁵⁴

Key Question 5

5.a. In Medicare eligible patients who have undergone bariatric therapy, what is the association between weight outcomes and eligible short- and long-term outcomes (other than weight outcomes)?

5.b. In Medicare eligible patients, what proportion of the bariatric intervention effect on eligible short- and long-term outcomes (other than weight outcomes) is accounted for by changes in weight outcomes?

KQ 5.a.

We identified three studies that reported measures of association between weight outcomes and health outcomes.

Wagner et al. examined whether the amount of weight loss is associated with return to work after RYGB in disabled patients with morbid obesity. They found no evidence that patients (30 percent) who lost more than the mean excess BMI in the studied population (i.e. >63 percent of excess BMI) were more likely to return to work compared to patients (44 percent) who lost less than the mean excess BMI. The same conclusions were reached when weight loss was defined as achieving BMI less than 35 kg/m² and less than 30 kg/m².⁶²

Wiklund et al. examined whether weight loss outcomes correlate with changes in physical health-related quality of life (HRQoL) as measured by the disability rating index in patients undergoing laparoscopic RYGB. The changes in both the weight and the BMI before and after surgery were weakly correlated with the change in the disability rating index (Spearman's $r=0.273$, $P<0.001$ for weight; and $r=0.273$, $P=0.022$ for BMI).¹⁰¹

Ramos-Levi et al. examine the association between weight loss and diabetes remission after RYGB, BPD or SG. Patients with diabetes remission experienced higher percent weight loss compared to patients without remission (35.5 \pm 8.1 vs. 30.2 \pm 9.5, $P=0.001$) as well as higher percent excess weight loss (73.6 \pm 18.4 vs. 66.3 \pm 22.8, $P=0.037$).¹⁰²

KQ 5.b.

We identified no studies that estimated the proportion of the effect of bariatric surgery on non-weight outcomes that is mediated by their effects on weight loss outcomes. As such, published data are not sufficient for performing a mediation analysis of the causal effect of bariatric surgery on health outcomes. Estimates of comparative treatments effects presented here represent average treatment effects of the eligible bariatric surgical procedures.

Discussion

Evidence Summary

We identified 70 studies, describing the spectrum of bariatric procedures and outcomes that have been studied in patients who resemble Medicare beneficiaries. Another 24 studies reported prediction models and risk factors for weight loss or absolute body weight after bariatric treatment that could be used to assess risk of failure to achieve weight loss.

In the Medicare eligible population, we did not identify any studies in patients undergoing bariatric endoscopic procedures. However, multiple studies have been conducted in regards to one or more bariatric surgical procedures. Most of the surgical procedures in this population were performed laparoscopically, and the most common procedures were AGB, RYGB, and SG. Most studies examined already widely-studied outcomes, such as weight loss, for which ample evidence exists in younger populations that suggests a beneficial effect of bariatric surgery.^{12, 103, 104} In addition, certain outcomes of primary interest to the Medicare population have not been extensively studied. These include health-related quality of life, hospital readmission after surgery, admission to skilled nursing facilities, and nutritional status. Same applies to bariatric procedures where evidence is limited or non-existent for certain procedures (e.g. bariatric endoscopy, vagal blockage), while there is abundant research for others (such as AGB which tends to be eliminated from clinical practice¹⁰⁵). Even for clinically-relevant outcomes that have been examined in the Medicare eligible population (such as mortality or polypharmacy), there is substantial heterogeneity in the outcome and/or procedure definitions that does not allow for the meaningful statistical synthesis of the available studies. As a result, very few studies exist in essence for each separate outcome.

Limited comparative evidence exists for the effects of different bariatric surgical procedures on weight loss and non-weight loss outcomes in the Medicare population. Even among the very few comparative non-randomized studies, the majority were deemed to have at most moderate risk of confounding, selection, or measurement biases because confounders and other prognostic factors associated with the studied outcomes are not accounted for in the design and analysis. The overwhelming majority of evidence is comprised of studies reporting changes in weight and/or non-weight outcomes after one or more bariatric surgical procedures using pre-post designs and estimating the difference of mean weight or BMI before and after surgery.

It should be acknowledged that substantial comparative evidence in younger patients exists. This evidence strongly suggests that bariatric surgery overall as well as certain procedures are both effective in achieving weight loss and reducing the risk of other non-weight loss outcomes (e.g. sleep apnea, cardiovascular events, etc.) and safe in regards to surgical complications. Nevertheless, evidence from studies in younger populations may not be directly generalizable to the Medicare eligible population. The main reason for lack of transportability of treatment effects include differences in the number and severity of comorbid conditions between adults age 65 and older (who comprise most of Medicare beneficiaries) and younger patients. In addition, age itself has a strong predictive effect on patients' ability to lose weight after surgery.⁸⁴ Although statistical methods for the transportability of treatment effects exist, a formal generalization of evidence from younger patients to the Medicare eligible population was beyond the scope of this technology assessment.

Despite the lack of direct evidence in the Medicare eligible population, patients and clinicians who consider bariatric surgery can still use evidence from younger patients to make clinical judgements at the individual level. For example, bariatric surgery may be a safe and

effective procedure for a healthy 70-year old patient with no comorbidities and long life expectancy, while it may pose important risks for a 40-year old patient with multiple comorbidities and short life expectancy.

Weight loss outcomes (i.e. change in a weight-related outcome before vs. after surgery) are measured as absolute weight loss in kilograms (kg), absolute BMI loss in kg/m^2 , percentage loss of total body weight, percentage loss of excess body weight, or percentage loss of excess BMI. Among those, percent EWL and percent WL are most commonly used to measure the effect of bariatric surgery. For non-weight outcomes, studies compare the prevalence of an outcome of interest (e.g. percentage of patients with diabetes) before surgery and after surgery. On average, weight and rates of various comorbidities appear to be reduced after bariatric surgery compared to their pre-surgery values.

Based on the evidence from studies reporting changes in weight outcomes before and after bariatric surgery, it is likely that bariatric surgery overall has a sustaining effect on weight loss outcomes over time. Although the follow-up rarely exceeded 1 year, in those studies with follow-up as long as 8 years, patients maintained their weight loss over time. However, it is possible that there are systematic differences between patients who attend follow-up visits compared to those who do not.¹⁰⁶ For example, patients who maintain their weight loss over time may be more likely to return to the scheduled visits after bariatric surgery. In addition, even if there is no association between data availability at follow-up and the likelihood of outcome events, loss to follow-up results in a smaller sample sizes over time which in turn reduces the statistical power for the estimates of weight loss at different time points.

Overall, for both weight loss and non-weight loss outcomes, the strength of the available evidence for establishing causal associations between bariatric surgical procedures and the respective outcomes in the Medicare eligible population is low to moderate. This is primarily because of the lack of randomized trials. Secondly, the available observational studies may be susceptible to unmeasured confounding that is not accounted for through design or statistical modeling. Moreover, based on the existing evidence base, it remains unclear to what extent the effect on weight-loss outcomes of bariatric surgery is direct or it is mediated through the effects of these procedures on weight loss.

A total of 40 different predictive models for weight loss or absolute body weight have been developed. The fit of these models, as reported in the eligible studies, varied extensively across studies. Even for models with adequate model fit, their clinical utility and validity may be undermined by two things. First, most studies did not adequately report measures of model performance that would allow a comprehensive assessment of their utility. Overall performance, as determined by the R^2 metric, was commonly reported but model calibration and/or discrimination were reported for only a few models. However, whenever these are reported, the respective models seem to perform well. Second, and most importantly, no model was internally or externally validated. All models were initially developed/trained in a cohort of patients undergoing one or more bariatric surgeries but no model's predictive ability was subsequently assessed in the same sample using techniques such as cross-validation or bootstrap (internal validation) or in an independent population (external validation).^{107, 108}

Evidence Limitations

There are no randomized studies regarding the effectiveness of bariatric surgeries in the Medicare eligible population. The evidence base consists primarily of observational studies, very few of which utilize an appropriate design and/or analytical approach that can yield unbiased

estimates of causal treatment effects by accounting for confounders and other prognostic factors associated with the studied outcomes. This is true for both weight loss and non-weight loss outcomes.

Randomized trials are the preferred design to estimate causal effects of bariatric procedures, because randomization ensures that, on average, the compared groups are similar in terms of measured and unmeasured effect modifiers. In the absence of randomization, the compared groups are likely to differ in terms of important prognostic factors (including confounders) that are known to be associated with the outcome of interest. Not accounting for these differences between the compared treatment groups is likely to result in biased estimates of treatment effects.¹⁹ For example, the anatomical modifications involved in sleeve gastrectomy are likely to lead to gastric reflux but the reduction in the stomach pouch during Roux-en-Y gastric bypass does not have such an effect.^{20, 21} Thus, patients who are at increased risk of gastro-esophageal reflux disease are more likely to receive Roux-en-Y gastric bypass rather than sleeve gastrectomy.²² When comparing the rates of gastro-esophageal reflux disease as an adverse event between sleeve gastrectomy and Roux-en-Y gastric bypass without taking into account (e.g. through statistical modeling) the fact the certain patient characteristics (e.g. baseline risk of gastro-esophageal reflux disease) are related to treatment selection (i.e. patients with increased risk of GERD are more likely to receive Roux-en-Y gastric bypass) is not sufficient to attribute differences in adverse event rates between surgeries to surgeries themselves. Moreover, non-randomized comparative studies ought to emulate (mimic) a target randomized trial in order to be maximally and reliably informative for policy actions based on the evidence base that they comprise.^{23, 24} By designing and/or analyzing observational data in a way that emulates a target randomized trial one can make inferences about causal treatment effects. This involves specification of the PICOTS elements as in the target trial and in addition emulation of the random treatment assignment to ensure that the groups being compared are similar. This can be achieved via matching using propensity score, stratification or regression, standardization or inverse probability weighting, g-estimation, or doubly robust methods.²⁴

Although bariatric surgical procedures have sustaining effects on weight loss outcomes over time in pre- vs. post-surgery studies (“before-after” studies), we cannot exclude the possibility that this is due to attrition bias that results from systematic differences in patients who attend follow-up visits. In addition, when follow-up data are analyzed using percent change from baseline as the raw data for analysis, this can be particularly problematic for the estimation of accurate treatment effects even when a comparison group exists.^{109, 110} Despite their easy and clinically relevant interpretation, percentage change as an outcome has many statistical limitations that may lead to overestimation of treatment effects. Hence, its use in statistical analysis is generally discouraged.¹⁰⁹

Pre- vs. post-surgery studies do not have an independent control group as each subject serves as their own control in the pre- versus post-intervention period. Therefore, these studies have greater statistical power (since the independent control group confers additional variation) and subject-specific time-invariant confounders are eliminated.¹¹¹ Furthermore, due to their temporal nature, pre-post studies can indicate changes in the outcome of interest over time, i.e. after the implementation of the intervention. Nevertheless, their major drawback is because of the absence of a control comparison group. In the absence of such a group, pre-post studies cannot reliably determine how much of the change in the outcome represents a causal effect due to surgery and how much may be due to changes occurring naturally over time. The lack of a control group does

not also allow inferences about which of two or more procedures is the most effective and safe. Finally, in pre-post surgery studies, it is not possible to control for time-varying confounders.¹¹¹

For example, in the case of weight loss outcomes, it is impossible to know whether patients, who experienced changes in body weight and/or BMI after the surgery, would not have done so without surgery since weight is very likely to change naturally over time, and if so to what extent. It should be acknowledged, however, that it is unlikely for a person to achieve weight loss of the magnitude reported in the eligible studies “naturally” so rapidly. Similarly, when pre-post studies suggest that the prevalence of an outcome after surgery is lower than before surgery, this difference does not necessarily mean that the outcome change occurred within the same person. For example, diabetes may be resolved after bariatric surgery in a fraction of diabetic patients but a smaller fraction of non-diabetic bariatric patients may develop diabetes after surgery, while the overall diabetes prevalence after surgery still appears lower than before surgery.

Hence, changes in the occurrence of the outcome before versus after the treatment cannot be completely attributed to the treatment per se since some outcomes, such as weight, may be subject to secular changes. Therefore, treatment effects from pre-post study designs are not necessarily causal effects of the studied interventions. As it has been argued before, pre-post studies have limited value for comparative effectiveness research.¹¹¹ Still, their findings can be indicative of potential treatment effects and should be interpreted as hypothesis-generating evidence for future controlled trials.

Studies on weight loss interventions, including drugs, devices, operative procedures (such as bariatric surgery), diets and lifestyle modifications are often susceptible to placebo effects.¹¹² This has been documented in trials evaluating the blockade of the vagal nerve using an implanted rechargeable pulse generator, in which patients randomized to a placebo device lost as much as 11 percent of their excess weight.^{113, 114} Due to the pragmatic nature of the studies included in this report which used routinely collected health data from registries and electronic health records, we anticipate that our findings are less susceptible to placebo effects compared to randomized trials.

Moreover, none of the included studies performed a competing risk analysis for the relevant outcomes. Competing risks occur when an outcome of interest (e.g. cardiovascular events) cannot be observed during the study period because participants experience a different event such as mortality that does not allow for the outcome of interest to occur (competing event).¹¹⁵ Competing risks are of particular concern when treating patients age 65 years and older or patients with multiple comorbidities, because these patients are likely to experience a competing event that decreases the likelihood of treatment benefit.¹¹⁶ These conditions particularly apply to studies of bariatric procedures in the Medicare eligible population. First, bariatric patients, regardless of age, tend to have multiple obesity-related comorbidities. Second, the majority of the Medicare eligible population are above 65 years of age when risks of all-cause mortality are substantially higher than in younger ages. The studies in the current technology assessment had a mean or median age of 55 years or greater and since most of them enrolled patients seen in routine clinical practice. Therefore, competing risks are likely to have substantial effects in the Medicare eligible population and should be accounted for when evaluating the comparative effectiveness of bariatric procedures in this population.

The lack of internally and/or externally predictive models for weight loss limits the clinical utility of the existing which have not passed the initial phase of development. Model validation is important for two reasons.¹¹⁷ First, model performance is usually overestimated when only the

training sample is used for evaluating a model.¹¹⁸ To avoid this “optimism” and derive more accurate model parameters, validation of the model can be performed either using a subset of the original sample; a variety of statistical techniques are available.^{107, 118} Second, a model is clinically useful when it can accurately predict the outcome of interest in a different population from the one developed and internally validated. This can be achieved by external validation using data that have not previously used for model development which come from an independent population with similar distribution of clinical characteristics as the original population from which the model was developed. External validation is important because it ensures the generalizability of the model to different settings and patients. Finally, very few models explicitly aim to predict “minimal weight loss”. Even among these models, there is considerable lack of standardized outcome definition as to how “minimal weight loss” is measured. This issue further complicates the applicability of the identified predictors in clinical practice, particularly in shared decision making. Variation in what constitutes “minimal weight loss” makes it difficult for patients and clinicians to set goals about the expected outcome of a particular bariatric surgical procedure given a set of patient-level characteristics.

There is very limited evidence on the extent to which the effects of bariatric surgery on non-weight outcomes are mediated through its effects on weight loss. A few studies reported the association between weight loss and other health outcomes but we were not able to identify any studies in which all relevant associations (i.e. average treatment effect of bariatric surgery on weight loss, average treatment effect of bariatric surgery on non-weight outcomes, and association between weight loss and non-weight outcomes) were reported within the same study.

Future Research Recommendations

Since no randomized evidence is available for the effectiveness of different bariatric procedures (surgical or endoscopic) in Medicare eligible obese patients, generating such evidence is critical for identifying both effective and safe procedures. Nevertheless, large, well-powered randomized trials are rarely conducted in adults age 65 and older or other populations that meet Medicare criteria (e.g. disabled) for a variety of reasons.¹¹⁹ Yet, various incentive mechanisms can be used to facilitate the conduct of randomized trials in the Medicare population, thus generating necessary evidence for policy decisions. Such incentives can be directed to both patients and clinicians/researchers to increase enrolment into pragmatic trials that better capture the real-world challenges of implementing bariatric procedures in the Medicare eligible patients.

Given the existing lack of randomized trials, evidence may be generated by using appropriate statistical methods and existing routinely collected health data that would allow unbiased estimates of treatment effects for bariatric surgical procedures.^{25, 120, 121} As very few studies are directly applicable to the Medicare population, existing research gaps in regards to the comparative effectiveness of different bariatric surgical procedures can be addressed by analyzing claims data from Medicare beneficiaries.^{122, 123} In particular, Medicare Parts A and B data include claims for all inpatient and outpatient services provided to Medicare beneficiaries (individuals 65 years and older and individuals with disabilities younger than 65 years) on a fee-for-service basis. The longitudinal nature of these data allows for the comparison of outcomes, such mortality, complications and others, in patients receiving different types of bariatric surgery. Similarly, other routinely collected health data can also be used to assess the comparative effectiveness of different bariatric surgical procedures in adults age 65 and older.^{120, 121, 123} One such example is the National Surgical Quality Improvement Program (NSQIP) by the

American College of Surgeons.¹²⁴ This clinical registry includes patient records with demographic, clinical, surgical, and outcome data for more than 600 hospitals. Among the quality programs for surgical outcomes included in the NSQIP is the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP), a national clinical registry to which all bariatric programs are required to report data to remain accredited. Using these and other analogous data sources, evidence on comparative treatment effects can be generated by using observational data and statistical methods that allow the emulation of a randomized trial in the target population.^{23, 125, 126}

Along these lines, other approaches can also be used for making inferences about the comparative effectiveness and safety of bariatric surgeries in populations with similar characteristics as those covered by Medicare. These approaches involve the transportability of randomized evidence across populations.¹²⁷ For example, statistical methodology can be used to generalize evidence from randomized trials and/or meta-analyses thereof in younger populations to adults age 65 and older.

Furthermore, routinely collected health data can also be used to externally validate existing models.¹²⁸ External validation of a particular risk prediction model depends on the availability of covariate information in other studies. Even when the same covariates have been measured across studies, the target study may have limited numbers of events making model validation difficult. These obstacles can be overcome with the use of registry data and electronic health records data from hospital and clinical practices that become increasingly accessible to researchers.¹²⁹ These sources include much larger number of patients than traditional epidemiological studies and better reflect the characteristics of patients seen in clinical practice. In addition, prediction models validated using electronic health records may be easier to be integrated in these systems. This can make their utilization in shared decision-making by patients and physicians more efficient in routine clinical practice. Towards this end, it will be important for all relevant stakeholders to identify a core of clinically meaningful and standardized definitions of the outcomes that these models should predict, particularly what should be considered “minimal weight loss” and how it should be measured (e.g. whether the definition pertains to percent excess weight loss or percent BMI loss etc.; and what the respective values should be).

Although randomized trials and high-quality comparative observational studies are limited in regards to the health outcomes of bariatric procedures in the Medicare eligible population, there is in fact a very large number of bariatric procedures (either surgical or endoscopic) as well as a very large number of short and long term outcomes. However, not all outcomes are equally important to patients and physicians for making informed treatment decisions and not all procedures are accompanied by the same rate of treatment success or the same severity of adverse events. These are all components that should be factored into the shared decision making process between patients and physicians. Given the sparsity of the existing evidence base, optimization of how to allocate future research resources is critical to ensure that the most relevant clinical outcomes and procedures are studied. Therefore, there is enormous value in undertaking efforts that can prioritize future research questions. In addition to qualitative approaches, such as a Delphi process, that can shape future research agendas, research prioritization can be contextualized through formal statistical methods. Towards this end, value of information analysis¹³⁰ and other decision analysis methods can benefit patients, clinicians, payers, and research. A value of information analysis applied to research prioritization can

quantify the benefits of acquiring further evidence through additional research on a given topic before making a decision.¹³⁰

Finally, more studies are needed to examine the mediating role of weight loss on the effect of bariatric surgeries on non-weight outcomes. As weight is a causal risk factor for multiple conditions, such as diabetes and cardiovascular disease, reducing weight through bariatric surgery is expected to also reduce the risk for non-weight loss outcomes. However, estimating the magnitude of this reduction requires estimation of direct and indirect treatment effects within each study.

Conclusions

Very few studies exist that address clinically relevant outcomes in Medicare eligible patients who undergo surgical or endoscopic bariatric procedures. Based on such sparse evidence, Medicare eligible patients undergoing bariatric surgery achieve sustained weight loss for most types of bariatric surgical procedures. Large gaps remain in the literature regarding the comparison of individual procedures for both weight loss and non-weight loss outcomes. Very little or no information exists on the extent to which the effects of bariatric surgery on non-weight outcomes are mediated through weight loss. In order for clinicians, patients and payers to make informed decisions regarding the benefits and harms of bariatric surgery in the Medicare eligible population, evidence from new randomized trials or high-quality comparative observational studies is needed.

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