Technology Assessment Program

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

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Technology Assessment Program– Technical Assessment

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

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AHRQ Publication No.

Purpose and Key Messages:

Purpose

- To examine the outcomes of bariatric procedures in patients eligible for Medicare

Key Messages

Among patients who are eligible for Medicare:

- 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 nonrandomized studies and none for endoscopic procedures.
- Bariatric surgery overall, and in particular the procedures of Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric banding, leads to improvements in weight loss outcomes beyond one year after surgery.
- Roux-en-Y gastric bypass performs better compared to sleeve gastrectomy or adjustable gastric banding for metabolic, cardiovascular outcomes, renal function outcomes and for postoperative complications; Roux-en-Y gastric bypass also performs better for weight loss outcomes.

This report is based on research conducted by the Brown Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00002-I). 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 AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may periodically be assessed for the currency of conclusions. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at www.effectivehealthcare.ahrq.gov. Search on the title of the report.

Persons using assistive technology may not be able to fully access information in this report. For assistance contact EffectiveHealthCare@ahrq.hhs.gov.

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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 (CMS) 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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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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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 nonfinancial conflicts may be retained. The Task Order Officer and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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

Structured Abstract

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

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

Results. Of 126 eligible studies, 83 described outcomes after bariatric therapy and 43 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 15 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 moderate evidence that Roux-en-Y gastric bypass performs better compared to sleeve gastrectomy or adjustable gastric banding for metabolic, cardiovascular, and renal function outcomes and for postoperative complications. Finally, no models to predict weight loss have undergone internal or external validation.

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

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Evidence Summary

Introduction

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

Bariatric surgical procedures result in anatomic manipulations of the gastrointestinal tract; and more recently similar anatomic modifications have been achieved through the use of endoscopic technologies. Many adults age 65 and older meet indications for bariatric treatment, but the utilization of these procedures remains low.[8, 9] Based on the U.S. National Health and Nutrition Examination Survey (NHANES), in 2012 35 percent of people 60 years and older had a BMI of 30 Kg/m^2 or more, 14 percent had a BMI of 35 Kg/m^2 or more, and six percent had a BMI of 40 Kg/m^2 or more, with a women-to-men ratio of almost 2:1 within each category.[10] Thus, a large number of Medicare-eligible people in the U.S. likely meet NIH indications for either surgical or endoscopic bariatric therapy.

We conducted a technology assessment to objectively summarize and appraise the current evidence regarding the effectiveness and safety of bariatric therapies 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:

KQ 1: What are the theorized mechanisms of action of bariatric procedures on weight loss and 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 postsurgical 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. nonbariatric therapies) on weight outcomes (including failure to achieve at least minimal weight loss)?

b) What patient- (KQ2a) and intervention- (KQ2b) level characteristics 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. nonbariatric 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. nonbariatric 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- (KQ2b) level 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?

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.[11] The PROSPERO registration number is CRD42017065285. There is no deviation from the registered protocol except for the addition of KQ3d; this question was added later given the increased rates of revisional bariatric surgery in the Medicare population.

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 certain 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) and studies in pregnant women. Because studies that are conducted exclusively in adults age 65 years and older are uncommon,[12] we included 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. For studies in which the total population did not meet these criteria, we sought to identify any reported subgroup analyses for these groups. For example, if the overall population in a study had a mean age of 40 years but the study reported a subgroup analysis in the group of patients aged 60 years or older, we included the results of this subgroup analysis. We also included any study that used claims data from people already enrolled in and receiving benefits from Medicare. Therefore, our eligibility criteria ensure that all Medicare-eligible populations (i.e. older adults, disabled, persons with end-stage renal diseases) are reflected in the selected studies.

The reason we excluded studies in younger patients (unless they met other Medicare-eligibility criteria) is that for young patients to qualify for Medicare benefits they need to have disability or end-stage renal disease. The clinical characteristics and prognosis of disabled persons with obesity or persons with obesity and end-stage renal disease are substantially different from younger patients with obesity but without disability or end-stage renal disease. Thus, these groups of patients may not be exchangeable with each other, limiting our ability to make robust inferences. Furthermore, although substantial evidence exists in regard to the effectiveness and safety of bariatric procedures in younger patients,[13-16] there is virtually no evidence that is specific to older adults or other Medicare-eligible populations. Because younger and older patients may differ substantially in their comorbidity burdens and frailty, evidence generated in younger patients may not be directly applicable to older adults, leading to differences in the expected benefits and/or harms.[17] Existing evidence on younger patients can (and should) still be used by patients and physicians in their decisionmaking processes, as long as all stakeholders have reasonable assumptions regarding the transportability of this evidence to older patients, who are not well represented in the evidence.

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 nonrandomized 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 regard 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 versus after surgery or by providing descriptive statistics. In this way, we aim to minimize unreliable inferences about causal treatment effects, while at the same time maximizing the utilization of the evidence base to provide estimates that are useful to stakeholders for purposes other than causal treatment effects.

Searching for the Evidence

We searched six bibliographic databases for studies with publication dates between January 1, 2000 and June 31, 2017, 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 were summarized in narrative form and in summary tables that tabulate the important features of the study populations, design, interventions, outcomes, and results.

Due to the sparsity of the 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 regard 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 126 studies met the eligibility criteria, of which 43 reported models to predict body weight loss or absolute body weight after bariatric surgery, and the remaining 83 studies pertained to the effectiveness and safety of bariatric procedures.

Of the 83 studies (total sample size, N=177,268) on treatment effects of bariatric surgery, 8 studies[18-24] 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 69 studies were on patients with a mean or median age of 55 or older. The characteristics of these studies are shown in Table A.

We did not identify any randomized controlled 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 41 nonrandomized studies reported data on more than one procedure, but only 16 of those had a design and/or analytical approach that explicitly attempted to address confounding bias. Treatment effects reported in the studies where confounding was accounted for approximate causal associations between bariatric procedures and weight loss outcomes, adverse events/complications, and other nonweight related health outcomes. The remaining studies reported weight changes in outcomes before and after bariatric surgery or provided descriptive statistics, such as incidence or prevalence of outcomes among patients undergoing bariatric surgery, without a comparison with an independent or paired group.

The 43 prediction studies reported a total of 81 distinct models predicting body weight loss or absolute body weight after bariatric surgery. None of these models was internally or externally validated. Few studies were conducted in U.S. settings. The majority of studies were conducted after 2010.

Table A. Baseline Patient Characteristics

Author, Year PMID	N	Mean Age y (SD) [range]	Mean BMI kg/m2 (SD) [range]	Mean weight kg (SD) [range]	BP mmHg mean (SD)	% female	% white	% black	% Hispanic	% Asian
Abbas 2015 26001882	83	63.4 (3.1)	47 (7.9)	122.4 (25.5)		80				
Altieri 2016 26201412	8990	[>= 45]								
Andalib 2016 26416373	234	47.26 (10.38)	47.04 (8.2)	134.84 (27.08)		56.84	45.73	38.46	7.69	
Ardestani 2015 25573879	5225	53.8 (10.2)	47.1 (8)			66.7	81.7			
Bergeat 2017 28035521	55	63.9 (2.5) [60, 71]	44.5 (6.3) [32, 60]			91				
Boules 2015 26243345	166	56.7 (8.6)	44.6 (8)	119.2 (24.2)		81.3				
Busetto 2008 18239641	216	64.1 (4)	44.2 (7.6)	116.4 (21.1)		85.2				
Clough 2011 20490708	113	63.6 [60, 73]	42.2	116.9		56.5				
Casillas 2017 28438494	429	67 [65, 79]	42.6 (5.4)			70				
Davidson 2016 26864395	1210	59 (3.4)	46 (7)			76.2				
Davis 2017 27681880	632	53 (11)				72				
Dorman 2012 22038414	18058	[50, 70]				76.8	80.8	10.5	3.1	0.7
Dunkle-Blatter 2007 17331804	61	62 [60-72]	49.3 (7.5) [38.0, 78.3]			67.2				
Flum 2005 16234496	1519									
Flum 2011 21975317	47030	52.9 (11.6)				75.48	81.01	14.73	2.05	
Freeman 2015 25708829	52	50 (10) [18-67]				54				
Gebhart 2015 25130515	6125	[>60]				68.65	84.22			

Author, Year PMID	N	Mean Age y (SD) [range]	Mean BMI kg/m2 (SD) [range]	Mean weight kg (SD) [range]	BP mmHg mean (SD)	% female	% white	% black	% Hispanic	% Asian
Ghio 2016 28259559	74	54.8 (9.6)	44.1 (5.5			65				
Giordano 2014 24318411	132	59.43 (3.81)	46.21 (7.47)	132.27 (28.97)		57.6				
Hallowell 2007 17576885	77	56 (9.5) [31, 66]	52.7 (6.5)			89.6				
Hazzan 2006 17138231	55	61.5 [60-70]	46.2 [38-61]			65.4				
Hernigou 2016 27130648	279	71.7 (8.74)	36 (7.15)	96.5 (20.0)		59.1				
Huang 2015 25859266	68	58.9 (4.3) [55, 79]	39.5 (6.8) [32, 60.4]	102.1 (19.4)		64.7				
Imam 2017 27927587	1428	58.25 (8.68)	44.15 (6.89)	269.85 (50.58)		76.6	56.2	18.3	22.5	
Irwin 2013 23744816	27	56.9 (9.2)	50.2 (7.5)			81.5				
Johnson 2012 22643265	349	55.1				65	86			
Lee 2016 27220823	162	55.2 (9.3)	42.9 (5.3)	131.4 (21.3)	125 (14.8)/74.78 (12.5)		59.3			
Lemaître 2016 27063637	494	45.5 [18, 75]	47.8 (7.8) [35.0, 82.3]	133.5 [84, 255]		74				
Leonetti 2012 22508671	60	54.5 (8.3)	40.2 (5.9)			68				
Loy 2014 24582414	55	72.4 (2.5) [70, 82]	45 (6.2)	123 (22)		60	94.5	5.5		
Luppi 2015 25088486	28	63.2 [60, 68]	43.3	113.2		64.3				
Mackay 2016 27778462	1362					82.6				
Maraka 2015 25611727	128	55	46.3 (9.0)			64.8				
Martin 2015 26530652	364	58.2 (7.3)	40.7 (9.7)			81				

Author, Year PMID	N	Mean Age y (SD) [range]	Mean BMI kg/m2 (SD) [range]	Mean weight kg (SD) [range]	BP mmHg mean (SD)	% female	% white	% black	% Hispanic	% Asian
McGlone 2015 26112136	50	[>60]	49.5 (6.1)			74				
Michaud 2016 26130180	102	62.3 (2)	50.9 (6.8)	133 (24)		61				
Miranda 2013 23604694	19	Median 65 [49, 78]	Median 50.9 [22, 64]	141.6 [98, 210]	134.6	47				
Mittermair 2008 18830777	134	55.6 (4.6) [50, 69]	43.9 (5.7) [35.3, 62.7]			76.1				
Mizrahi 2014 24442420	52	62.9 (0.3) [60, 70]	42.6 (0.7)	117.3 (2.8)		56				
Moon 2016 26220238	353	62.9 (2.5) [60-71]	44.5 (6.6) [32.9, 74.5]			71.4				
Mozer 2015 25832986	138	Median 48 (10.6)	Median 46	Median 294		51.4				
Nagao 2014 24519024	52	55.1 (3.7)	46.4 (6)	127.4 (24.1)		82				
Navarrete 2017 28214166	206	55.4 (10.2)	46.0 (17.2)			80.6				
Nearing 2017 28011119	102	102	80.39							
Nickel 2016 27179771	5918					83				
O'Keefe 2010 20532834	197	67.3 (2.3) [65-78]	48.1 (6.9) [35.6, 73]	72.9 (17.8) [38.7, 127.1]		72.1				
Ochner 2013 23700235	157					100				
Omalu 2007 17938303	2022	[>55]								
Papasavas 2004 15479593	71	59 [55, 67]	50.2 [37, 65]			76.1				
Pajecki 2015 26537266	46	64 [60, 71]	49.63 [38, 66]			89				
Peraglie 2016 25814071	88	64 [60, 74]	43 [33, 61]	118 [78, 171]		62				
Perry 2008 18156918	11903	[65, 75]				77.6				

Author, Year PMID	N	Mean Age y (SD) [range]	Mean BMI kg/m2 (SD) [range]	Mean weight kg (SD) [range]	BP mmHg mean (SD)	% female	% white	% black	% Hispanic	% Asian
Persson 2017 28506731	47859									
Praveenraj 2016 27279392	86	57.5 (6.1) [50, 75]	43.2 (8.7) [29, 87]	108.2 (23.1) [65, 200]		53.5				
Qin 2015 25373923	3616	56.7 (5.1)	45.2 (7.6)			74.8	76.1	14.9		0.8
Quebbemann 2005 16925254	27	68 [65.8, 72.6] [65.8, 72.6]	47.4 (7.4)			63				
Quirante 2017 28039650	393		41.6			58	83	5	11	
Ramirez 2012 22551574	42	73.5 [71, 80]	44 [34-81]	124.5 [80.1-219.1]		52.4				
Ritz 2014 24708912	154	[>60]								
Saleh 2015 25868831	667	50.7 (11.7)	47 (7.4)			65.5		25.8		
Scott 2013 22014480	2432	[50, 79]								
Serrot 2011 22000180	34	Median 59	34.3	Median 225.5	Median SBP 126 IQR 30	55.9				
Sosa 2004 15603658	22	64.4 [60, 75]	48.5 [40, 62]							
Soto 2013 23733390	35	66.3 [60-79]	46.3 [33.7, 77.6]			68.6				
Spaniolas 2014 24913586	1005		44 (7)			69.2				
Sugerman 2004 15273547	65	63 (3) [60.1, 74.5]	49 (7)	133 (22)		78	85	14	1	
Sun 2016 26264895	367	[>60]								
Tiwari 2011 21459686	905									
Trieu 2007 17400516	92	62.2 [60-74]	48.45 [35-68]	136.63 [86.4, 215.9]		63				
Valderas 2009 19517199	52	57.8 (4.3)	36.4 (8.7)			100			100	
van Rutte 2013 23344504	135	[55, 70]	43.8 [29.8, 65.1]			69.6				

Author, Year PMID	N	Mean Age y (SD) [range]	Mean BMI kg/m2 (SD) [range]	Mean weight kg (SD) [range]	BP mmHg mean (SD)	% female	% white	% black	% Hispanic	% Asian
Varela 2006 17058723	1339	[>60]				73	82.2			
Wagner 2007 17938305	54	48.9 [27, 63] [27, 63]	56.8 [34, 113]			75.9				
Werner 2015 26071250	79	[65, 84]	[>40]			78.1				
Wiklund 2017	70	47 (12)	44.7 (5.8)	133.7 (24.5)		58.6				
Willkomm 2010 20870182	100	68 [65, 77]	45 [33, 61]							
Wise 2016 26091994	117	59.3 (5.7)	43.6 (6.2)			77.8		6.8		
Wittgrove 2009 19705206	120	62 [60, 74]	43 [34, 70]			48				
Wool 2009 18855082	60	56.7	49 [37, 71]			0				
Yuan 2009 18996764	282	48.5 (11.78)	52.4 (10)			74.47				
Y. Van Noeiwenhove 2016	56	63.8 (3.2)		122 (26)		57				
Zaveri 2016 27795883	53	72.7 (2.5) [70, 81.4]	43.3 (5.8)	264.6 (40.7)		66				

KQ1: Theorized Mechanisms

Bariatric surgery includes 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 is to restrict 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 are dominant in the early weight loss period after surgery.[25] In the long term, however, additional mechanisms appear to be responsible for maintaining weight loss. 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.[26] 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 postoperatively by affecting insulin secretion and sensitivity, reducing appetite, and increasing satiety.[27]

KQ2: Patient Characteristics, Interventions, and Outcomes in the Medicare-eligible population

The patient characteristics in studies of bariatric surgical procedures, shown in detail in Table A, are as follows:

- Mean or median BMI at baseline ranged from 34.3 kg/m^2 to 56.8 kg/m^2.
- Two studies[28, 29] included only female patients undergoing bariatric surgery
- One study [30] included only male patients.
- In the remaining studies, the percentage that were women ranged from 51.4 to 89.6.

The frequency of comorbidities was as follows:

- Three studies were conducted entirely in patients with type 2 diabetes,[31-33]
- In another 33 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.[34]
- Prevalence of pulmonary comorbidities ranged from 2 percent to 44.3 percent.
- Six studies reported on 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.
- Fifteen studies reported on musculoskeletal comorbidities, mainly osteoarthritis and other degenerative joint disorders.
- Prevalence of congestive heart failure ranged from 11.1 percent to 32.4 percent, and one study examined bariatric surgery exclusively in patients with congestive heart failure.[35]

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

Table B. Method of surgery by bariatric procedure studied in the Medicare-eligible population.
The numbers correspond to the study arms across all eligible studies.

	Method of surgery			
Bariatric Procedure	Open only	Laparoscopic only	Either open or laparoscopic	Not reported
AGB		23		1
MGB		1		
Multiple surgeries	1	7	7	10
RYGB	4	26	7	5
SADS		1		
SG		25	2	1
VBG		1		
BPD-DS	1	1	1	

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

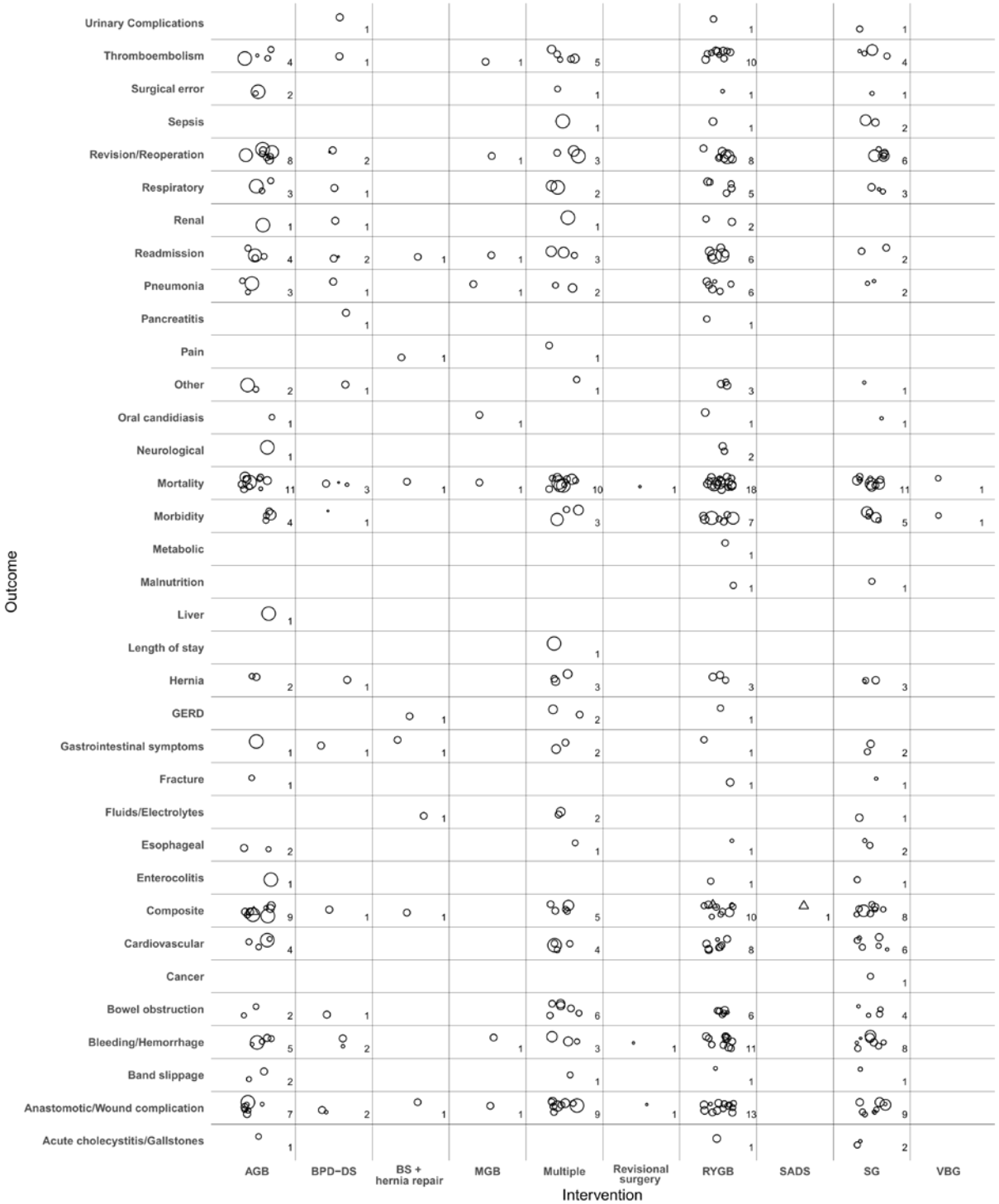
Weight loss outcomes measured in the Medicare-eligible population include percent excess weight loss (EWL), percent weight loss (WL), percent excess BMI loss (EBMIL), absolute body weight loss, and absolute BMI loss, while a few studies reported the mean body weight and BMI before and after bariatric 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 with weight loss outcomes after VBG, and there are is limited evidence regarding mini-gastric bypass and SADS. Most outcomes pertained to laparoscopically conducted surgeries, with only five outcomes examined after open surgeries. These include EBMIL and changes in BMI after open RYGB[36]; and percent EWL, percent WL, and changes in BMI after open BPD-DS.[37]

The adverse events and/or surgical complications reported in the 90-day postoperative period after bariatric surgical procedures is shown in Figure A. This figure shows the different bariatric procedures on the horizontal axis and the various adverse events/surgical complications on the vertical axis for each of the eligible studies. Each data point (showed as hollow circle) corresponds to a patient population that had undergone a specific bariatric procedure and had the respective outcome measured (i.e., each data point corresponds to a treatment arm with a specific adverse event/surgical complication measured). The size of the data point (hollow circle) is relative to the sample size of the treatment arm (i.e., arms with larger number of patients are

shown by larger circles). In each cell, the number of circles corresponds to the total number of treatment arms with the respective outcome, while the numeric value in the right-bottom corner denotes the size of the treatment arms with a respective outcome measure. For example, the cell that is identified at the point where the “Renal” and the “AGB” columns cross each other contains four data points; this is a graphical representation of the fact that we identified four treatment arms that had undergone AGB and for whom the respective primary studies reported on renal outcomes. Similarly, in the cell that corresponds to the point where “Sepsis” and “AGB” meet each other, there are no data points; this means that we did not identify any studies in which data on sepsis were reported for at least one treatment arm pertaining to AGB. Because certain studies reported on more than one procedure, the total number of treatment arms is greater than the number of studies. Overall, this figure descriptively summarizes the current state of the evidence in regard to adverse events/surgical complications and provides a map of the evidence gaps (e.g., outcomes and/or procedures with few or no studied populations), as well as of the procedures and outcomes where multiple populations were studied. The sample sizes for these outcomes vary across procedures, with the largest sample sizes in AGB, RYGB, and SG, and evidence for BPD-DS, MGB, SADS, and VBG from smaller samples.

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

Each circle denotes an adverse event reported in regard to the bariatric procedures shown on the horizontal axis in an eligible study; the diameter of each circle is proportional to the logarithm of the sample size of the arm for the largest applicable arm in each study

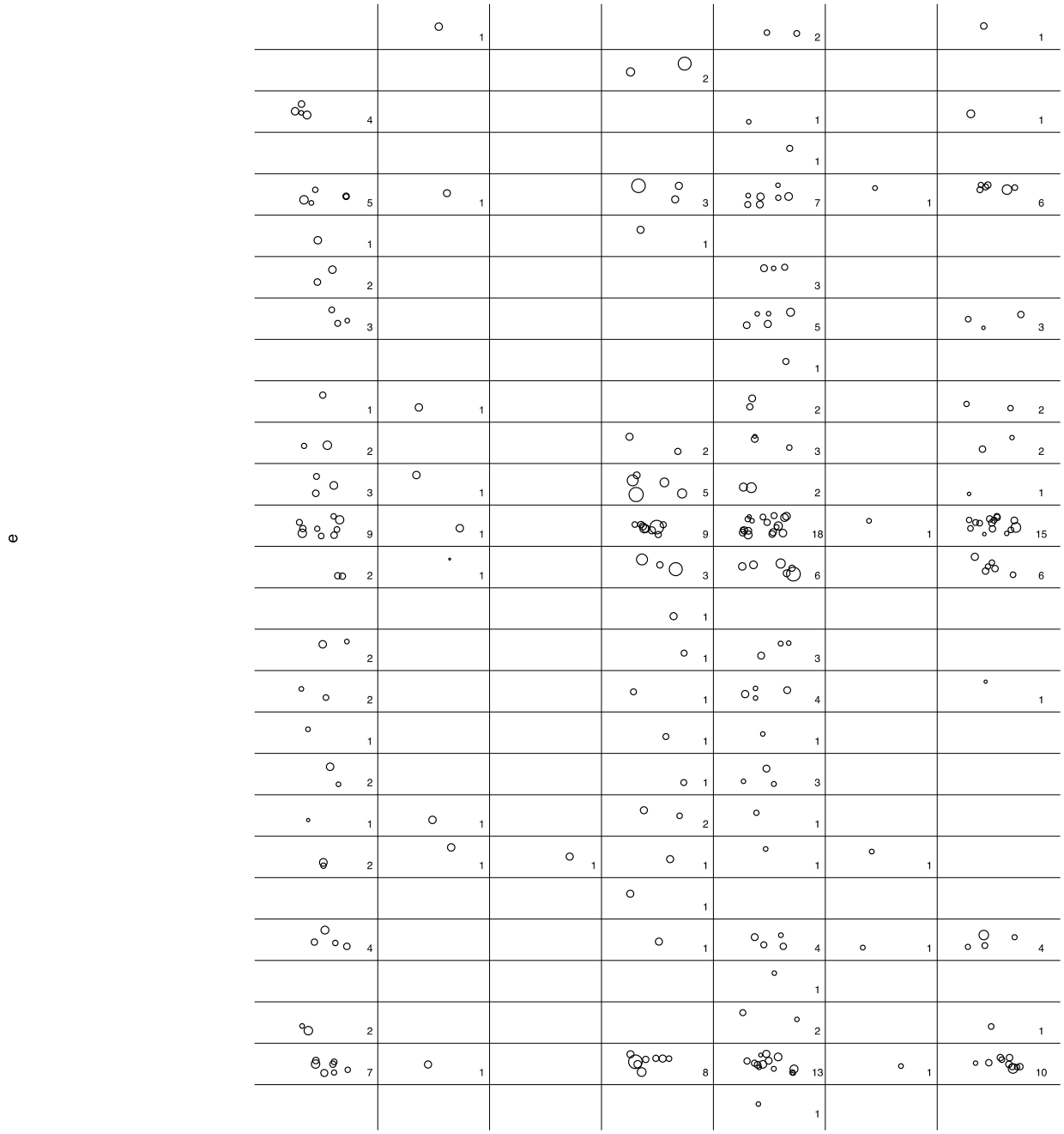


AGB: adjustable gastric banding; BS: bariatric surgery; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; VBG: vertical band gastroplasty; BPD-DS: biliopancreatic diversion with duodenal switch; GERD: gastroesophageal reflux disease

The most commonly reported outcomes other than weight loss were respiratory outcomes (23 studies), metabolic/diabetes-related outcomes (53 studies), and cardiovascular outcomes (40 studies). 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 as shown in Figure B. This figure shows the different bariatric procedures on the horizontal axis and the various health outcomes (other than weight loss or adverse events/surgical complications) on the vertical axis for each of the eligible studies. Each data point (showed as hollow circle) corresponds to a patient population (treatment arm) that had undergone a specific bariatric procedure and had the respective outcome measured. In addition, the size of the data point (hollow circle) is relative to the sample size of the treatment arm (i.e., arms with larger number of patients are shown by larger circles). In each cell, the number of circles corresponds to the total number of treatment arms with the respective outcome, while the numeric value in the right-bottom corner denotes the size of the treatment arms with a respective outcome measure. For example, the cell that is identified at the point where the "Mortality" and the "AGB" columns cross each other contains one data point; this is a graphical representation of the fact that we identified one treatment arm that had undergone AGB and for whom the study reported on mortality outcomes. Similarly, in the cell that corresponds to the point where "Mortality" and "SADS" meet each other, there are no data points; this means that we did not identify any studies in which data on mortality were reported for at least one treatment arm pertaining to SADS. Because certain studies reported on more than one procedure, the total number of treatment arms is greater than the number of studies. Overall, this figure descriptively summarizes the current state of the evidence in regard to health outcomes other than weight loss and adverse events/surgical complications and provides a map of evidence gaps (e.g., outcomes and/or procedures with few or no studied populations), as well as of procedures and outcomes where multiple populations are studied.

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

Each circle denotes an outcome that has been reported in the bariatric procedures shown on the horizontal axis in 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

KQ3: Weight Loss Outcomes

Five studies assessed the comparative effects on weight change of different bariatric surgeries with each other or conventional (nonsurgical) treatment. Of these, only four reported numerical data.[32, 38-40] In two studies, RYGB resulted in greater improvements for all weight-loss outcomes compared to SG up to 4 years after surgery. Moreover, RYGB and SG achieved better outcomes than LAGB.[38] In a second study, patients undergoing LSG experienced 71 percent weight loss compared to 2.8 percent weight regain in the conventional therapy group, which included pharmaceutical agents and lifestyle modifications (diet and physical activity) at 18 months after the intervention. In the same study, the mean BMI loss in the LSG group was 13.5 kg/m^2 compared to a mean 0.17 kg/m^2 BMI increase in the conventional treatment group.[32] In a third study, weight loss at one year after surgery was higher for RYGB and SG compared to LAGB. 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.[39] Finally, a fifth study reported no numerical results but the authors note that throughout the 3-year follow up, weight loss was greater for RYGB as compared to SG, as well as for patients undergoing any bariatric surgery compared to nonsurgical controls.[41]

The clinical and methodological heterogeneity introduced by the different modeling strategies and the different covariates in these two studies do not allow for a meaningful statistical synthesis of the results.

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 (See Table C).

Table C. 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 nonrandomized study addresses this question (N=162). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
RYGB results in greater improvements in weight outcomes compared to SG at 1, 2, 3, and 4 years after surgery (1) Mean BMI loss (2) Mean percent weight loss (3) Mean percent excess weight loss	Low for (1), (2), (3)	[Not rated]	Moderate for (1), (2), (3),	High for (1), (2), (3)	Moderate SoE for (1), (2), (4)	- Only 1 nonrandomized study compares weight changes for all three outcomes at 1, 2, 3, and 4 years (N=429). - Follow-up rates for this study were high (100% at year 1, 95% at year 2, 91% at year 3, and 75% at year 4). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*

Conclusion statement	RoB (evidence-base)	Consistency	Precision	Directness and Applicability	Overall Rating	Comments
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 nonrandomized study compares weight changes for all four outcomes at 6 months (N=162). - Only 1 nonrandomized study compares weight changes for (1), (2), and (4) at 12 months (N=162). - Only two nonrandomized studies (N=316) compare weight changes at 12 months for (3). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
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 nonrandomized study compares weight changes for all four outcomes at 6 months (N=162). - Only 1 nonrandomized study compares weight changes for (1), (2), and (4) at 12 months (N=162). - Only two nonrandomized studies (N=316) compare weight changes at 12 months for (3). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
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). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*

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

A total of 81 different predictive models of weight loss outcomes were reported in the eligible studies. Outcome definitions were rarely consistent across models. There was no global agreement on the definition of "minimal weight loss" and no model explicitly used this outcome definition. Twenty-six models directly predicted the probability of successful or 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 EWL >50 percent (good outcome/successful weight loss). Values of the R^2 metric for model fit ranged from 2 percent[42] to 99.7 percent.[43] Finally, a model with diabetes, sleep apnea, age, gender, bariatric center, hypertension, GERD, BMI and body fat as predictors had the highest clinical utility (sensitivity, 71 percent; specificity, 91 percent; positive

predictive value, 72 percent; and negative predictive value, 91 percent) for predicting percent EWL at 1 and 3 months.[44]

KQ4: Outcomes Other Than Weight Loss

We identified 31 studies which compared bariatric surgical procedures to each other, to nonbariatric treatments, or to conventional or no treatment. We found no randomized trials in the Medicare-eligible population.

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 procedures[45] were used in 12 studies.

Below we summarize the outcomes that were reported in these 15 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 Appendix H.

Mortality

Six nonrandomized comparative studies examined the effects of bariatric surgical procedures on mortality. Results are given as hazard ratios (HR) and 95% confidence intervals (CI).

In one study, RYGB resulted in lower all-cause mortality rates (HR, 0.50; 95% CI 0.31, 0.79; P<0.003) compared to a nonsurgical 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.[46] Moreover, lower mortality rates were observed among patients undergoing RYGB compared to those undergoing SG, although the number of events were too small to allow statistical comparisons.[47]

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 noncardiovascular mortality (HR 0.60; 95% CI 0.26, 1.39; P=0.233) compared to patients with morbid obesity undergoing orthopedic or gastrointestinal surgeries, although these differences did not achieve statistical significance.[48]

Two other studies found that bariatric surgery resulted in lower risk of all-cause mortality either when compared to gastrointestinal surgical procedures (HR 0.45, 95% CI 0.33, 0.60)[49] or to no surgical controls (HR 0.72; 95% CI 0.56, 0.93).[50] Finally, bariatric surgery was associated with lower mortality rates at 2 years after surgery in morbidly obese Medicare beneficiaries 65 years and older with morbid obesity compared to nonsurgical controls (8 percent vs. 12.2 percent, P<0.001). However, mortality rate was increased in the 30-day postoperative period (1.55 percent vs. 0.53 percent; P<0.001).[23]

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

Three nonrandomized comparative studies examined postoperative complications of different bariatric surgical procedures showing not significantly different complications rates between

RYGB and SG.[51] Overall complication rates were higher for LRYGB than SG, a difference that is attributed to the higher rates of major complications with LRYGB than SG.[50]

Finally, concomitant bariatric surgery and hiatal hernia repair did not result in higher complications rates than bariatric surgery alone.[52]

Diabetes and Metabolic-Related Outcomes

Four nonrandomized 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.[31]

In another study, there was no evidence in the improvement of diabetes among patients receiving bariatric surgery compared to nonsurgical controls at 6 months and 1 year after surgery; however, there was an improvement at 2 years.[23]

In a third study, RYGB resulted in larger reductions than SG in LDL and total cholesterol at 6 and 12 months after surgery; and in larger increases in HDL-cholesterol at 6 but not at 12 months after surgery. Similarly, LAGB results in larger reductions than SG in LDL and total cholesterol at 6 and 12 months after surgery.[38]

Finally, LSG was associated with statistically significantly 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. Greater 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 greater changes in the levels of LDL or total cholesterol.[32]

Cardiovascular Outcomes

One study found that patients undergoing bariatric surgery had a lower risk of myocardial infarction (MI) compared with control patients undergoing orthopedic surgery (HR 0.59, 95% CI 0.44, 0.79), as well as compared with patients undergoing gastrointestinal surgery (HR 0.49; 95% CI 0.36, 0.68).[49] Bariatric surgery was associated with lower risk of MI, stroke, or all-cause mortality compared to orthopedic surgery (HR 0.72, 95% CI 0.58-0.89) and gastrointestinal surgery (HR 0.48, 95% CI 0.39-0.61).[49]

A second study found evidence of improvement in coronary artery disease at 6 months after surgery compared to nonsurgical controls, which was maintained at 1 and 2 years after surgery.[23] There was also evidence of lower rates of hypertension and hyperlipimdemia compared to nonsurgical controls at 1 and 2 years after surgery, but no evidence of improvement in the first 6 months.

A third study found no evidence that either systolic or diastolic blood pressure were lower at 6 or 12 months after surgery after RYGB, SG or LAGB compared to each other.[38]

A fourth study found that, compared to conventional therapy that included pharmaceutical agents and lifestyle modifications (diet and physical activity), LSG was not associated with a difference in the prevalence of hypertension at 18 months after treatment.[32]

Bariatric surgery was found to reduce the risk of heart failure/heart failure hospitalizations in one study (HR=0.35; 95% CI 0.25, 0.49).[50]

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).[49]

Respiratory Disease

One study found evidence of improvement in sleep apnea in the 6-month period after surgery, but there was no evidence of improvement at 1 and 2 years.[23]

Orthopedic/Musculoskeletal Outcomes

In one study, RYGB 1 to 5 years prior to the time of outcome measurements was found to be associated with the prevalence of hyperparathyreoidism.[29]

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 reoperated due to any cause (HR 2.5; 95% CI 1.2 to 6.2; P = 0.02). 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 reoperated due to any cause (HR 2.4; 95% CI 1.2 to 3.3; P = 0.02), as well as to undergo revisional surgery (HR 2.2; 95% CI 1.1 to 6.5, P = 0.04).[53]

A third study found no effect of bariatric surgery on the risk of joint dislocation after total hip arthroplasty.[54] Patients who underwent bariatric surgery before total knee arthroplasty or total hip arthroplasty had decreased operative times and length of stay regarding their orthopedic surgery compared to patients than underwent bariatric surgery after arthroplasty. The study found no effect on postoperative complication rates.[55]

Renal Function

According to a single study, patients undergoing bariatric surgery experienced improved kidney function as measured by the estimated glomerular filtration rate (eGFR). Differences in mean eGFR between the bariatric surgery and control groups were 12.58 mL/min/1.73 m^2 (95% CI 10.46, 14.7) at 3 months, 13.29 mL/min/1.73 m^2 (95% CI 11.84, 14.74) at 6 months, 12.27 mL/min/1.73 m^2 (95% CI 10.87, 13.67) at 1 year, 12.66 mL/min/1.73 m^2 (95% CI 11.15, 14.17) at 2 years, and 9.84 mL/min/1.73 m^2 (95% CI 8.05, 11.62) at 3 years.[41]

Between procedures, RYGB was associated with a greater effect on eGFR compared to SG. Differences in mean eGFR between the two procedures were 4.22 mL/min/1.73 m^2 (95% CI 0.49, 7.95) at 3 months, 4.75 mL/min/1.73 m^2 (95% CI 2.21, 7.29) at 6 months, 5.03 mL/min/1.73 m^2 (95% CI 2.53, 7.54) at 1 year, 7.52 mL/min/1.73 m^2 (95% CI 4.84, 10.2) at 2 years, and 6.6 mL/min/1.73 m^2 (95% CI 3.42, 9.78) at 3 years.[41]

Polypharmacy

In one study, patients undergoing RYGB experienced a greater reduction in the number of prescribed medications for chronic conditions at 6 and 12 months after surgery compared to patients undergoing SG or LAGB.[38]

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 (from 0.4 to 0.2).[32]

In a third study,[56] 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 compared to patients undergoing endoscopic retrograde cholangiopancreatography.[56]

Strength of Evidence

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

Table D. 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 nonbariatric surgery/conventional treatment in regard to: (1) Mortality (2) Metabolic outcomes (3) Cardiovascular outcomes (4) Musculoskeletal outcomes (5) Warfarin dose after surgery (6) Respiratory outcomes (7) Renal function outcomes	High for (2), (3), (4), (5), (6) Low for (1), (7)	[Not rated]	Low for (4), (5) Moderate for (1), (2), (3), (6), (7)	Moderate for (1), (2), (3), (4), (5), (6), (7)	Moderate SoE for (1), (2), (3), (4), (5), (6), (7)	There are no randomized studies available in the Medicare-eligible population. The evidence-base consists of nonrandomized comparative studies. Use of inappropriate control groups limits applicability/generalizability. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
RYGB results in favorable outcomes compared to SG in regard to: (1) Postoperative complications (2) Metabolic outcomes (3) Polypharmacy (4) Cardiovascular outcomes (5) Renal function outcomes	Moderate for (1), (2), (3), (4) Low for (5)	[Not rated]	Low for (1), (2), (3), (4), Moderate for (5)	High for (1), (2), (3), (4), (5)	Moderate SoE for (1), (2), (3), (4) High SoE of (5)	There are no randomized studies available in the Medicare-eligible population. The evidence-base consists of nonrandomized comparative studies. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
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 nonrandomized comparative studies. Only one study addressed this question. Technical aspects of the surgical procedures may limit the feasibility of these surgeries across surgeons. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*

Conclusion statement	RoB (evidence-base)	Consistency	Precision	Directness and Applicability	Overall Rating	Comments
RYGB results in favorable outcomes compared to LAGB in regard 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)	There are no randomized studies available in the Medicare-eligible population. The evidence-base consists of nonrandomized comparative studies. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
SG results in favorable outcomes compared to LAGB in regard 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 nonrandomized comparative studies. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*

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

Discussion

Evidence Summary

In the Medicare-eligible population, we found multiple studies evaluating one or more bariatric surgical procedures, but we did not identify any studies in patients undergoing bariatric endoscopic procedures. Limited comparative evidence exists about the effects of different bariatric surgical procedures on weight loss and non-weight-loss outcomes. 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 specific procedures, are effective in 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 improved after bariatric surgery compared to their presurgery values. However, because of the nonrandomized 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 studies with follow-up as long as 8 years, patients maintained their weight and/or BMI loss over time. Our findings of a low to moderate strength of evidence for the effects of bariatric surgery on non-weight-loss outcomes agree with the conclusions of the American

College of Cardiology, the American Heart Association, and the Obesity Society as highlighted in their clinical practice guidelines for the management of overweight and obesity in adults.[57]

Although many models are available to predict successful body weight loss or absolute body weight after bariatric surgery, none have 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 that did, the majority were deemed to have at least moderate risk of confounding, selection, or measurement biases.

The major drawback of pre-post study designs is the absence of a control comparison group that would capture changes in the outcome of interest when the studied procedure is not performed.[58] Nevertheless, the findings of these studies 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 models.

Since no randomized evidence is available for the effectiveness of different bariatric surgeries in Medicare eligible persons with obesity, generating such evidence is important for identifying effective and safe surgeries. Nevertheless, large, well-powered randomized trials are rarely conducted in patients age 65 and older or with multiple comorbidities.[59] Evidence may be generated by using Medicare claims data and electronic health records can be used to design nonrandomized comparative studies to contrast bariatric surgeries to each other.[60-62]

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 models[63] and overcome issues related to low numbers of events and granularity of clinical predictors.[64] 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. Moreover, future studies should inform their outcomes by incorporating patient values and preferences, which may guide the collection and analysis of patient-centered outcomes related to function and quality of life for patients undergoing bariatric surgery. Towards this end, an ongoing study funded by the Patient-Center Research Institute (PCORI; https://www.pcori.org/research-results/2015/comparing-benefits-and-harms-three-types-weight-loss-surgery-pcornet-bariatric) is expected to provide meaningful data upon its completion.

It should be acknowledged that the type of and the conditions under which bariatric procedures covered by Medicare and other payers will be affect the populations analyzed in studies using routinely-collected health data. For example, gastric bypass, adjustable gastric banding, and duodenal switch are currently covered under Medicare's National Coverage Determination (NCD), while coverage of laparoscopic sleeve gastrectomy and revisional bariatric surgery are at the discretion of the local Medicare Administrative Contractors (MACs). By contrast, balloon devices, mini gastric bypass, and several other similar procedures are excluded from coverage. Additionally, many public and private payers have criteria that limit

access to bariatric surgery based on comorbidities with some requiring severe comorbidities to allow coverage and others being less restrictive. Because of these coverage restrictions, published studies using routinely-collected health data are scarce, and it is likely that the clinical characteristics of patients in these studies will vary due to eligibility criteria determined by coverage type rather than by relevance to clinical practice. Therefore, generation of comprehensive real-world evidence regarding the effectiveness and safety of many bariatric procedures will require that patients' insurance covers the bariatric procedures and relevant services only in the context of a clinical study.

Conclusions

Very few studies address clinically relevant outcomes in Medicare eligible patients who undergo surgical or endoscopic bariatric procedures. Based on this 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 about the extent to which the effects of bariatric surgery on nonweight 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),[6, 65-67] mortality,[68, 69] decreased quality of life,[70] and increased healthcare costs,[66, 67, 71] especially among adults age 65 and older in whom chronic conditions are more prevalent. Obesity carries a substantial health burden,[72] 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.[6, 65-67] 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/m^2 were approximately $1,400 higher than those with a normal BMI (between 18.5 and 24.9 Kg/m^2).[71] This cost-of-care differential between people with high versus normal BMI is probably even higher for people with more severe obesity (BMI $\geq$35 kg/m^2). Among employed Americans, the 3 percent with severe obesity account for 21 percent of the health care costs associated with obesity.[71]

Treatments for severe obesity include lifestyle modifications (exercise, diet), use of medications (e.g., orlistat, phentermine), endoscopically-placed devices (e.g. gastric balloons), and bariatric surgery. Most nonsurgical treatments for obesity fail to achieve long-term weight loss, particularly among patients with severe obesity.[1] In contrast, bariatric surgery is perceived to be an effective obesity treatment, especially long-term, and reduces morbidities.[2-4] It has become the preferred therapy for persons with severe obesity refractory to medical therapy.[5] According to a National Institutes of Health (NIH) Panel, bariatric surgery is indicated for patients with a BMI of 40 kg/m^2 or more (obesity grade 3), or a BMI of 35 Kg/m^2 or more (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 adults with moderate obesity (obesity grade 1, BMI 30-34.9 kg/m^2).[7] Yet, despite the fact that a large number of U.S. adults are eligible for bariatric surgery, its utilization remains low.[8, 9]

Bariatric surgery procedures result in anatomic manipulations of the gastrointestinal (GI) tract and more recently similar anatomic modifications have been 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 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 35 percent of people 60 years and older had a BMI of 30 Kg/m^2 or more, 14 percent had a BMI of 35 Kg/m^2 or more, and six percent had a BMI of 40 Kg/m^2 or more.[10] In these people, obesity was more prevalent among women than men, with almost twice as many women than men meeting the criteria for bariatric surgery, and varied across ethnicities, being highest among nonHispanic blacks (49

percent) and Hispanics (47 percent) and lowest among Asians (9 percent).[10] Thus, a large number of Medicare eligible people likely meet NIH indications for bariatric therapy.

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:

KQ 1: What are the theorized mechanisms of action of bariatric procedures on weight loss and 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 postsurgical 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. nonbariatric therapies) on weight outcomes (including failure to achieve at least minimal weight loss)?
b) What patient- (KQ2a) and intervention- (KQ2b) level characteristics 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. nonbariatric 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. nonbariatric 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- (KQ2b) level characteristics modify the effects of the bariatric therapies on the outcomes other than weight loss in KQ2c?

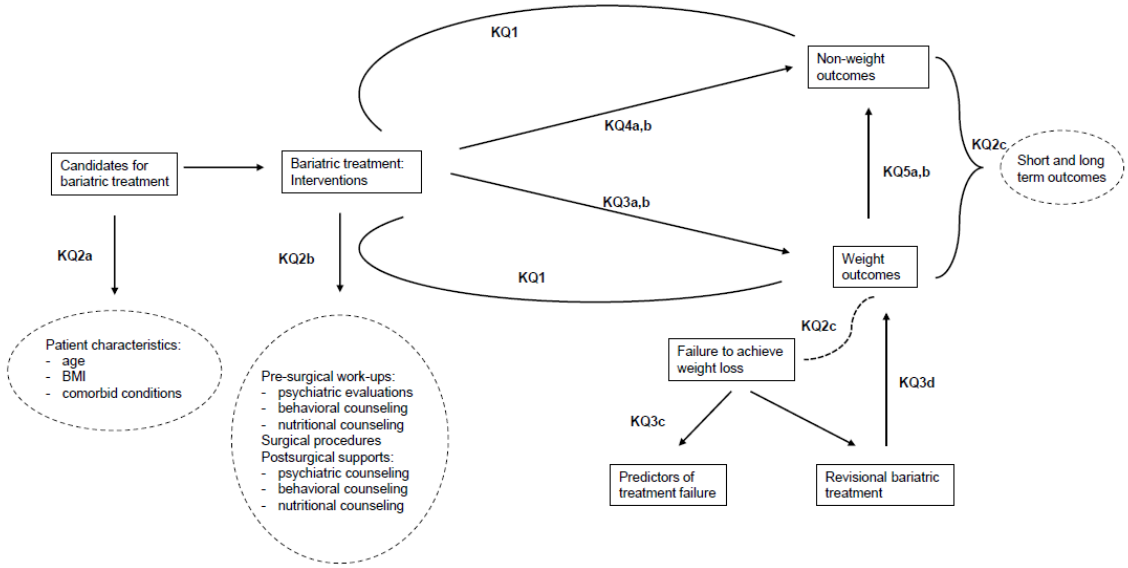
KQ 5

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?

Analytic Framework

To guide the assessment of studies, the analytic framework maps the specific linkages associating the populations, interventions, and outcomes of interest. The analytic framework (Figure 1) depicts the chains of logic that evidence must support to link the 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.[11] 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. There is no deviation from the registered protocol except for the addition of KQ3d; this question was added later given the increased rates of revisional bariatric surgery in the Medicare population.

Eligibility Criteria

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

Population	**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.**
Interventions	Bariatric treatments including anatomic alteration, FDA-approved device placements, open surgical procedures, as well as laparoscopic and endoscopic procedures
	A. Surgical bariatric therapies 1.Adjustable gastric banding (AGB) 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 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.Jejunoileal bypass 6.Biliopancreatic diversion (BPD) 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
	B. Endoscopic bariatric therapies 1.Space-occupying endoscopic bariatric therapies a. Intragastric balloons b. Nonballoon devices 2.Aspiration therapy 3.Endoscopic sleeve gastroplasty 4.Endoscopic gastrointestinal bypass devices a. Duodenojejunal bypass sleeve b. Gastroduodenojejunal bypass sleeve 5.Duodenal mucosal resurfacing 6.Self-assembling magnets for endoscopy
Comparisons	comparisons between different bariatric therapies, or between bariatric and nonbariatric therapies
Outcomes	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:
	a. Mortality b. Weight loss c. Reoperations/need for revisional bariatric surgery d. Postoperative complications including mortality e. Metabolic/diabetes-related outcomes 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. Nonalcoholic steatohepatitis (NASH) and/or nonalcoholic fatty liver disease (NAFLD) f. Reflux g. Cardiovascular outcomes i. Myocardial infraction ii. Stroke

	iii. Hypertension h. Respiratory disease i. Asthma ii. COPD iii. Sleep apnea including the discontinuation of CPAP or BiPAP i. Orthopedic/musculoskeletal outcomes 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 n. Mental health outcomes 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., 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
Timing	Studies published since 2000
Setting	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) and studies in pregnant women. Because studies that are conducted exclusively adults age 65 years and older are uncommon,[12] we included 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. For studies in which the total population did not meet these criteria, we sought to identify any reported subgroup analyses for these groups. For example, if the overall population in a study had a mean age of 40 years but the study reported a subgroup analysis in the group of patients aged 60 years or older, we included the results of this subgroup analysis. We also included any study that used claims data from people already enrolled in and receiving benefits from Medicare. Therefore, our eligibility criteria ensure that all Medicare-eligible populations (i.e. older adults, disabled, persons with end-stage renal diseases) are reflected in the selected studies.

The reason that we excluded studies in younger patients (unless if they met other Medicare-eligibility criteria) was that for young patients to qualify for Medicare benefits they need to have disability or end-stage renal disease. The clinical characteristics and prognosis of disabled persons with obesity or persons with obesity and end-stage renal disease are substantially different from younger patients with obesity but without disability or end-stage renal disease. Thus, these groups of patients may not be exchangeable to each other, limiting our ability to make robust inferences. Furthermore, although substantial evidence exists in regard to the effectiveness and safety of bariatric procedures in younger patients,[13-16] there is virtually no evidence that is particular to older adults or other Medicare-eligible populations. Because younger and older patients may differ substantially in their comorbidity burdens and frailty, evidence generated in younger patients may not be directly applicable to older adults leading to differences in the expected benefits and/or harms.[17] Existing evidence on younger patients can (and should) still be used by patients and physicians in their decisionmaking processes, as long as all stakeholders have reasonable assumptions regarding the transportability of this evidence to older patients, who are not well-represented in the evidence.

For all Key Questions, we included studies of bariatric therapies (i.e., any open or laparoscopic surgical 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 nonbariatric 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, postsurgical 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, single-arm studies with sample size less than 50, case reports, letters, comments, and 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 and 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 noncomparative studies (registries, cross-sectional studies, cohort studies).
- For Key Questions 3a, 3b, and 3d, we included both comparative and noncomparative studies.
- For Key Question 3c, we included prospective cohort studies that report on predictive models for the success or failure of bariatric surgery in regard 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, were eligible.
- For Key Question 5a, we included both comparative and noncomparative studies, while for Key Question 5b we included randomized and nonrandomized 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.[45] 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.[73, 74] 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.[75] Comparing the rates of gastro-esophageal reflux disease between sleeve gastrectomy and Roux-en-Y gastric bypass without taking into account (e.g. through statistical modeling) the fact that certain patient characteristics (e.g. baseline risk of gastro-esophageal reflux disease) are related to treatment selection is not sufficient to attribute differences in adverse event rates to the surgeries themselves.

Moreover, nonrandomized 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.[76, 77] This is because multiple biases relevant to observational studies can be overcome when a target trial is specified to guide the design and analysis of the observational studies.[77] 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, or other more advanced methods, such as g-estimation or doubly robust methods.[60]

Therefore, in the current technology assessment, estimates of treatment effects reported in nonrandomized 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 regard 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).[45] 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 described treatment effects by comparing outcome values before versus after surgery or by providing descriptive statistics. In this way, we aim to minimize unreliable inferences about causal treatment effects while at the same maximizing the utilization of the evidence base to provide estimates that are 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 June 31, 2017 to identify primary research studies meeting our criteria. 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.

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/).[78, 79] 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 postsurgical 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,[11] 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 Nonrandomized Studies - of Interventions (ROBINS-I) tool.[77] 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 were 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 scientific information packet requests.

For Key Question 1, we conducted a narrative review, searching editorials, published narrative and systematic reviews, and textbooks in relevant medical specialties. We employed a systematic and replicable, but nonexhaustive, methodology to efficiently appraise the available evidence, as well as to identify major knowledge gaps.[80]

Descriptive analyses for KQ 2 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 to support valid 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 Key Questions 3a, 3d, and 4a, we intended to conduct quantitative syntheses for all primary outcome categories and for those secondary outcome categories for which at least four studies were available based on the evidence map. However, due to the sparsity of the 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 regard to interventions, outcomes, and populations did not allow for a synthesis, the findings of which would be informative of treatment effects. For the same reasons, no meta-regression was performed for probing statistical between-study heterogeneity in treatment effect estimates.

All procedures identified have been approved by the FDA and are currently used in U.S. clinical practice. We therefore did not conduct subgroup analysis by excluding nonFDA approved procedures or surgeries not practiced in the United States.

For Key Questions 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, 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).[81]

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.[82] 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, the study designs, the study limitations (i.e., risk of bias and overall methodological quality), the relevance of the evidence to the Key Questions, 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 identified a lack of sufficient 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

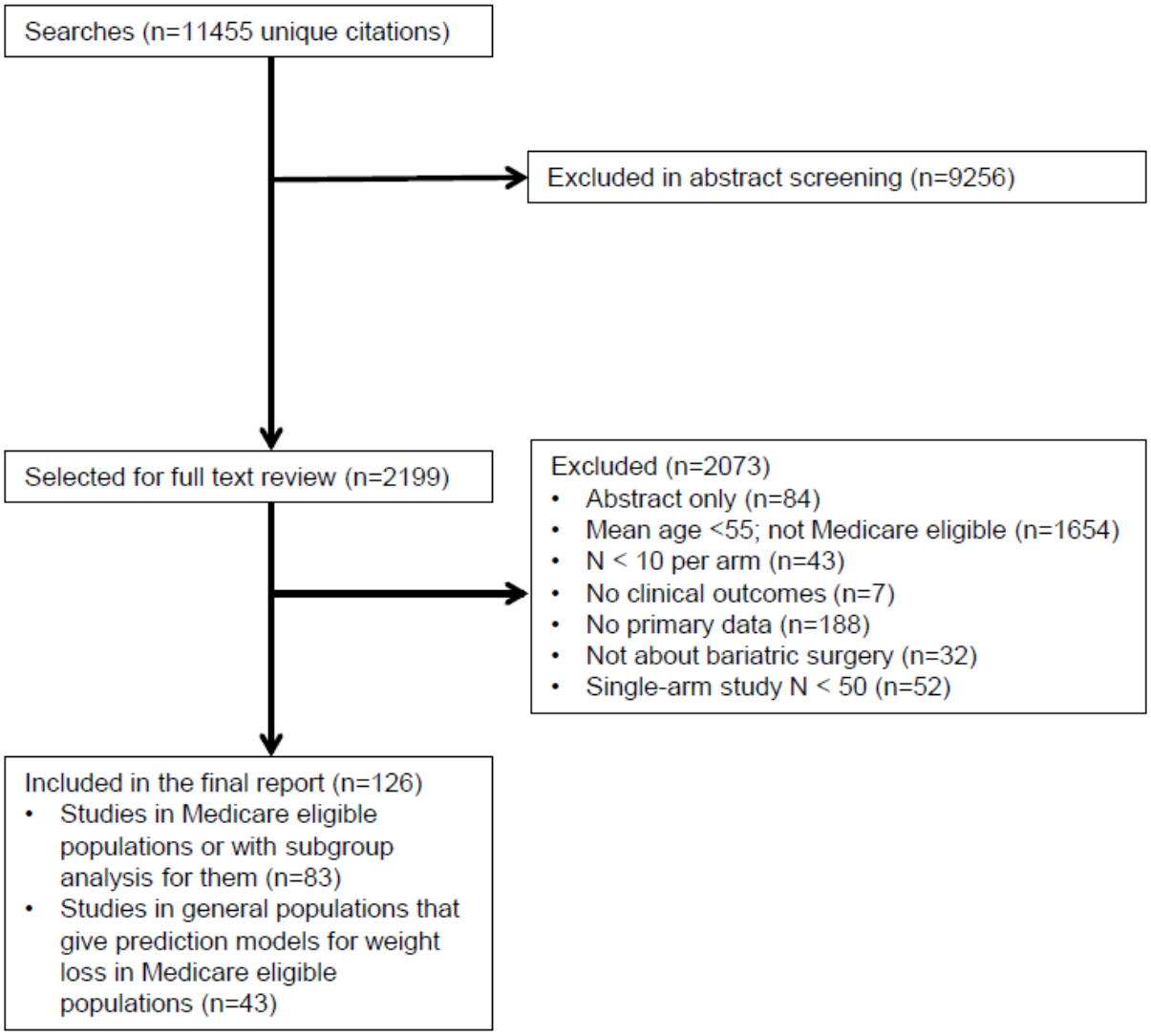
The literature search yielded 11,455 citations (Figure 2) that were screened for eligibility. Of those, 9,273 were excluded in abstract screening. A total of 126 studies met the eligibility criteria, of which 43 reported models to predict weight loss or absolute body weight after bariatric treatment, and the remaining 83 studies pertained to the effectiveness and safety of bariatric procedures. Appendix B lists the articles that were reviewed in full text that were excluded along with reasons for exclusion.

Appendix E describes in detail the patient characteristics in the studies reporting effectiveness or safety data in the Medicare-eligible population. Of the 83 studies (total sample size, N=177,268), 8 studies[18-24, 83] 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 69 on patients with a mean or median age of 55 or older.

We did not identify any randomized controlled 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 41 nonrandomized studies reported data on more than one bariatric procedure, but only 16 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 than weight loss (non-weight-loss outcomes). The remaining studies reported weight changes in outcomes before and after bariatric surgery or provided descriptive statistics, such as incidence or prevalence of outcomes among patients undergoing bariatric surgery without a comparison with an independent or paired group. Details about study design, baselines, and treatments are given in Appendix C, D, and E, respectively.

Appendixes F and G describe in detail the characteristics of the 43 studies reporting a total of 81 distinct prediction models of weight loss outcomes. There was no study with internal or external model validation. Few studies were conducted in U.S. settings. The majority of studies were conducted 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 includes 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 to restrict 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 reduced absorption of ingested food. These mechanisms are dominant in the early weight loss period after surgery.[25] In the long term, however, additional mechanisms appear to be responsible for maintaining weight loss. 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.[26] 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 postoperatively by affecting insulin secretion and sensitivity, reducing appetite, and increasing satiety.[27]

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.[84]

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 the smaller LSG postoperative 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.[84] Ghrelin, a hormone involved in appetite stimulation produced in the gastric fundus, is reduced after LSG.[85]

The Roux-en-Y gastric bypass (RYGB) is classically defined as "restrictive/malabsorptive." 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. The digestive enzymes and food 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 malabsportion (increased fecal fat, decreased albumin, diarrhea) when patients follow the 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.[86-88] Similarly to what is seen after LSG, ghrelin levels are decreased postoperatively, 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.[89] 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.[90] 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.[89, 90]

Food preferences also change after RYGB.[84, 91] Patients report less interest in eating calorie-dense foods, with a lower preference for high-sugar and high-fat foods than before surgery.[92] 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 award-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 postsurgical surgical work-ups (e.g., psychiatric evaluations, behavioral and nutritional counseling),**
c) **the outcomes that have been measured, including perioperative (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 59 studies and ranged from 34.3 to 56.8 percent. Sixty-nine studies reported the ratio between male and female patients. Two studies[28, 29] included only female patients undergoing bariatric surgery, while one[30] included only male patients. In the remaining studies, 47 to 91 percent of the study population was female. Results are presented in Table 1.

Appendix E describes the comorbid conditions in the eligible studies. Four studies were conducted entirely in patients with type 2 diabetes,[31-33] while in another 33 studies at least 50 percent of patients had type 2 diabetes. One study compared outcomes in patients with type 1 or type 2 diabetes.[93] The prevalence of hypertension at baseline ranged from 35.2 to 97.7 percent. One study was exclusively conducted on patients who were on chronic dialysis.[34] The prevalence of pulmonary comorbidities ranged from 2 to 44.3 percent. Six studies reported on the prevalence of chronic obstructive pulmonary disease. Psychiatric comorbidities were reported in nine studies, with the most commonly reported psychiatric comorbid condition being depression (5 studies). Hypercholesterolemia and other lipid disorders were reported as comorbidities in 30 studies; the percentage of bariatric patients with these comorbidities ranged from 11.9 to 95 percent. Gastroesophageal reflux disease was reported in 14 studies and its prevalence ranged from 1.35 to 64.8 percent. Fifteen studies reported on musculoskeletal comorbidities, mainly osteoarthritis and other degenerative joint disorders. The prevalence of congestive heart failure

was reported in eight studies and ranged from 11.1 to 32.4 percent, while one study examined bariatric surgery in patients with congestive heart failure exclusively.[35]

Table 1. Baseline Patient Characteristics

Author, Year PMID	N	Mean Age y (SD) [range]	Mean BMI kg/m2 (SD) [range]	Mean weight kg (SD) [range]	BP mmHg mean (SD)	% female	% white	% black	% Hispanic	% Asian
Abbas 2015 26001882	83	63.4 (3.1)	47 (7.9)	122.4 (25.5)		80				
Altieri 2016 26201412	8990	[>= 45]								
Andalib 2016 26416373	234	47.26 (10.38)	47.04 (8.2)	134.84 (27.08)		56.84	45.73	38.46	7.69	
Ardestani 2015 25573879	5225	53.8 (10.2)	47.1 (8)			66.7	81.7			
Bergeat 2017 28035521	55	63.9 (2.5) [60, 71]	44.5 (6.3) [32, 60]			91				
Boules 2015 26243345	166	56.7 (8.6)	44.6 (8)	119.2 (24.2)		81.3				
Busetto 2008 18239641	216	64.1 (4)	44.2 (7.6)	116.4 (21.1)		85.2				
Clough 2011 20490708	113	63.6 [60, 73]	42.2	116.9		56.5				
Casillas 2017 28438494	429	67 [65, 79]	42.6 (5.4)			70				
Davidson 2016 26864395	1210	59 (3.4)	46 (7)			76.2				
Davis 2017 27681880	632	53 (11)				72				
Dorman 2012 22038414	18058	[50, 70]				76.8	80.8	10.5	3.1	0.7
Dunkle-Blatter 2007 17331804	61	62 [60-72]	49.3 (7.5) [38.0, 78.3]			67.2				
Flum 2005 16234496	1519									
Flum 2011 21975317	47030	52.9 (11.6)				75.48	81.01	14.73	2.05	
Freeman 2015 25708829	52	50 (10) [18-67]				54				
Gebhart 2015 25130515	6125	[>60]				68.65	84.22			
Ghio 2016 28259559	74	54.8 (9.6)	44.1 (5.5			65				
Giordano 2014 24318411	132	59.43 (3.81)	46.21 (7.47)	132.27 (28.97)		57.6				
Hallowell 2007 17576885	77	56 (9.5) [31, 66]	52.7 (6.5)			89.6				
Hazzan 2006 17138231	55	61.5 [60-70]	46.2 [38-61]			65.4				
Hernigou 2016 27130648	279	71.7 (8.74)	36 (7.15)	96.5 (20.0)		59.1				
Huang 2015 25859266	68	58.9 (4.3) [55, 79]	39.5 (6.8) [32, 60.4]	102.1 (19.4)		64.7				
Imam 2017 27927587	1428	58.25 (8.68)	44.15 (6.89)	269.85 (50.58)		76.6	56.2	18.3	22.5	
Irwin 2013 23744816	27	56.9 (9.2)	50.2 (7.5)			81.5				
Johnson 2012 22643265	349	55.1				65	86			
Lee 2016 27220823	162	55.2 (9.3)	42.9 (5.3)	131.4 (21.3)	125 (14.8)/74.78 (12.5)		59.3			
Lemaître 2016 27063637	494	45.5 [18, 75]	47.8 (7.8) [35.0, 82.3]	133.5 [84, 255]		74				

Author, Year PMID	N	Mean Age y (SD) [range]	Mean BMI kg/m2 (SD) [range]	Mean weight kg (SD) [range]	BP mmHg mean (SD)	% female	% white	% black	% Hispanic	% Asian
Leonetti 2012 22508671	60	54.5 (8.3)	40.2 (5.9)			68				
Loy 2014 24582414	55	72.4 (2.5) [70, 82]	45 (6.2)	123 (22)		60	94.5	5.5		
Luppi 2015 25088486	28	63.2 [60, 68]	43.3	113.2		64.3				
Mackay 2016 27778462	1362					82.6				
Maraka 2015 25611727	128	55	46.3 (9.0)			64.8				
Martin 2015 26530652	364	58.2 (7.3)	40.7 (9.7)			81				
McGlone 2015 26112136	50	[>60]	49.5 (6.1)			74				
Michaud 2016 26130180	102	62.3 (2)	50.9 (6.8)	133 (24)		61				
Miranda 2013 23604694	19	Median 65 [49, 78]	Median 50.9 [22, 64]	141.6 [98, 210]	134.6	47				
Mittermair 2008 18830777	134	55.6 (4.6) [50, 69]	43.9 (5.7) [35.3, 62.7]			76.1				
Mizrahi 2014 24442420	52	62.9 (0.3) [60, 70]	42.6 (0.7)	117.3 (2.8)		56				
Moon 2016 26220238	353	62.9 (2.5) [60-71]	44.5 (6.6) [32.9, 74.5]			71.4				
Mozer 2015 25832986	138	Median 48 (10.6)	Median 46	Median 294		51.4				
Nagao 2014 24519024	52	55.1 (3.7)	46.4 (6)	127.4 (24.1)		82				
Navarrete 2017 28214166	206	55.4 (10.2)	46.0 (17.2)			80.6				
Nearing 2017 28011119	102	102	80.39							
Nickel 2016 27179771	5918					83				
O'Keefe 2010 20532834	197	67.3 (2.3) [65-78]	48.1 (6.9) [35.6, 73]	72.9 (17.8) [38.7, 127.1]		72.1				
Ochner 2013 23700235	157					100				
Omalu 2007 17938303	2022	[>55]								
Papasavas 2004 15479593	71	59 [55, 67]	50.2 [37, 65]			76.1				
Pajecki 2015 26537266	46	64 [60, 71]	49.63 [38, 66]			89				
Peraglie 2016 25814071	88	64 [60, 74]	43 [33, 61]	118 [78, 171]		62				
Perry 2008 18156918	11903	[65, 75]				77.6				
Persson 2017 28506731	47859									
Praveenraj 2016 27279392	86	57.5 (6.1) [50, 75]	43.2 (8.7) [29, 87]	108.2 (23.1) [65, 200]		53.5				
Qin 2015 25373923	3616	56.7 (5.1)	45.2 (7.6)			74.8	76.1	14.9		0.8
Quebbemann 2005 16925254	27	68 [65.8, 72.6] [65.8, 72.6]	47.4 (7.4)			63				
Quirante 2017 28039650	393		41.6			58	83	5	11	

Author, Year PMID	N	Mean Age y (SD) [range]	Mean BMI kg/m2 (SD) [range]	Mean weight kg (SD) [range]	BP mmHg mean (SD)	% female	% white	% black	% Hispanic	% Asian
Ramirez 2012 22551574	42	73.5 [71, 80]	44 [34-81]	124.5 [80.1-219.1]		52.4				
Ritz 2014 24708912	154	[>60]								
Saleh 2015 25868831	667	50.7 (11.7)	47 (7.4)			65.5		25.8		
Scott 2013 22014480	2432	[50, 79]								
Serrot 2011 22000180	34	Median 59	34.3	Median 225.5	Median SBP 126 IQR 30	55.9				
Sosa 2004 15603658	22	64.4 [60, 75]	48.5 [40, 62]							
Soto 2013 23733390	35	66.3 [60-79]	46.3 [33.7, 77.6]			68.6				
Spaniolas 2014 24913586	1005		44 (7)			69.2				
Sugerman 2004 15273547	65	63 (3) [60.1, 74.5]	49 (7)	133 (22)		78	85	14	1	
Sun 2016 26264895	367	[>60]								
Tiwari 2011 21459686	905									
Trieu 2007 17400516	92	62.2 [60-74]	48.45 [35-68]	136.63 [86.4, 215.9]		63				
Valderas 2009 19517199	52	57.8 (4.3)	36.4 (8.7)			100			100	
van Rutte 2013 23344504	135	[55, 70]	43.8 [29.8, 65.1]			69.6				
Varela 2006 17058723	1339	[>60]				73	82.2			
Wagner 2007 17938305	54	48.9 [27, 63] [27, 63]	56.8 [34, 113]			75.9				
Werner 2015 26071250	79	[65, 84]	[>40]			78.1				
Wiklund 2017	70	47 (12)	44.7 (5.8)	133.7 (24.5)		58.6				
Willkomm 2010 20870182	100	68 [65, 77]	45 [33, 61]							
Wise 2016 26091994	117	59.3 (5.7)	43.6 (6.2)			77.8		6.8		
Wittgrove 2009 19705206	120	62 [60, 74]	43 [34, 70]			48				
Wool 2009 18855082	60	56.7	49 [37, 71]			0				
Yuan 2009 18996764	282	48.5 (11.78)	52.4 (10)			74.47				
Y. Van Noeiwenhove 2016	56	63.8 (3.2)		122 (26)		57				
Zaveri 2016 27795883	53	72.7 (2.5) [70, 81.4]	43.3 (5.8)	264.6 (40.7)		66				

BP: blood pressure; SD: standard deviation; PMID: PubMed ID (not reported for articles not indexed in PubMed but retrieved through other databases)

Interventions

We did not identify any studies in the Medicare-eligible population that reported on endoscopically performed bariatric procedures. In particular, there are no studies in the Medicare-eligible population in regard to intragastric balloons or other nonballoon space-occupying endoscopic bariatric devices, aspiration therapy, endoscopic sleeve gastroplasty, endoscopic duodenojejunal or gastroduodenojejunal bypass sleeve, duodenal mucosal resurfacing, and self-assembling magnets for endoscopy. Overall, the 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 2 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 (48 studies), followed by sleeve gastrectomy (SG; 28 studies) and adjustable gastric banding (AGB; 24 studies). Twenty-five studies used a combined treatment group that consisting of two or more bariatric surgical procedures. The pertinent data were reported in only seven studies and included RYGB and SG;[30, 94] RYGB, AGB, vertical banded gastroplasty (VBG), and biliopancreatic diversion with duodenal switch (BPD-DS)[95]; gastric bypass and AGB[48]; AGB, SG, RYGB, and revisional surgery;[19] laparoscopic SG and laparoscopic one anastomosis gastric bypass;[96] VBG, AGB, RYGB, and duodenal bypass. We found one study on mini-gastric bypass (MGB) alone, one on revisional surgery alone, one on single-anastomosis duodenal switch (SADS) alone, one on VBG alone, and three on bilipancreatic diversion alone. One study evaluated outcomes in patients who concurrently received bariatric surgery and hiatal hernia repair.[52] We did not identify any studies on gastric plication, vagal blockade, omentum removal (omentectomy), gastric stimulation, or mucosal ablation.

Table 2 also shows how many bariatric surgeries were performed though 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 performed either open or laparoscopically (RYGB, n=7; SG, n=2; BPD-DS, n=1).

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

Table 2. Method of surgery by bariatric procedure studied in the Medicare-eligible population.
The numbers correspond to the study arms across all eligible studies.

	Method of surgery			
Bariatric Procedure	Open only	Laparoscopic only	Either open or laparoscopic	Not reported
AGB		23		1
MGB		1		
Multiple surgeries	1	7	7	10
RYGB	4	26	7	5
SADS		1		
SG		25	2	1
VBG		1		
BPD-DS	1	1	1	

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

Outcomes

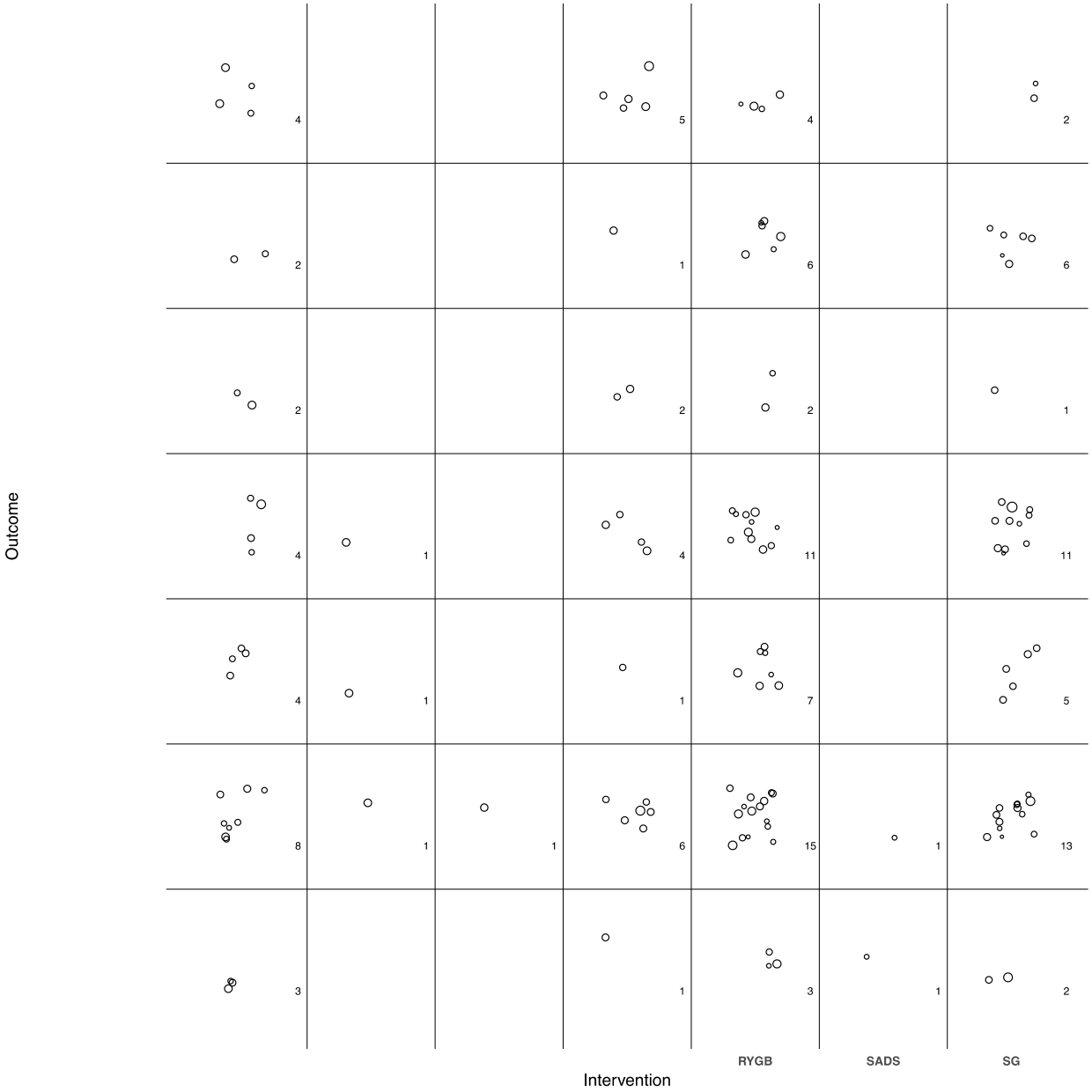
Because of the wide variety of outcome definitions, we classified outcomes in hierarchical categories based on their clinical importance for the management of bariatric patients (see Methods).

Figure 3 shows the weight loss outcomes measured in Medicare eligible patients undergoing bariatric surgery. The figure shows the different bariatric procedures on the horizontal axis and the measure of weight loss outcomes on the vertical axis for each of the eligible studies. Each data point (showed as hollow circle) corresponds to a patient population that had undergone a specific bariatric procedure and had the respective outcome measured. (i.e., each data point corresponds to a treatment arm with a specific adverse event/surgical complication measured). The size of the data point (hollow circle) is relative to the sample size of the treatment arm (i.e., arms with larger number of patients are shown by larger circles). In each cell, the number of circles corresponds to the total number of treatment arms with the respective outcome, while the numeric value in the right-bottom corner denotes the size of the treatment arms with a respective outcome measure. For example, the cell that is identified at the point where the "Weight loss – absolute" and the "AGB" columns cross each other contains four data points; this is a graphical representation of the fact that we identified four treatment arms that had undergone AGB and for whom the respective primary studies reported absolute weight loss. Similarly, in the cell that corresponds to the point where "Weight loss – absolute" and "MGB" meet, there are no data points; this means that we did not identify any studies in which at least one treatment arm pertained to MGB. Because certain studies reported on more than one procedure, the total number of treatment arms is greater than the number of studies. Overall, this figure descriptively summarizes the current state of the evidence in regard to weight loss outcomes and provides a map of the evidence gaps (e.g., outcomes and/or procedures with few or no studied populations), as well as of the procedures and outcomes where multiple populations were studied.

Percent excess weight loss (EWL) and percent weight loss (WL) were examined for the vast majority bariatric surgical procedures, while absolute changes in weight and BMI were studied less commonly. Of note, there are no studies about weight outcomes after VBG, and there are is limited evidence regarding MGB and SADS. Most outcomes pertained to laparoscopically conducted surgeries, while only five outcomes were examined after open surgeries (Table 3). These are percent excess BMI loss (EBMIL) and changes in BMI after open RYGB[36]; and percent EWL, percent WL, and changes in BMI after open BPD-DS.[37]

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

Each circle denotes an outcome that has been reported in regard to the bariatric procedures shown on the horizontal axis in an 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



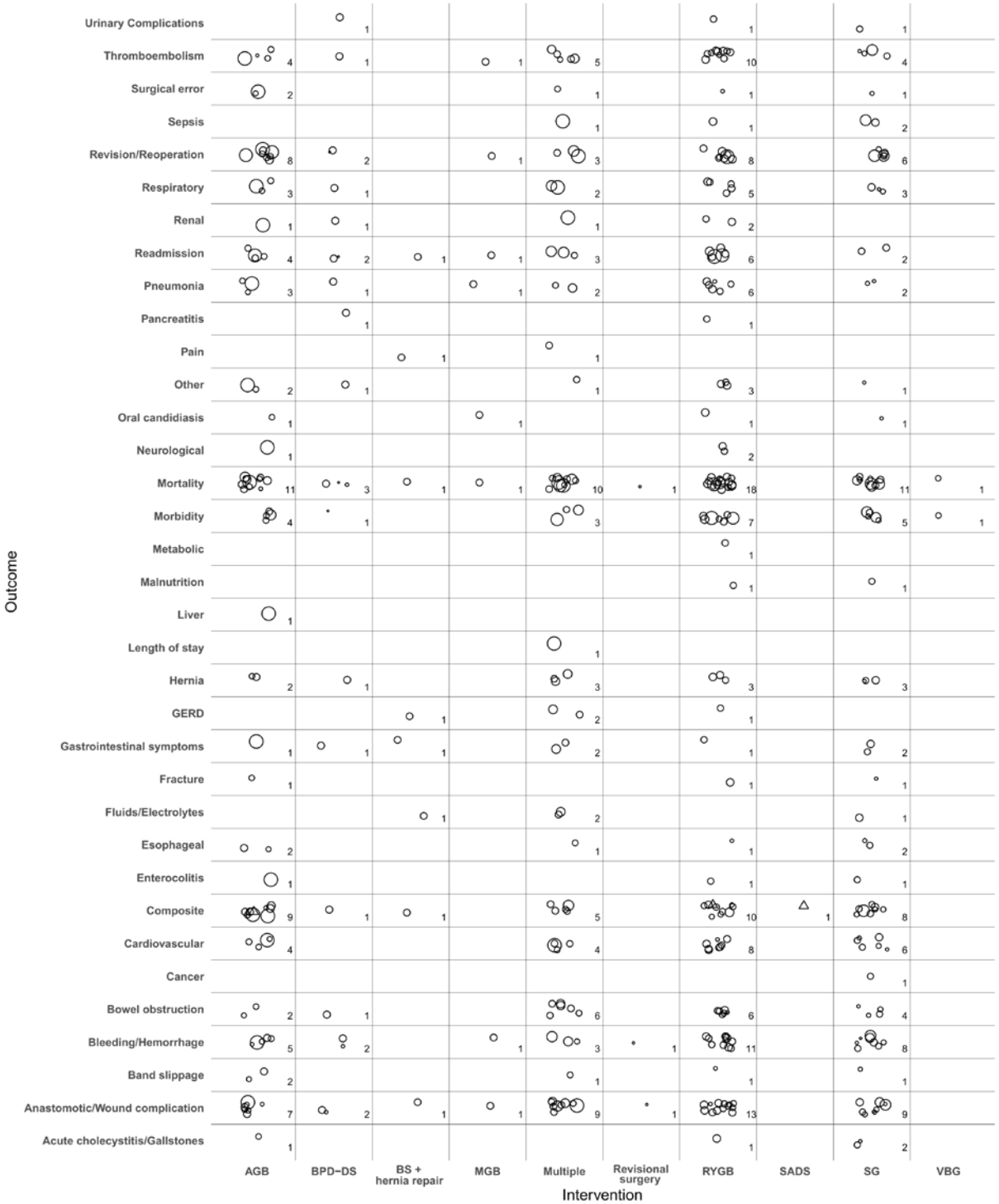
AGB: adjustable gastric banding; BS: bariatric surgery; MGB: mini-gastric bypass; RYGB: Roux-en-Y gastric bypass; SADS: single anastomosis duodenal switch; SG: sleeve gastrectomy; BPD-DS: biliopancreatic diversion with duodenal switch; BMI: body mass index; %EBMIL: percent excess BMI loss; %EWL: percent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

The incidence of a wide variety of adverse events and/or surgical complications in the 90-day postoperative period after bariatric surgical procedures is shown in Figure 4. The figure shows the different bariatric procedures on the horizontal axis and the various adverse events/surgical complications on the vertical axis in each of the eligible studies. Each data point (showed as hollow circle) corresponds to a patient population that had undergone a specific bariatric

procedure and had the respective outcome measured (i.e., each data point corresponds to a treatment arm with a specific adverse event/surgical complication measured). The size of the data point (hollow circle) is relative to the sample size of the treatment arm (i.e., arms with larger number of patients are shown by larger circles). In each cell, the number of circles corresponds to the total number of treatment arms with the respective outcome, while the numeric value in the right-bottom corner denotes the size of the treatment arms with a respective outcome measure. For example, the cell that is identified at the point where the "Renal" and the "AGB" columns cross each other contains four data points; this is a graphical representation of the fact that we identified four treatment arms that had undergone AGB and for whom the respective primary studies reported on renal outcomes. Similarly, in the cell that corresponds to the point where "Sepsis" and "AGB" meet each other, there are no data points; this means that we did not identify any studies in which data on sepsis were reported for at least one treatment arm pertaining to AGB. Because certain studies reported on more than one procedure, the total number of treatment arms is greater than the number of studies. Overall, this figure descriptively summarizes the current state of the evidence in regard to adverse events/surgical complications and provides a map of the evidence gaps (e.g., outcomes and/or procedures with few or no studied populations), as well as of the procedures and outcomes where multiple populations were studied. The sample sizes for these outcomes vary across procedures, with the largest sample sizes in AGB, RYGB, and SG, and evidence for BPD-DS, MGB, SADS, and VBG from smaller sample sizes.

Only 17 types of adverse events/surgical complications were reported for patients undergoing open surgery (Table 3). These include postoperative mortality[24, 97] and bleeding, leaks, bowel obstruction, wound infection, incisional hernia, deep venous thrombosis, and pulmonary embolism[97] after open RYGB; and the following 16 outcomes after open BPD-DS:[37] 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. Postoperative (0 to 90 days after bariatric surgery) adverse events and surgical complications studied in the Medicare-eligible population according to bariatric procedure.
Each circle denotes an adverse event reported in regard to the bariatric procedures shown on the horizontal axis in an 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

Other outcomes that have been studied in patients undergoing bariatric surgery are shown in Figure 5. The figure shows the different bariatric procedures on the horizontal axis and the various health outcomes other than weight loss or adverse events/surgical complications on the vertical axis in each of the eligible studies. Each data point (showed as hollow circle) corresponds to a patient population that had undergone a specific bariatric procedure and had the respective outcome measured. (i.e., each data point corresponds to a treatment arm with a specific adverse event/surgical complication measured). The size of the data point (hollow circle) is relative to the sample size of the treatment arm (i.e., arms with larger number of patients are shown by larger circles). In each cell, the number of circles corresponds to the total number of treatment arms with the respective outcome, while the numeric value in the right-bottom corner denotes the size of the treatment arms with a respective outcome measure. For example, the cell that is identified at the point where the "Mortality" and the "AGB" columns cross each other contains one data point; this is a graphical representation of the fact that we identified one treatment arm that had undergone AGB and for whom the study reported on mortality outcomes. Similarly, in the cell that corresponds to the point where "Mortality" and "SADS" meet each other, there are no data points; this means that we did not identify any studies in which data on mortality were reported for at least one treatment arm pertaining to SADS. Because certain studies reported on more than one procedure, the total number of treatment arms is greater than the number of studies. Overall, this figure descriptively summarizes the current state of the evidence in regard to health outcomes other than weight loss and adverse events/surgical complications and provides a map of evidence gaps (e.g., outcomes and/or procedures with few or no studied populations), as well as of procedures and outcomes where multiple populations are studied.

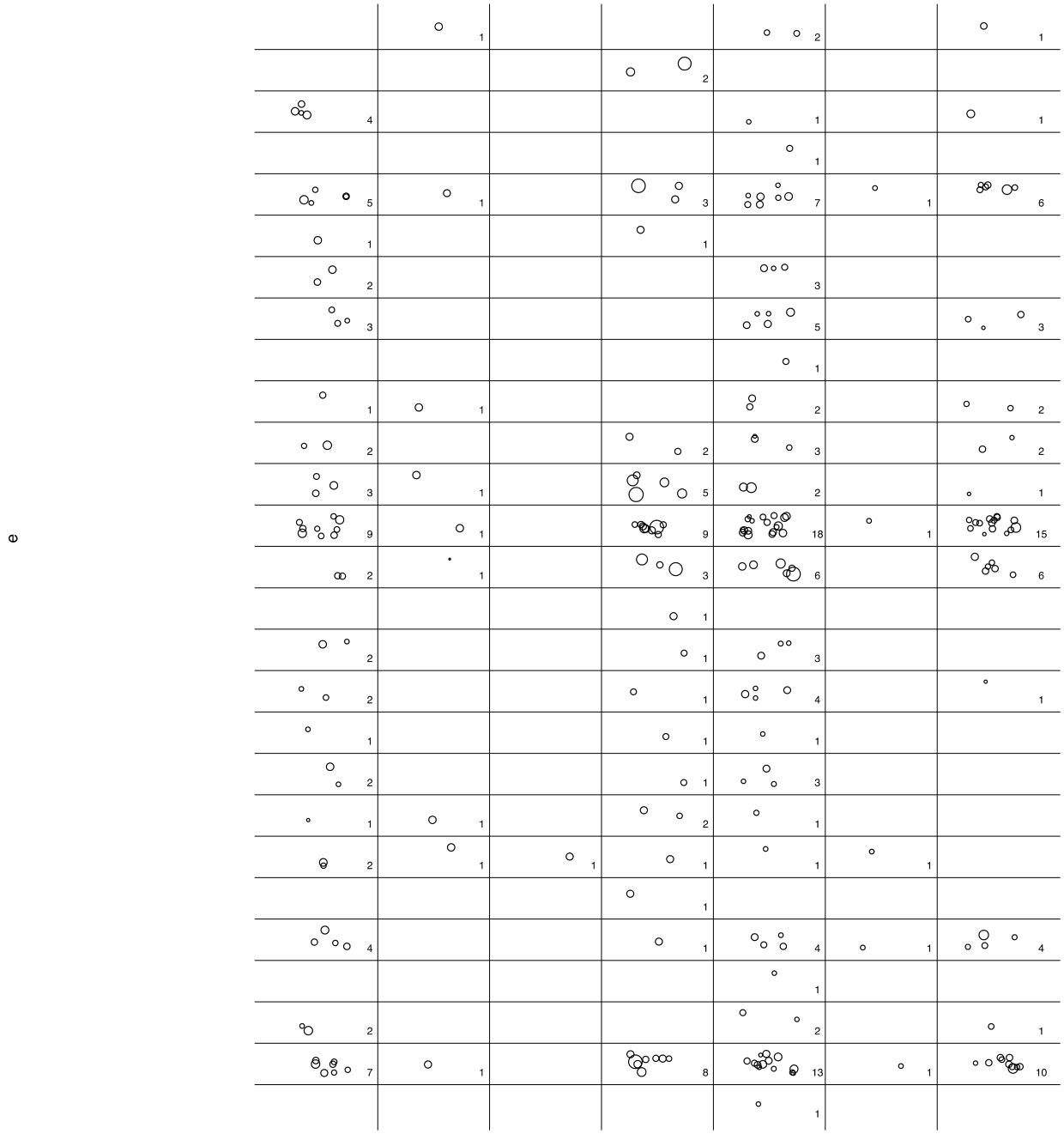
Based on Figure 5, respiratory outcomes (26 studies), metabolic/diabetes-related outcomes (59 studies), and cardiovascular outcomes (44 studies) are most commonly reported. Health-related quality of life, whether physical, mental, or overall, has not been extensively studied in Medicare eligible patients. The majority of evidence pertains to RYGB, but limited evidence also exists for other procedures.

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

As with weight outcomes and adverse events/surgical complications, all but 29 outcomes pertain to laparoscopic surgeries (Table 3). 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, renal 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 denotes an outcome that has been reported in the bariatric procedures shown on the horizontal axis in an 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 3. Summary of outcomes after bariatric surgery by procedure and method of surgery (open versus laparoscopic) in the Medicare-eligible population.

The numbers (N) correspond to the study arms across all eligible studies.

	Adverse Events, N		Weight/BMI, N		Other Outcomes, N	
Bariatric Procedure	Open	Laparoscopic	Open	Laparoscopic	Open	Laparoscopic
AGB		81		27		54
MGB		8		1		
Multiple surgeries		36		15		18
RYGB	1	117	2	39	10	63
SADS		1		2		5
SG		86		41		53
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

a) In Medicare-eligible patients, what are the effects of different bariatric therapies (contrasted between them or vs. nonbariatric 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. nonbariatric therapies) on weight outcomes?

KQ 3.a. Comparative Studies

Five studies assessed the comparative effects of bariatric surgeries on weight change, of which only four reported numerical data.[32, 38-40]

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 for patients receiving RYGB (N=84), SG (N=48), or LAGB (N=30). As shown in Table 4, 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.[38]

Table 4. 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/m^2)						
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 patients (N=30) receiving conventional treatment with pharmaceutical agents and lifestyle modifications (diet and physical activity), a higher proportion of patients undergoing LSG (N=30) achieved better weight outcomes at 18 months of follow-up. There was a 71 percent EWL among patients in the LSG group, compared to 2.8 percent weight regain in the conventional therapy group. Similarly, the mean BMI loss in the LSG group was 13.5 kg/m^2 compared to a mean 0.17 kg/m^2 increase in the conventional treatment group.[32]

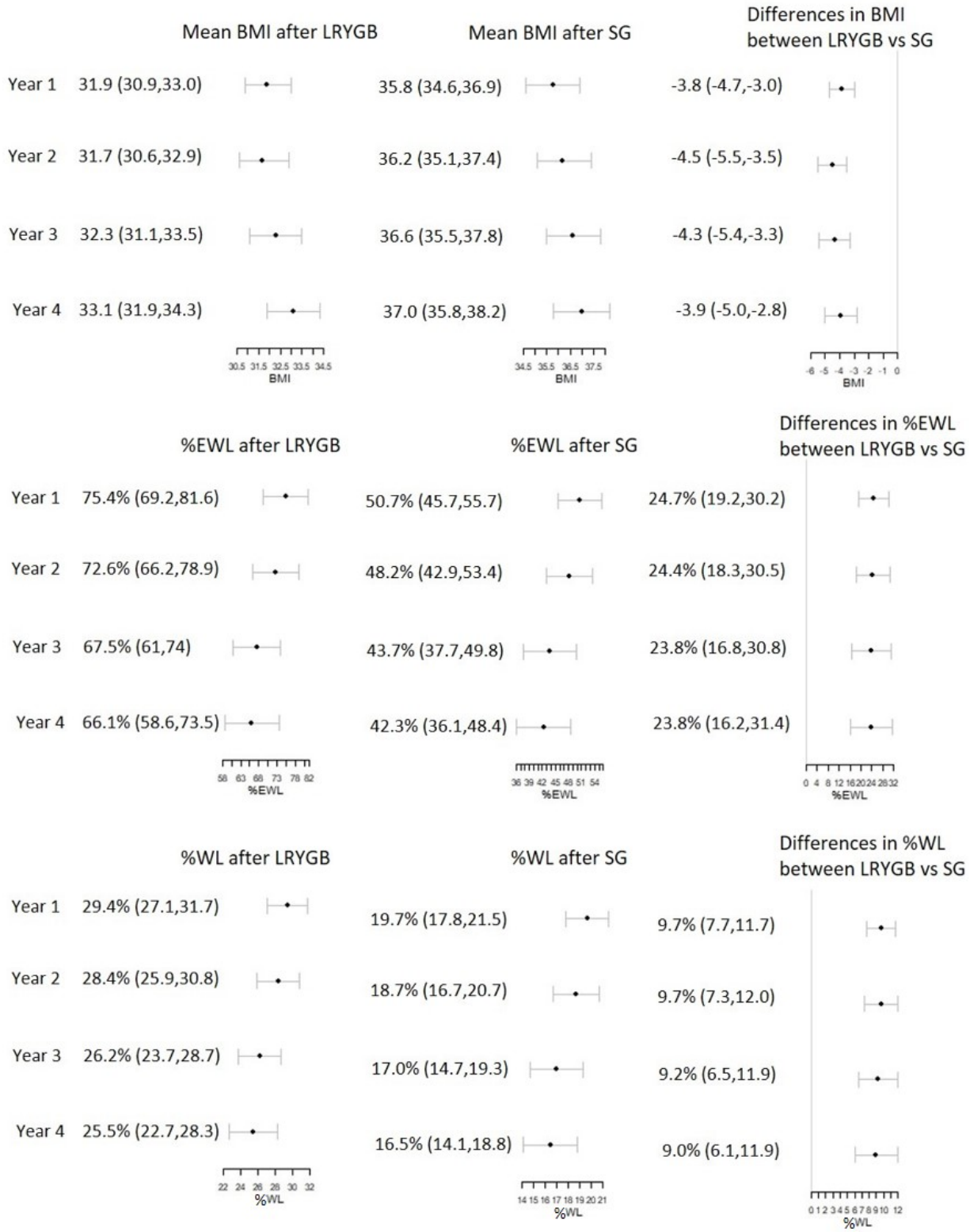
Ritz et al. found that for patients 60 years of age or older, 1 year after surgery, weight loss was higher for RYGB (N=57) and SG (N=47) compared to LAGB (N=50). The percent of initial weight lost was 9.2 percent higher for those undergoing RYGB and 5.5 percent higher for those undergoing SG compared to patients receiving LAGB.[39]

Imam et al. compared patients undergoing RYGB (N=234) to propensity score matched patients undergoing SG (N=234), as well as patients undergoing any bariatric surgery (N=714) to propensity score matched nonsurgical controls (N=714). Although no numerical results are reported for weight loss outcomes, the authors note that throughout the 3-year follow up, weight loss was greater for RYGB compared to SG and for patients undergoing any bariatric surgery compared to nonsurgical controls.[41]

Finally, Casillas et al. compared weight loss outcomes for patients aged 65 years of older who underwent LRYGB (N=177) compared to those who underwent SG (N=252), matched using propensity scores. During a median follow-up of 4 years, LRYGB results in significantly (P<0.001) larger improvements in BMI, percent WL, and percent EWL compared to SG. The magnitudes of these effects are shown in Figure 6.[40]

Although 3 studies (Lee et al., Ritz et al., and Casillas 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 used to account for confounders and other prognostic factors associated with weight loss as well as the differences in the modelled covariates do not allow for a meaningful statistical synthesis of the results.

Figure 6. Comparative effects of LRYGB vs. SG on body mass index, percent excess weight loss, and percent weight loss.



LRYGB: laparoscopic Roux-en-Y gastric bypass; SG: sleeve gastrectomy; BMI: body mass index; %EWL: percent excess weight loss; %WL: percent weight loss

KQ 3.b. Pre- Versus Post-Surgery Studies

A total of 54 studies reported the effect of bariatric surgeries by estimating the differences in weight outcomes between baseline and at different time points during follow-up.

Multiple Bariatric Surgery Procedures

O'Keefe et al. reported that the average percent EWL among patients undergoing either 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.[98]

Ghio et al. graphically showed the trajectory of percent EWL among patients with insulin-treated type 2 diabetes who underwent either RYGB or SG. Excess weight was reduced at 4 and at 12 months after surgery and this reduction was maintained on average up to 7 years after surgery.[99]

Hernigou et al. reported that among 85 patients undergoing any bariatric surgery before total hip arthroplasty, mean BMI declined from 42 kg/m^2 (SD 7.4) to 27.6 kg/m^2 (SD 4.2).[54]

Nearing et al. also reported that in patients who underwent any bariatric surgery either before or after total hip arthroplasty or total knee arthroplasty, BMI declined from 49.6 kg/m^2 (SD 5.8) to 37.8 kg/m^2 (SD 7.1) and from 46.3 kg/m^2 (SD 5.6) to 43.9 kg/m^2 (SD 8.7), respectively, at 1 year of follow-up.

Adjustable Gastric Banding

Table 5 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 EBMIL ranged from 35.5 to 43.3 percent at 1 year. The mean percent EWL at 1 year ranged from 16 to 50 percent and the percent WL from 12 to 13.7 percent. Finally, the mean BMI reduction at 1 year ranged from 5 to 8.4 kg/m^2 and the mean weight reduction ranged from 40.7 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- versus post-surgery comparisons and cannot account for temporal trends that are not due to bariatric surgery.

In addition to mean percent EWL (Table 5), Moon et al. also evaluated the effect of LAGB on weight-loss failure, defined as percent EWL less than 30. At the time of last follow-up, 40/68 LAGB patients (58.8 percent) failed to achieve weight loss, and three (4.4 percent) gained weight.[100]

O'Keefe et al. reported the average percent EWL among patients undergoing RYGB, LAGB or VSG.[98] This study is described under “Multiple bariatric surgery procedures”.

Ritz et al. graphically present percent WL at 3, 6, 9 and 12 months after AGB surgery, which consistently increased at each time point of follow-up.[39]

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.[101]

Table 5. 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	Baseline N	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	113					43.3 (NR)							44.1 (NR)		
Moon 2016 26220238	68			29.8 (NR)		35.5 (NR)		37 (NR)	35.6 (NR)						
Zaveri 2016 27795883	24		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															
Quebbemann 2005 16925254	14					32 (NR)			35 (NR)						
Ramirez 2012 22551574	22					32.8 (17)									
Wise 2016 26091994	117			27.2 (12.6)		30.2 (19.2)									
Moon 2016 26220238	68			26.1 (NR)		30.9 (NR)		32.8 (NR)	31.5 (NR)						
Lee 2016 27220823	30			13.9 (14.3)		16.1 (15.9)									
Ochner 2013 23700235	325					50 (NR)[g]			53 (NR)[g]						
Zaveri 2016 27795883	24		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	68			11.8 (NR)		13.7 (NR)		15 (NR)	14.3 (NR)						
Lee 2016 27220823	30			10.3 (10.4)		12 (11.7)									
BMI (kg/m^2)															
Ramirez 2012 22551574	22	44 (NR)[a]				35.8 (4.5)									
BMI loss (kg/m^2)															
Mittermair 2008 18830777	124					8.4 (NR)			11.0 (NR)	12.3 (NR)	12.4 (NR)	11.8 (NR)	12.5 (NR)	10.2 (NR)	
Lee 2016 27220823	30			4.4 (4.5)		5 (5)									
O'Keefe 2010 20532834	34			8.1 (6.1)[e]		6.5 (7)[e]									

Author Year PMID	Baseline N	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
Loy 2014 24582414	55			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	22	124.5 (NR)[a]				96.1 (14.1)									
Weight loss (kg)															
Lee 2016 27220823	30			14 (14.1)		15.3 (15.7)									
Clough 2011 20490708	113												23.2 (NR)		
O'Keefe 2010 20532834	34			21.3 (22.6)[e]		17.3 (24.1)[e]									
Loy 2014 24582414	55			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	124					23.5 (NR)[b]			29.5 (NR)[a]	29.5 (NR)[a]	27.5 (NR)[a]	28.5 (NR)[a]	32.5(NR)[a]	19.5 (NR)[a]	
Mittermair 2008 18830777	99					24 (NR)[c]			30 (NR)[b]	29 (NR)[b]	28 (NR)[b]	29 (NR)[b]	33 (NR)[b]	19 (NR)[b]	
Mittermair 2008 18830777	25					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; EBMIL: 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. Baseline weight and BMI were not reported separately by procedure at baseline. Therefore, we did not compute the difference in weight between baseline and different time points after surgery.

[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 present the trajectory of percent EWL at 6, 12, 24, 36, 48, and 60 months after BPD-DS in 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) lost less than 25 percent of their initial excess weight.[37]

Mini-Gastric Bypass

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, respectively. 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.[102]

Roux En Y Gastric Bypass

Table 6 shows the changes over time after RYGB in different weight outcomes by study.

Across all studies, the mean percent EBMIL ranged from 73.1 to 80.6 percent at 1 year. The mean percent EWL at 1 year ranged from 41.4 to 82.8 percent, and the percent WL from 25 to 31.8 percent. Finally, the mean BMI reduction at 1 year ranged from 16.5 to 13.4 kg/m^2, and the mean weight reduction ranged from 40.7 to 93.8 kg. Because the standard deviation of weight change was not consistently reported across studies, we concluded that a meta-analysis of the subset of studies reporting relevant data would not be informative.

O'Keefe et al. reported the average percent EWL among patients undergoing RYGB, LAGB or VSG.[98] This study is described under "Multiple bariatric surgery procedures".

Miranda et al. evaluated the changes in weight among patient with heart failure undergoing RYGB bariatric surgery. During a median follow-up of 4.3 years, mean BMI was reduced from 55 kg/m^2 to 35 kg/m^2, and weight was reduced from 146 kg to 99 kg. The mean percent weight loss was 42.[35]

Moon et al., in addition to mean percent EWL (Table 6), also evaluated the effect of RYGB on weight-loss failure, defined as percent EWL less than 30. At the time of last follow-up, 29/210 RYGB patients (14 percent) failed to achieve weight loss.[100]

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.[103]

Ritz et al. graphically present the percent WL at 3, 6, 9 and 12 months after RYGB surgery, which consistently increased at each time point of follow-up.[39]

Imam et al. graphically present the trajectory of absolute weight loss (in pounds) for patients undergoing RYGB at 3 months, 1 year, 2 years, and 3 years after surgery. Weight loss peaked at 13.6 months and was sustained up to 3 years after surgery.[41]

Macano et al. graphically present changes in BMI over time after LRYGB. Patients had a median BMI of 44.4 kg/m^2 (range, 34.8-66) before surgery. BMI was sequentially lower at 6 weeks, 6 months, and 1 year after surgery, while the 1 year mean BMI value was sustained up to 2 years.[94]

Van Nieuwenhove et al. graphically present the trajectory of percent WL up to 4 years after LRYGB in 56 patients older than 60 years. The results support a sustainable weight change for all the duration of follow-up.[104]

Casillas et al.[47] report changes in weight outcomes at 1, 2, 3, and 4 years after LRYGB. Results are shown in Figure 6.

Table 6. 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	N	0 mo	3 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	3 y	3.5 y	4 y	Last follow-up
percent EBMIL	Wagner 2007 17938305	38	.	.	.	.	.	.	.	.		62.6 (26.4)[g]		
	Moon 2016 26220238	210	.	.	64.9 (NR)	.	73.1 (NR)	.	78.5 (NR)	76.1 (NR)		.		
	Zaveri 2016 27795883	14	.	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	13	.	.	.	.	71.0 (NR)	.	.	.		.		
	Trieu 2007 17400516	93	.	38.4 (NR)	.	55 (NR)	.	.	68.3 (NR)	.		.		
	Willkomm 2010 20870182	100	.	.	.	.	74.8 (NR)	.	.	83.4 (NR)		.		
	Serrot 2011 22000180	17	.	.	.	.	70.0 (21.0)	.	.	.		.		
	Ramirez 2012 22551574	8	.	.	.	.	63.6 (32.2)	.	.	.		.		
	Giordano 2014 24318411	132	.	.	51.2 (38.4)	.	62.6 (41.8)	.	.	64.5 (18.4)		.		
	Huang 2015 25859266	44	.	.	.	.	65.1 (NR)[a]	.	.	.		.		
	Huang 2015 25859266	12	.	.	.	.	49.5 (NR)[b]	.	.	.		.		

Outcome	Author Year PMID	N	0 mo	3 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	3 y	3.5 y	4 y	Last follow-up
	Huang 2015 25859266	27	.	.	.	.	69.8 (NR)[c]	.	.	.		.		
	Huang 2015 25859266	39	.	.	.	.	63.5 (NR)[d]	.	.	.		.		
	Moon 2016 26220238	210	.	.	57.4 (NR)	.	64.8 (NR)	.	69.4 (NR)	67.5 (NR)		.		
	Boules 2015 26243345	61	.	.	.	.	59.7 (42.3)	.	.	.		.		
	Lee 2016 27220823	84	.	.	34.2 (9.4)	.	41.4 (11.6)	.	.	.		.		
	Praveenraj 2016 27279392	32	.	.	.	.	82.8 (34.3)	.	.	.		.		
	Zaveri 2016 27795883	14	.	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	23	.	.	.	.	65 (NR)	.	.	.		.		
	Ochner 2013 23700235	1031	.	.	.	.	69.0 (NR)[h]	.	.	71.0 (NR)[h]		.		
	Soto 2013 23733390	92	.	.	.	.	.	.	68.2 (NR)	.		.		
	Ghio 2017 28259559	24												61.1 (27.6)
	Mackay 2016 27778462	108					79 (NR)							
percent WL	Serrot 2011 22000180	17	.	.	.	.	25.0 (6.0)	.	.	.		.		

Outcome	Author Year PMID	N	0 mo	3 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	3 y	3.5 y	4 y	Last follow-up
	Moon 2016 26220238	210	.	.	27.4 (NR)	.	31.8 (NR)	.	34.0 (NR)	33.9 (NR)		.		
	Lee 2016 27220823	84	.	.	26.0 (7.2)	.	31.5 (8.5)	.	.	.		.		
	Praveenraj 2016 27279392	32	.	.	.	.	28.0 (7.2)	.	.	.		.		
	Mackay 2016 27778462	108					33 (NR)							
	Pajecki 2015	30[k]												68 (NR)
	Pajecki 2015	16[l]												72 (NR)
	Van Nieuwenhove 2016 27426660	56							30.6 (11.5)				26.7 (15.2)	
BMI (kg/m^2)	Ramirez 2012 22551574	8	44 (NR)[e]	.	.	.	34.0 (9.1)	.	.	.		.		
BMI loss (kg/m^2)	Sosa 2004 15603658	23	.	.	.	.	16.5 (NR)	.	.	.		.		
	Lee 2016 27220823	84	.	.	11.1 (4.0)	.	13.4 (14.1)	.	.	.		.		
	Wiklund 2015	70	.	.	.	.	.	.	13.5 (5.5)[f]	.		.		
	Wagner 2007 17938305	38	.	.	.	.	.	.	.	.		21.8 (14.5)[f,g]		
	Valderas 2009 19517199	26	.	.	.	.	.	.	.	.		14.1 (4.9)[f]		
	O'Keefe 2010 20532834	157	.	.	12.4 (6.5)[f]	.	15.8 (6.3)[f]	.	.	.		.		

Outcome	Author Year PMID	N	0 mo	3 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	3 y	3.5 y	4 y	Last follow-up
	Serrot 2011 22000180	17	.	.	.	.	8.8 (2.2)[f]	.	.	.		.		
	Giordano 2014 24318411	132	.	.	7 (8.5)[f]	.	12.9 (7.8)[f]	.	.	31.9(8.4)[f]		.		
	Trieu 2007 17400516	93		10.1 (NR)	.	9.5 (NR)	.	.	17.6 (NR)	.		.		
	Huang 2015 25859266	44	.	.	.	.	11.7 (6.5)[f]	.	.	.		.		
	Davis 2016 27681880				40 (9)									
Weight (kg)	Ramirez 2012 22551574	8	124.5 (NR)[e]	.	.	.	93.8 (14.7)	.	.	.		.		
	Davis 2016 27681880	NR			111 (31)									
Weight loss (kg)	Sosa 2004 15603658	23	.	.	.	.	43.2 (NR)	.	.	.		.		
	Giordano 2014 24318411	132	.	.	28.2 (22.1)	.	40.8 (22.1)	.	.	41.5 (17.5)		.		
	Lee 2016 27220823	84	.	.	34.0 (12.9)	.	40.7 (14.5)	.	.	.		.		
	Wiklund 2015	70	.	.	.	.	.	.	40.6 (22.1)[f]	.		.		
	O'Keefe 2010 20532834	157	.	.	34.8 (20.4)[f]	.	43.6 (20.4)[f]	.	.	.		.		
	Serrot 2011 22000180	17	.	.	.	.	57 (22.8)[f]	.	.	.		.		

Outcome	Author Year PMID	N	0 mo	3 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	3 y	3.5 y	4 y	Last follow-up
	Huang 2015 25859266	44	.	.	.	.	29.9 (15.7)[f]	.	.	.		.		
	Mackay 2016 27778462	108					40 (NR)							
	Trieu 2007 17400516	93		27.3 (NR)	.	31.6 (NR)	.	.	49.0 (NR)	.		.		

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. Baseline weight and BMI were not reported separately by procedure at baseline. Therefore, we did not compute the difference in weight between baseline and different time points after surgery.

[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.

[i] SD computed from 95% confidence interval

[j] Values correspond to median

[k] Age group: 60-65 years

[l] Age group: above 65 years

Single Anastomosis Duodenal Switch

Zaveri et al. found that the percent EBMIL at 3, 6, 9, 12, 15, and 18 months after SADS was 49.1 (95% confidence interval [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).[105]

Sleeve gastrectomy

Table 7 shows the changes over time in different weight outcomes by study. Changes in weight outcomes at 1 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 EBMIL ranged between 60 and 64.6 percent at 1 year. The mean percent EWL at 1 year ranged from 26 to 74.3 percent, and the percent WL from 5.5 to 26.5 percent. Finally, Lee et al. reported a mean BMI reduction at 1 year of 7.9 kg/m^2 and a mean weight reduction of 24.4 kg.[38] Because the standard deviation of weight change was not consistently reported across studies, we concluded that a meta-analysis of the subset of studies reporting relevant data would not be informative.

O'Keefe et al. reported the average percent EWL among patients undergoing RYGB, LAGB or VSG.[98] This study is described under “Multiple bariatric surgery procedures”.

In addition to mean percent EWL (Table 7), Moon et al. 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 LSG patients (20.5 percent) failed to achieve weight loss.[100]

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.[32]

Ritz et al. graphically present the percent WL at 3, 6, 9 and 12 months after SG, which consistently increased at each time point of follow-up.[39]

Imam et al. graphically present the trajectory of absolute weight loss (in lbs.) for patients undergoing SG at 3 months, 1 year, 2 years, and 3 years after surgery. Weight loss peaked at 102. months and was sustained up to 3 years after surgery.[62]

Macano et al. graphically present changes in BMI over time after LSG. Patients had a median BMI of 49.44 kg/m^2 (range, 38-59.3) before surgery. BMI remained practically unchanged up to 6 weeks after surgery but was then sequentially lower at 6 months and 1 year after surgery, while the 1 year mean BMI value was sustained up to 2 years.[94]

Casillas et al.[47] report changes in weight outcomes at 1, 2, 3, and 4 years after SG. Results are shown in Figure 6.

Table 7. 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	N	Prior to surgery	3 mo	6 mo	12 mo	18 mo	2 y	3 y	4 y	After surgery	Last follow-up
percent EBMIL	Moon 2016 26220238	73	.	.	55.1 (NR)	64.6 (NR)	67.5 (NR)	68.9 (NR)			.	.
	Lemaitre 2016 27063637	384	.	.	.	60.0 (19.2)	.	64.6 (22.0)			.	.
percent EWL	Ramirez 2012 22551574	12	.	.	.	39.4 (15.4)	.	.			.	.
	van Rutte 2013 23344504	73	.	.	52.8 (16.1)[a]	.	.	.			.	55.2 (17.8)[a]
	van Rutte 2013 23344504	50	.	.	49.9 (12.2)[b]	.	.	.			.	52.2 (14.4)[b]
	van Rutte 2013 23344504	12	.	.	52.4 (10.7)[c]	.	.	.			.	59.9 (14.9)[c]
	Soto 2013 23733390	35	.	.	.	.	.	43			.	.
	Nagao 2014 24519024	61	.	.	48.0 (15.5)	54.6 (15.3)	.	54.4 (15.4)			.	.
	Huang 2015 25859266	24	.	.	.	68.5 (NR)[g]	.	.			.	.
	Huang 2015 25859266	12	.	.	.	68.1 (NR)[h]	.	.			.	.
	Huang 2015 25859266	8	.	.	.	65.0 (NR)[i]	.	.			.	.
	Huang 2015 25859266	4	.	.	.	74.3 (NR)[j]	.	.			.	.
	Moon 2016 26220238	73	.	.	48.8 (NR)	56.6 (NR)	59.8 (NR)	60.8 (NR)			.	.
	Boules 2015 26243345	22	.	.	.	51.8 (39.8)	.	.			.	.
	Lemaitre 2016 27063637	384	.	.	.	64.8 (24.6)	.	67.4 (24.0)			.	.
	Lee 2016 27220823	48	.	.	24.6 (18.2)	26.7 (27.6)	.	.			.	.
	Praveenraj 2016 27279392	54	.	.	.	60.2 (17.5)	.	.			.	.

Outcome	Author Year PMID	N	Prior to surgery	3 mo	6 mo	12 mo	18 mo	2 y	3 y	4 y	After surgery	Last follow-up
	Luppi 2015 25088486	28	.	.	.	49 (NR)	.	45 (NR)			.	.
	Bergeat 2017 28035521	40										65.0 (20.2)
	Ghio 2017 28259559	50										60.2 (24.1)
	Navarrete 2017 28214166	103		34.3 (NR)	57.5 (NR)	73.5 (NR)		60.9 (NR)	55.7 (NR)			
percent WL	van Rutte 2013 23344504	73	.	.	24.5 (6.5)[a]	.	.	.			.	25.6 (7.6)[a]
	van Rutte 2013 23344504	50	.	.	23.3 (6.1)[b]	.	.	.			.	23.4 (9.2)[b]
	van Rutte 2013 23344504	12	.	.	23.1 (4.3)[c]	.	.	.			.	26.5 (6.9)[c]
	Moon 2016 26220238	73	.	.	22.1 (NR)	26.5 (NR)	27.3 (NR)	28.0 (NR)			.	.
	Lee 2016 27220823	48	.	.	18.5 (13.7)	20.2 (21.5)	.	.			.	.
	Praveenraj 2016 27279392	54	.	.	.	25.0 (5.4)	.	.			.	.
	Navarrete 2017 28214166	103		15.1 (NR)	25.2 (NR)	32.4 (NR)		26.7 (NR)	24.9 (NR)			
BMI (kg/m^2)	O'Keefe 2010 20532834	6	50.0 (12.0)	.	42.0 (8.1)	42.0 (8.4)	.	.			.	.
	Leonetti 2012 22508671	30	41.3 (6.0)	35.1 (3.8)	31.6 (3.9)	29.4 (4.9)	28.3 (5.4)	.			.	.
	Ramirez 2012 22551574	12	44 (NR)[k]	.	.	36.1 (4.3)	.	.			.	.
	van Rutte 2013 23344504	73	45.1 (6.9)[a]	.	34.5 (5.7)[a]	.	.	.			.	33.6 (6.2)[a]
	van Rutte 2013 23344504	50	45.4 (5.8)[b]	.	34.5 (3.9)[b]	.	.	.			.	35.0 (5.2)[b]
	van Rutte 2013 23344504	12	46.2 (8.9)[c]	.	34.2 (5.9)[c]	.	.	.			.	34.2 (5.0)[c]

Outcome	Author Year PMID	N	Prior to surgery	3 mo	6 mo	12 mo	18 mo	2 y	3 y	4 y	After surgery	Last follow-up
	Mizrahi 2014 24442420	52	42.6 (0.7)	.	.	.	.	31.8 (0.5)			.	.
	Nagao 2014 24519024	61	46.4 (6.0)	.	36.1 (6.4)	34.3 (6.0)	.	34.8 (6.0)			.	.
	Luppi 2015 25088486	28	43.3 (NR)	.	.	32.8 (NR)	.	33.2 (NR)			.	.
	Freeman 2015 25708829	52	43.0 (5.4)	.	.	.	.	.			36.3 (5.3)	.
	Huang 2015 25859266	24	37.6 (5.2)	.	.	28.2 (4.9)	.	.			.	.
	Lemaitre 2016 27063637	384	46.2 (6.4)	.	.	31.5 (5.8)	.	31.3 (6.4)			.	.
	Praveenraj 2016 27279392	54	43.8 (9.7)	.	.	.	.	.			.	.
	Macano 2017	16	49.55 (NR)[n]									
	Navarrete 2017 28214166	103	45.8 (22.8)	38.7 (NR)	34.1 (NR)	30.7 (NR)		33.3 (NR)	34.6 (NR)			
BMI loss (kg/m^2)	Lee 2016 27220823	48	.	.	7.8 (6.1)	7.9 (7.3)	.	.			.	.
Weight (kg)	Ramirez 2012 22551574	12	124.5 (NR)[k]	.	.	111.4 (18.1)	.	.			.	.
Weight loss (kg)	Lee 2016 27220823	48	.	.	23.5 (17.9)	24.4 (22.1)	.	.			.	.
	O'Keefe 2010 20532834	6	.	.	25.2 (21.3)[l]	26.7 (23.2)[l]	.	.			.	.
	Luppi 2015 25088486	28		.	.	27.9 (NR)	.	25.3 (NR)			.	.
	van Rutte 2013 23344504[a]	73		.	30.6 (19.8)[l]	.	.	.			.	31.9 (21.0)[l]
	van Rutte 2013 23344504[b]	50		.	29.3 (16.9)[l]	.	.	.			.	29.8 (16.9)[l]
	van Rutte 2013 23344504[c]	12		.	36.2 (26.7)[l]	.	.	.			.	34.3 (26.4)[l]
	Mizrahi 2014 24442420	52		.	.	.	.	30.1 (2.5)[l]			.	.

Outcome	Author Year PMID	N	Prior to surgery	3 mo	6 mo	12 mo	18 mo	2 y	3 y	4 y	After surgery	Last follow-up
	Freeman 2015 25708829	52		.	.	.	.	.			19.9 (21.4)[l]	.
	Huang 2015 25859266	24		.	.	25.1 (18.8)[l]	.	.			.	.

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

[m] SD computed from 95% confidence interval

[n] Values correspond to median.

Strength of the Evidence

Grades for strength of evidence for weight loss outcomes based on the three comparative studies are summarized in Table 8. 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 nonsurgical treatments, or to no treatment. Although enough nonrandomized studies report data on more than one procedure, only four studies were designed and/or analyzed adequately to compare treatment groups amongst each other. Even among these four studies, it is likely that unmeasured confounding may be substantial. Based on the available body of evidence and given these limitations, there is moderate SoE that RYGB results in greater improvements in weight loss outcomes compared to SG up to four years after surgery. SoE is low for other comparisons. In addition, many studies did not have a control group (uncontrolled before-after surgery studies) but reported changes in outcomes before versus 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 8. 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 nonrandomized study addresses this question (N=162). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
RYGB results in greater improvements in weight outcomes compared to SG at 1, 2, 3, and 4 years after surgery (1) Mean BMI loss (2) Mean percent weight loss (3) Mean percent excess weight loss	Low for (1), (2), (3)	[Not rated]	Moderate for (1), (2), (3),	High for (1), (2), (3)	Moderate SoE for (1), (2), (4)	- Only 1 nonrandomized study compares weight changes for all three outcomes at 1, 2, 3, and 4 years (N=429). - Follow-up rates for this study were high (100% at year 1, 95% at year 2, 91% at year 3, and 75% at year 4). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
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 nonrandomized study compares weight changes for all four outcomes at 6 months (N=162). - Only 1 nonrandomized study compares weight changes for (1), (2), and (4) at 12 months (N=162). - Only two nonrandomized studies (N=316) compare weight changes at 12 months for (3). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
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 nonrandomized study compares weight changes for all four outcomes at 6 months (N=162). - Only 1 nonrandomized study compares weight changes for (1), (2), and (4) at 12 months (N=162). - Only two nonrandomized studies (N=316) compare weight changes at 12 months for (3). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
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). *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*

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 9. A third study examined the predictive value of preoperative comorbidities related to obesity rather than conducting subgroup analyses.[36]

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 nondiabetic patients, and therefore heterogeneity of treatment effect cannot be explored formally. 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.[106]

Freeman et al. found that, compared to diabetic patients, nondiabetics 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 kg/m^2 was significantly shorter among patients with baseline BMI of 40 kg/m^2 or less compared to those with BMI > 40 kg/m^2 at baseline (P=0.02).[107]

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.[108]

The study by Soto et al. was the only one to examine treatment effect heterogeneity according to bariatric surgical procedure characteristics, specifically, 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.[109]

Finally, Wagner et al. found no association between comorbidities and return to work after RYGB. No relevant data were reported.[36]

Table 9. 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
				Bougie size 46	62	
				Bougie size 38	56	
	48 mo	Soto	LSG	Bougie size 52	27	NR
				Bougie size 46	82	
				Bougie size 38	NA	
	6 mo	Freeman	LSG	Males	30.0 (5.3)	0.60
				Females	32.9 (21.1)	
				Caucasian	30.7 (20.5)	0.74
				African American	32.6 (14.5)	
				Diabetes	26.6 (16.8)	0.04[a]
				No diabetes	36.5 (18.6)	
				BMI > 40	32.2 (16.2)	0.65
				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)	
percent WL	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 gastroplasty; 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 81 different models (Appendix G, Table 10, and Table 11) were reported in the eligible studies (some studies reported more than one model). Outcome definitions were rarely consistent across models. There was no global agreement in regard to the definition of "minimal weight loss" and no model explicitly used this outcome definition. Table 12 shows in detail the 26 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 6 months after surgery [110], 1 year after surgery[44, 111, 112], or 2 years after surgery.[113-115] Ortega et al. defined surgical success as percent EWL of 60 percent or more at 1 year. Alarcón del Agua[116] used two models to predict successful weight loss as percent EWL more than 30 and one model to predict failed weight loss defined as percent EWL less than 20 at one year. Fried defined suboptimal weight loss as residual BMI more than 35.9 at 6 months,[117] while Dolezalova-Kormanova [118] defined optimal weight loss as residual BMI less than 35 or 40 among patients with superobesity. Yanos et al. developed a model to predict regaining of at least 20 percent initial weight loss versus less than 20 percent initial weight loss,[119] while Sharaiha[120] developed a model to predict percent WL more than 15, and Lopez-Nava,[121] for percent WL at least 10 at 24 months. Two models (Manning et al.) predicted maximal percent WL (percent WL of 20% or more),[122] and one model (Yanos et al.) predicted nadir weight loss as the percentage of total weight lost at the patient's lowest self-reported postoperative weight (percent WL).[119] Arterburn et al. developed three models, each predicting more than 25 percent, more than 30 percent or more than 35 percent weight loss at 1 year after any bariatric surgery. da Silva[123] and Shantavasinkul[124] studied percent postoperative weight regain more than 10 and more than 15 at one year respectively. 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.[125]

In each of two studies, a single set of predictors was used to predict multiple outcomes after the same bariatric surgical procedure[125] or a single outcome but after different bariatric surgical procedures.[126] 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.[42] 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.[122, 127] 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.[113-115] Manning et al.,

Martin et al., Obeidat et al., Yanos et al. , da Silva et al. [123], Alfonsson et al. [128], Shantavasinkul et al. [124] Sockalingam et al.[129], Mitchell et al. [130], Wood et al.[131], and Al-Khyatt et al.[132] each report different sets of predictors for different outcomes among patients receiving the same bariatric surgical procedure.[119, 122, 133, 134] 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 81 models were internally or externally validated after their initial derivation.[135] Alarcón del Agua[116] used two models to predict percent EWL more than 30 at 12 months by adding to the second model the cognitive-restraint eating behavior measured by the three-factor eating questionnaire. Alfonsson et al. [128] used the same model to predict both BMI loss at 12 months and percent BMI loss at 12 months. Mitchell et al [130] reported three separate models for both Roux-en-Y gastric bypass and laparoscopic adjustable gastric banding (LAGB), stratified in three different behavioral patterns each. Paone et al.[136] used different models to predict percent EWL at 3 and 12 months. Steinbeisser et al.[137] also used different models to predict EBWL and change in BMI postoperatively. Freese et al.[138] evaluated the addition of type of surgery to a model predicting percent EBMIL at 12 months. Slotman et al.[139] used the same set of variables to predict weight/weight loss at five different time points. Mack et al.[140] predicted follow-up BMI and percent EWL overall and stratified by sex, using different sets of predictors for each model.

Twenty models (models 7, 26, 28, 29, 31, 32, 43, 60, 61, 62, 64, 65, 69, 75, 76, 77, 78, 79, 80, 81) predicted weight outcomes after SG; eight models (models 6, 9, 10, 12, 16, 17, 21, 22) after AGB; one model (model 37) after BPD; 20 models (models 2, 3, 4, 5, 11, 13, 27, 30, 39, 40, 47, 48, 49, 50, 53, 54, 55, 56, 63, 68) after RYBG; three models (models 41, 51, 52) after endoscopic sleeve gastroplasty; three models (models 44, 45, 46) after gastric electrical stimulation; three models (models 57, 58, 59) after LAGB; one model (model 15) after plication; one (model 42) after laparoscopic greater curvature plication; and one after VBG. The remaining 20 models (models 1, 8, 14, 18, 19, 20, 23, 24, 25, 33, 34, 35, 36, 66, 67, 70, 71, 72, 73, 74) 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. prespecified 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 59 studies for which model performance was reported, performance was assessed through the coefficient of determination (R^2) alone, both R^2 and adjusted R^2 in 35 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 two models; simple correlation coefficient was reported for one model. The performance of the remaining 8 models was assessed using other metrics such as predictive accuracy, or classification rate (Table 11).

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.[134] The AUC ranged from 0.58 for 3-year weight change to 0.85 for percent EWL more than 50 percent

(good outcome/successful weight loss) [model 1].[127] 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 percent[42] to 99.7 percent.[43]

Two models 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.[141] Cottam et al. used a model of percent EWL at 1 month and at 3 months with sensitivity 71 percent, specificity 91 percent, positive predictive value 72 percent and negative predictive value 91 percent.[44]

Table 10. Characteristics of the populations used in prediction models of weight loss.

First Author PMID	Sample size	Men (N, %)	Age			Bariatric Intervention
			Mean/Median	SD	Range	
Aguëra 2015 26377595	139	31 (22.3%)	40.6	10.3	18-62	Gastric bypass; Duodenal switch; Vertical sleeve; Laparoscopic gastric plication
Arterburn 2013 24304479	370	274 (74)	51.6	NR	NR	Gastric bypass surgery
Benoit 2014 24570089	40,352	8713 (21.6)	45.8	11.28	NR	Roux-en-Y gastric bypass
Brandao 2015 26122195	150	137 (91.3)	NR	NR	21-64	Roux-en-Y gastric bypass, Laparoscopic adjustable gastric banding
Brown 2013 23636997	127	25 (19.80)	43.6	12.4	15-71.4	Laparoscopic adjustable gastric banding
Courcoulas 2015 25824474	1738	NR	46	NR	NR	Roux-en-Y gastric bypass
Dallal 2009 19277799	1168	218 (18.7)	45.2	12	NR	Gastric bypass
de Raaff 2016 26220241	816	162 (19.9)	44.4	10.6	NR	Laparoscopic Roux-en-Y gastric bypass; Laparoscopic sleeve gastrectomy
Fried 2012 22648797	105	17 (31.5)	47.5	10.3	NR	Laparoscopic greater curvature plication
Galtier 2006 16477271	73	0 (-)	39.1	10.4	18.4-64.8	Laparoscopic adjustable gastric banding
Gouillat 2012 21870049	262	29 (11)	36.4	9.7	18.0-61.0	Laparoscopic adjustable gastric banding
Gras-Miralles 2014 24927691	14	0	44	IQR 41-55	NR	Laparoscopic Roux-en-Y gastric bypass; Laparoscopic sleeve gastrectomy
Lee 2007 18074500	249	72 (28.9)	33	9	NR	Laparoscopic mini-gastric bypass and laparoscopic adjustable gastric banding
Lee 2009	74	22 (29.7)	31.7	9.1	NR	Laparoscopic adjustable gastric banding
Lee 2009 20214230	251	68 (27.1)	33	NR	NR	Laparoscopic mini-gastric bypass and laparoscopic adjustable gastric banding
Manning 2015 25239175	538	145 (27)	46.5	11.1	NR	Sleeve gastrectomy
Martin 2015 25929176	292	87 (29.8)	41.5	11.1	NR	Laparoscopic sleeve gastrectomy
Melton 2008 18071836	495	91 (18)	42	NR	19-66	Roux-en-Y gastric bypass
Obeidat 2016 26428251	146		34	10.8	NR	Sleeve gastrectomy
Ortega 2012 22234587	407	98 (24)	44	NR	18-65	Roux-en-Y gastric bypass; Sleeve gastrectomy
Robinson 2014 24913590	274	11 (4)	51.14	8.39	NR	Gastric bypass; Lap band; Gastric sleeve; Other
Valera-Mora 2005 15941878	107	22 (20.6)	37	10	NR	Biliopancreatic diversion (BPD)
van Hout 2009 18317854	112	14 (12.5)	38.8	8.3	NR	Vertical band gastroplasty
Yanos 2015 25519772	97		56.11	11.26	NR	Roux-en-Y gastric bypass

First Author PMID	Sample size	Men (N, %)	Age			Bariatric Intervention
Sharaiha 2017 28017845	91	29 (31.9)	43.66	11.26	19–66	Endoscopic Sleeve Gastroplasty
Dolezalova-Kormanova 2017 28560523	212	39 (18.4)	45.8	10.9	44.3, 47.3	Laparoscopic Greater Curvature Plication
Cottam 2017 28545916	613	129	47.2	11.5	NR	sleeve gastrectomy
Alarcón del Agua 2017 28013450	97	25	39	10.8	19-59	closed loop Gastric electrical stimulation
da Silva 2016 27544005	80	9 (11.2)	46	16	NR	Roux-en-Y gastric bypass
Alfonsson 2017 28229317	158	57 (36)	47.5	9.02	NR	Roux-en-Y gastric bypass
Shantavasinkul 2016 27989521	1,426	0.158	45.1	10.7	18–76	Roux-en-Y gastric bypass
Lopez-Nava 2017 28451929	248	27	44.5	10	NR	Endoscopic Sleeve Gastroplasty
Sockalingam 2017 28807141	156	30 (19)	45.23	9.3	NR	Roux-en-Y gastric bypass
Mitchell 2016 27096225	2,022	445 (22)	47	IQR 38-55	NR	Roux-en-Y gastric bypass; laparoscopic adjustable gastric banding (LAGB)
Susmallian 2017	300	100	41.65	11.05	18-64	laparoscopic sleeve gastrectomy
Paone 2017 28353096	75	15	40.8	6.12	22–60	laparoscopic sleeve gastrectomy
Wood 2016 27532274	726	123 (16.9)	45.2	10.7	18-72	Roux-en-Y gastric bypass
Steinbeisser 2017 28050788	204	54 (26)	45.1	10.8		laparoscopic sleeve gastrectomy
Freese 2017 28660099	63	0	46	IQR 34-53	NR	Roux-en-Y gastric bypass or sleeve gastrectomy or laparoscopic gastric banding
Al-Khyatt 2016 27943095	227	0.25	48.6	11	NR	Roux-en-Y gastric bypass
Dilektasli 2017 27401183	100	0.19	37	IQR 27–43	NR	laparoscopic sleeve gastrectomy
Slotman 2017 28583814	166,601		NR	NR	NR	RYGB or LRYGB or LAGB or SG or BPD/DS
Mack 2016 27178406	75	27	45.2	11.6	NR	laparoscopic sleeve gastrectomy

Table 11. Summary of 83 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; Negelkerke'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
14	de Raaff	2016	Multivariable logistic regression analysis with backward selection	Nagelkerke R^2; Hosmer and Lemeshow; AUC	Nagelkerke R^2=0.208 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
19	Lee	2007	Logistic regression	Classification rate	0.887
20			Articficial Neural Network Model	Classification rate	0.94
21	Lee	2009	Multivariate logistic regression	NR	NR
22			Articficial Neural Network Model	NR	NR

Model Number	Author	Year	Modeling method	Metric of Model Performance	Model Performance
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
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
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
41	Sharaiha	2017	Multivariate logistic regression	NR	NA
42	Dolezalova-Kormanova	2017	2-step cluster analysis	Sensitivity	0.9102 sensitivity = 0.71 specificity = 0.91 PVP = 0.72
43	Cottam	2017	Multivariate logistic regression	Sensitivity, specificity, PVP, PVN	PVN = 0.91

Model Number	Author	Year	Modeling method	Metric of Model Performance	Model Performance
44	Alarcón del Agua	2017	best subset analysis to choose the variables for the multiple logistic regression model resulting in the highest percent of correctly predicted success and failure outcomes	Deviance, R^2 adjusted	7.94%
45	Alarcón del Agua	2017	best subset analysis to choose the variables for the multiple logistic regression model resulting in the highest percent of correctly predicted success and failure outcomes	Deviance, R^2 adjusted	9.41%
46	Alarcón del Agua	2017	best subset analysis to choose the variables for the multiple logistic regression model resulting in the highest percent of correctly predicted success and failure outcomes	Deviance, R^2 adjusted	9.83%
47	da Silva	2016	multiple logistic regression model including independent variables associated with weight regain in bivariate analysis ($P < 0.1$)	NR	NA
48	Alfonsson	2017	multiple linear regression analyses using a backward deletion process	Coefficient of determination (R^2)	0.55
49	Alfonsson	2017	multiple linear regression analyses using a backward deletion process	Coefficient of determination (R^2)	0.23
50	Shantavasinkul	2016	Multivariate logistic regression	Coefficient of determination (R^2)	0.283
51	Lopez-Nava	2017	Multivariate linear regression	NR	NA
52	Lopez-Nava	2017	Multivariate logistic regression	NR	NA
53	Sockalingam	2017	multivariate regression analysis model using all clinically relevant demographic and significant psychosocial variables ($p < 0.10$ in bivariate analysis)	NR	NA
54	Mitchell	2016	Multivariate linear regression	NR	NA
55	Mitchell	2016	Multivariate linear regression	NR	NA
56	Mitchell	2016	Multivariate linear regression	NR	NA
57	Mitchell	2016	Multivariate linear regression	NR	NA
58	Mitchell	2016	Multivariate linear regression	NR	NA
59	Mitchell	2016	Multivariate linear regression	NR	NA
60	Susmallian	2017	stepwise regression model	NR	NA
61	Paone, 2017	2017	Multivariate linear regression with variables that were significantly correlated with %EWL at 12 months	Adjusted R^2	0.08
62	Paone, 2017	2017	Multivariate linear regression with variables that were significantly correlated with %EWL at 3 months	Adjusted R^2	0.05
63	Wood	2016	Forward stepwise linear regression with variables that were significant in a univariate analysis (age, sex, and BMI were included in the model regardless of significance level)	NR	NA
64	Steinbeisser	2017	Manual backward stepwise linear regression	NR	NA
65	Steinbeisser	2017	Manual backward stepwise linear regression	NR	NA
66	Freese	2017	Multivariate linear regression	NR	NA

Model Number	Author	Year	Modeling method	Metric of Model Performance	Model Performance
67	Freese	2017	Multivariate linear regression	NR	NA
68	Al-Khyatt	2016	Stepwise regression model	r	0.23
69	Al-Khyatt	2016	Stepwise regression model	r	0.3
70	Al-Khyatt	2016	Stepwise regression model	r	0.37
71	Al-Khyatt	2016	Stepwise regression model	r	0.41
72	Al-Khyatt	2016	Stepwise regression model	r	0.44
73	Dilektasli	2017	Multivariate logistic regression	NR	NA
74	Slotman	2017	Forward stepwise logistic regression model	Coefficient of determination (R^2)	0.91
75	Slotman	2017	Forward stepwise logistic regression model	Coefficient of determination (R^2)	0.813
76	Slotman	2017	Forward stepwise logistic regression model	Coefficient of determination (R^2)	0.725
77	Slotman	2017	Forward stepwise logistic regression model	Coefficient of determination (R^2)	0.638
78	Slotman	2017	Forward stepwise logistic regression model	Coefficient of determination (R^2)	0.613
79	Mack	2016	Stepwise linear regression model	Coefficient of determination (R^2)	0.28
80	Mack	2016	Stepwise linear regression model	Coefficient of determination (R^2); Adjusted R^2	R^2=0.48; Adjusted R^2=0.435
81	Mack	2016	Stepwise linear regression model	Coefficient of determination (R^2)	0.246
82	Mack	2016	Stepwise linear regression model	Coefficient of determination (R^2)	0.08
83	Mack	2016	Stepwise linear regression model	Coefficient of determination (R^2)	0.302
84	Mack	2016	Stepwise linear regression model	Coefficient of determination (R^2)	0.167
85	Mack	2016	Stepwise linear regression model	Coefficient of determination (R^2)	0.375

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

Table 12. Models predictive of successful or failed weight loss after bariatric surgery.

	Arterburn, 2013	Arterburn, 2013	Arterburn, 2013	Agüera, 2015	de Raaff, 2016	Fried, 2012	Lee, 2007 (M1)	Lee, 2007 (M2)	Lee, 2009a (M1)	Lee, 2009a (M2)	Lee, 2009b (M1)	Lee, 2009b (M2)	Lee, 2009b (M3)	Ortega, 2012	Yanos, 2015	Yanos, 2015	Sharaiha, 2017	Dolezalova-Kormanova, 2017	Cottam, 2017	Alarcón del Agua, 2017 (M1)	Alarcón del Agua, 2017 (M2)	Alarcón del Agua, 2017	da Silva, 2016	Shantavasinkul, 2016	Lopez-Nava, 2017	Dilektasli, 2016
	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	percent WL **≥15**	residual BMI <35 or <40 if surgeries	**percent WL ≥55**	precent EWL > 30	precent EWL > 30	precent EWL < 20	percent postoperative weight regain>10	percent postoperative weight regain>15	percent TBWL at 24 months >=10	percent EWL>=percent 50 at 6 months
Age	2.18	3.92	1.57	0.88	1.035									1.40[a]			0.85[b]		NR[a]	3.59[bc]	4.15[bc]	0.28[ac]		0.97[b]		0.956[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	1.41	0.79	0.69																							
ASA class 4	1.28	0.54	0.39																							
Bariatric center																			NR[a]							
BMI					1.148	1.90								1.90[a]			1.1[a]		NR[a]	0.44[a]	0.44[a]					
Body fat																		0.8[b]								
Carbohydrates																							1.03[a]			

	Arterburn, 2013	Arterburn, 2013	Arterburn, 2013	Agüera, 2015	de Raaff, 2016	Fried, 2012	Lee, 2007 (M1)	Lee, 2007 (M2)	Lee, 2009a (M1)	Lee, 2009a (M2)	Lee, 2009b (M1)	Lee, 2009b (M2)	Lee, 2009b (M3)	Ortega, 2012	Yanos, 2015	Yanos, 2015	Sharaiha, 2017	Dolezalova-Kormanova, 2017	Cottam, 2017	Alarcón del Agua, 2017 (M1)	Alarcón del Agua, 2017 (M2)	Alarcón del Agua, 2017	da Silva, 2016	Shantavasinkul, 2016	Lopez-Nava, 2017	Dilektasli, 2016
Case number>35																	18.6[b]									
Childhood obesity																										0.39[b]
Depression				0.23												NR[b]										
Diabetes					1.921														NR[a]							
DCG score																										
Score = 1-2	1.22	1.20	0.74																							
Score = 2+	1.85	1.52	1.98																							
Education status																										
High school																										2.273[a]
University and higher																										3.772[b]
Gastroesophageal reflux disease																			NR[a]							
Gender										NR[a]									NR[a]							
Male														1.60[b]												
Female	2.03	2.48	2.04		1.645												0.47[a]									
HbA1c								NR[a]			NR[b]	NR[b]		1.20[b]												
HEI																							0.95[b]			
Hypertension																			NR[a]							
Insulin										NR[a]	NR[b]															
Lipids								NR[a]						1.20[b]									1.06[a]			
Liver function											NR[b]	NR[b]	NR[b]													
Marital status																										

	Arterburn, 2013	Arterburn, 2013	Arterburn, 2013	Agüera, 2015	de Raaff, 2016	Fried, 2012	Lee, 2007 (M1)	Lee, 2007 (M2)	Lee, 2009a (M1)	Lee, 2009a (M2)	Lee, 2009b (M1)	Lee, 2009b (M2)	Lee, 2009b (M3)	Ortega, 2012	Yanos, 2015	Yanos, 2015	Sharaiha, 2017	Dolezalova-Kormanova, 2017	Cottam, 2017	Alarcón del Agua, 2017 (M1)	Alarcón del Agua, 2017 (M2)	Alarcón del Agua, 2017	da Silva, 2016	Shantavasinkul, 2016	Lopez-Nava, 2017	Dilektasli, 2016
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																							
percent WL																										
at 1 month																			NR[b]							
at 3 months																			NR[b]							
Personality traits				1.05																						
Psychological counseling attendance																							0.36[a]			
Race/ethnicity																										
Unknown/missing	4.17	2.05	1.08																							
Caucasian	2.69	2.31	2.28																							
Sleep apnea																			NR[a]							
Smoking	1.83	1.39	0.51																							
SNPs																										
rs4684846										NR[a]																
rs660339										NR[a]																
Surgery time																							1.08[b]			
Sweets avoidance																NR[b]										
TFEQ																										
TFEQ F1 cognitive-restraint																				1.16[a]	0.69[b]					

	Arterburn, 2013	Arterburn, 2013	Arterburn, 2013	Agüera, 2015	de Raaff, 2016	Fried, 2012	Lee, 2007 (M1)	Lee, 2007 (M2)	Lee, 2009a (M1)	Lee, 2009a (M2)	Lee, 2009b (M1)	Lee, 2009b (M2)	Lee, 2009b (M3)	Ortega, 2012	Yanos, 2015	Yanos, 2015	Sharaiha, 2017	Dolezalova-Kormanova, 2017	Cottam, 2017	Alarcón del Agua, 2017 (M1)	Alarcón del Agua, 2017 (M2)	Alarcón del Agua, 2017	da Silva, 2016	Shantavasinkul, 2016	Lopez-Nava, 2017	Dilektasli, 2016
TFEQ F2 disinhibition																				0.86 [b]	0.88 [a]					
Time between surgery and follow-up visit																								1.62 [b]		
Type of bariatric surgery					1.961		NR [a]	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																						
Vomiting																						4.49 [a]				
White blood cells count								NR [b]	NR [b]	NR [b]	NR [b]	NR [b]														
Waist circumference														0.7 [b]												
Weight loss																									0.18 [b]	

[a] Not statistically significant (P>0.05)
[b] Statistically significant (P<0.05)
[c] Age>50 years
OHAS: oral hypoglycemic agents; BMI: body mass index; VSG: vertical sleeve gastrectomy; SNPs: single-nucleotide polymorphisms; WL: weight loss; ASA: American Society of Anesthesiologists; DCG: diagnostic cost group; HEI: Health Eating Index adapted to the Brazilian Healthy Eating Guide; TFEQ: Three-Factor Eating Questionnaire

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.[142]

Flum et al. used Medicare fee-for-service claims data to evaluate mortality after bariatric surgery. A total of 1,225 (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).[18]

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.[143]

Lemaitre et al. evaluated weight loss after LSG performed as revisional bariatric surgery after a previously failed LAGB (n=57), intragastic 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 intragastic ballon, 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).[21]

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.[144]

Key Question 4

4.a. In Medicare-eligible patients, what is the comparative effectiveness of different bariatric interventions (contrasted between them or vs. nonbariatric 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 31 studies that compared bariatric surgical procedures to each other, to nonbariatric treatments, or to conventional or no treatment. We found no randomized trials in the Medicare-eligible population.

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 procedures[45] were used in 15 studies. These factors included demographic characteristics (age,[23, 29, 31, 32, 38, 41, 46, 48, 50, 52, 56] gender,[23, 31, 32, 38, 48, 52 40, 50] race[38, 48 41]) one or more comorbid conditions (hypertension,[23, 48 40, 41, 50] dyslipidemia,[23, 48] history of diabetes,[23, 40, 41, 48, 50] duration of diabetes,[32, 51] obstructive sleep apnea,[23, 48] tobacco abuse,[48] history of transient ischemic attack,[48] cardiovascular event history,[23, 48, 50] gallstones,[23] fatty liver disease,[23] venous stasis,[23] cellulitis,[23] deep vein thrombosis,[23] pulmonary embolisms,[23] arthritis,[23] gastro-esophageal reflux disease [GERD],[23] stress incontinence,[23] back pain,[23] disc disease,[23] Charlson comorbidity score[38, 40]); BMI;[29, 31, 32, 38, 40, 46, 52, 53] year of surgery;[23, 40, 56]] international normalized ratio;[56] type of bariatric surgery for concomitant effects of bariatric and other surgeries;[52] body weight;[38, 41] glucose levels;[38] percent EWL;[31] and cholesterol levels.[32] One study did not report on potential confounders or other prognostic factors.[49]

The potential confounders and other prognostic factors associated with the outcome of interest were accounted for though adjustment for these covariates in models based on multiple regression;[32, 41, 46, 48-51, 53, 56] through matching[29, 31, 52]; or through construction of propensity scores which were subsequently used for estimating inverse probability of treatment weights[38, 40] or for weighted propensity score analyses.[23, 41]

Below we summarize the outcomes that were reported in these 15 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 six nonrandomized comparative studies examined the effects of bariatric surgical procedures on mortality in the period after 90 days from surgery. Results are given as hazard ratios (HR) and 95% confidence intervals (CI).

In Davidson et al., RYGB resulted in lower all-cause mortality rates compared to a nonsurgical control group (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 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 regard 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).[46]

Johnson et al. compared all-cause, cardiovascular, and noncardiovascular mortality in patients receiving gastric bypass or AGB compared to patients with morbid obesity 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 noncardiovascular mortality.[48]

Scott et al. compared mortality outcomes in patients who received any bariatric surgery with two nonbariatric 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).[49]

Perry et al. report lower mortality rates at 2 years after surgery in Medicare beneficiaries 65 years and older with morbid obesity undergoing any bariatric surgery compared to nonsurgical 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 nonsurgical controls (4.5 percent versus 8.6 percent, P<0.001). They also note an increased mortality rate in the 30-day postoperative period for patients aged 65 and over (1.55 percent vs. 0.53 percent; P<0.001) and disabled patients younger than 65 (1.27 percent vs. 0.49 percent; P<0.001). However, mortality rates did not differ between the surgical and nonsurgical 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.[23]

Casillas et al. compared mortality rates for patients aged 65 years of older who underwent LRYGB (N=177) compared with those who underwent SG (N=252), matched using propensity scores. Mortality rate 90 days after surgery was 1.7 per 100 patients in the LGYGB arm but there were no deaths in the SG arm. At 1 year the respective mortality rates were 2.8 and 0.4 percent; because of the small number of events, a formal statistical comparison was not feasible.[40]

Persson et al. examined the association between any bariatric surgery and overall mortality in Sweden using Cox regression, comparing 2,605 patients between the ages of 55-74 years who

underwent bariatric surgery to 6,486 nonsurgical controls. They found that bariatric surgery is associated with a lower risk of overall death (HR 0.72; 95% CI 0.56, 0.93).[50]

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 appendix 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

Three nonrandomized comparative studies examined postoperative complications of different bariatric surgical procedures. Results are shown as odds ratios (OR) and corresponding 95% CI.

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 on overall (OR 1.0; 95% CI 0.55, 1.82) or serious (OR 1.10; 95% CI 0.51, 2.38) morbidity, including postoperative bleeding, organ-specific infection, pulmonary embolism, reoperation, surgical site infection, and septic occurrences.[51]

Boules et al. evaluated postoperative 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.[52]

Casillas et al. compared mortality rates for patients aged 65 years of older who underwent LRYGB (N=177) compared to those who underwent SG (N=252), matched using propensity scores. They report overall higher complication rates for LRYGB than SG (30.5 percent vs. 15.9 percent; P<0.0001). Minor complications were similar (i.e., significantly different at P=0.05) between the two groups; however, LRYGB was associated with higher rates of major complications requiring reintervention or reoperation than SG (5.6 percent vs. 1.6 percent); this applies to both early (P=0.015) and late (P=0.0005) major complications.[40]

The rates of postoperative complications in studies that did not account for confounders or other prognostic factors associated with the outcomes of interest are shown in Appendix H, which 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 nonrandomized 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 versus 7 percent (P=0.02) at 1 month; 28.0 versus 12.9 percent (P=0.001) at 3 months; 30.7 versus 19.3 percent (P=0.01) at 6 months; and 35.7 versus 24.4 percent (P=0.01) at 12 months.[31]

Perry et al. found no evidence of improvement of diabetes among patients receiving bariatric surgery compared to nonsurgical controls at 6 months and 1 year after surgery; however, there was an improvement at 2 years.[23]

Lee et al. examined all pairwise comparisons between RYGB, SG, and LAGB using inverse-probability treatment weighting in regard 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.[38]

Lee et al. found that RYGB resulted in larger reductions than SG in LDL- and total-cholesterol at 6 and 12 months after surgery; and in larger increases in HDL-cholesterol at 6 but not at 12 months after surgery. Similarly, LAGB resulted in larger reductions than SG in LDL- and total-cholesterol at 6 and 12 months after surgery. However, they found no evidence that the effects of RYGB, LAGB or SG triglycerides at 6 or 12 months after surgery relate to each other.[38]

Leonetti et al. compared LSG to conventional therapy, including pharmaceutical agents and lifestyle modifications (diet and physical activity), in regard 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 greater decreases in triglycerides and HDL in the LSG group compared to the conventional therapy group. Greater 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 greater changes in the levels of LDL-cholesterol or total-cholesterol compared to conventional treatment.[32]

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 postsurgical period compared to baseline/presurgical 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 regard 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 cardiovascular outcomes occurring after 90 days from bariatric surgery. Cardiovascular outcomes within 90 days were considered as surgery-related postoperative complications/adverse events and are described earlier under "Postoperative Complications" and in Appendix H.

Scott et al. compared the effect on myocardial infarction (MI) of multiple bariatric surgical procedures combined into a single treatment arm. Compared with patients undergoing orthopedic surgery (controls), patients undergoing bariatric surgery had a lower risk (HR 0.59, 95% CI 0.44, 0.79) of 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).[49]

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).[49]

Perry et al. found an improvement in coronary artery disease 6 months after surgery, which was maintained at 1 and 2 years after surgery. Lipid profile was also improved at 1 and 2 years after surgery, but there was no evidence of improvement at 6 months. The difference in outcomes between bariatric patients and nonsurgical controls increased between 6 months, 1 year, and 2 years.[23]

Lee et al. found no evidence that either systolic or diastolic blood pressure were lower at 6 months after surgery after any of RYGB, SG or LAGB compared to each other.[38] Results were similar for the effects at 1 year after surgery, except for a larger decrease in systolic blood pressure after RYGB compared to LAGB.

Leonetti et al. compared LSG versus conventional therapy, consisting of pharmaceutical agents and lifestyle modifications (diet and physical activity), in regard to the prevalence of hypertension at 18 months after treatment. They found no difference between the two treatment groups.[32]

Scott et al. also compared the effect on stroke of a treatment arm comprising multiple bariatric surgical procedures. There was evidence of a lower risk for stroke in bariatric patients (HR 0.49; 95% CI 0.24, 0.98) compared to patients undergoing orthopedic surgery (controls). Patients undergoing bariatric surgery also had a lower, though not statistically significantly so, risk of stroke (HR 0.69; 95% CI 0.40, 1.30).[49]

Persson et al. examined the association between bariatric surgery and heart failure in Sweden using Cox regression, comparing 2,605 patients between the ages of 55-74 years who underwent bariatric surgery to 6,486 nonsurgical controls. Incidence rates of heart failure were consistently lower among bariatric surgery patients: age 55-59 years (11.2, 95% 9.6, 12.9 vs. 2.3; 95% CI 1.1-3.6), 60-64 years (19.2; 95% 16.5, 21.8 vs. 7.2; 95% 3.8, 10.6), 65-69 years (30.8; 95% 26.0, 35.5 vs. 10.6; 95% 1.3, 19.9), and 70-74 years (39.9; 95% 32.5, 47.4 vs. 0). Subsequently, they also found that bariatric surgery is associated with statistically significant lower risk of heart failure hospitalization (HR=0.35; 95% CI 0.25, 0.49).[50]

Due to the heterogeneous nature of the bariatric surgical procedures and outcomes across studies, we determined 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

Only one study was identified in the Medicare-eligible population that gave results for respiratory outcomes. 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.[23]

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 that RYGB was associated with an increased prevalence of hyperparathyroidism.[29]

Martin et al. evaluated the effect of bariatric surgery on outcomes after total knee arthroplasty (TKA). They compared outcomes in TKA patients who had received 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/m^2 at the time of TKA (i.e., similar to the prebariatric surgery BMI of the study group), while the low BMI group had a mean BMI of 37.2 kg/m^2 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 reoperated (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 reoperated for any reason (HR 2.4; 95% CI 1.2 to 3.3; P = 0.02), as well as to 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 infections were different.[53]

Another study found no effect of bariatric surgery on the risk of joint dislocation after total hip arthroplasty,[54] while patients who underwent bariatric surgery before total knee arthroplasty or total hip arthroplasty had decreased operative times (71 versus 113.5 minutes; P<0.0001) and length of stay (2.9 versus 3.8 days; P=0.0002) after their orthopedic surgery compared to patients than underwent bariatric surgery after arthroplasty. However, they found no effect on postoperative complication rates.[55]

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 in the Medicare-eligible population. 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

Only one comparative nonrandomized study on renal function was found in the Medicare-eligible population.

Imam et al. compared the effects on kidney function as measured by the estimated glomerular filtration rate (eGFR) of any bariatric surgery (N=714) versus nonsurgical controls (N=714), as well as of RYGB (N=234) versus SG (N=234). Patients in both comparisons were matched based on propensity scores. Patients undergoing bariatric surgery experienced increases in eGFR when compared nonsurgical controls over a 3-year period. Differences in mean eGFR between the bariatric surgery versus the control group were 12.58 mL/min/1.73 m^2 (95% CI 10.46, 14.7) at 3 months, 13.29 mL/min/1.73 m^2 (95% CI 11.84, 14.74) at 6 months, 12.27 mL/min/1.73 m^2 (95% CI 10.87, 13.67) at 1 year, 12.66 mL/min/1.73 m^2 (95% CI 11.15, 14.17) at 2 years, and 9.84 mL/min/1.73 m^2 (95% CI 8.05, 11.62) at 3 years.

Between procedures, RYGB was associated with a greater effect on eGFR compared to SG. Differences in mean eGFR between the two procedures were 4.22 mL/min/1.73 m^2 (95% CI 0.49, 7.95) at 3 months, 4.75 mL/min/1.73 m^2 (95% CI 2.21, 7.29) at 6 months, 5.03 mL/min/1.73 m^2 (95% CI 2.53, 7.54) at 1 year, 7.52 mL/min/1.73 m^2 (95% CI 4.84, 10.2) at 2 years, and 6.6 mL/min/1.73 m^2 (95% CI 3.42, 9.78) at 3 years.[41]

Studies reporting on changes in these outcomes before versus after surgery, with no comparison to a control group, are show in Appendix H.

Compliance with Follow-Up

We did not identify any studies that compared bariatric surgeries in regard 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 regard to mental health outcomes. Changes in the prevalence and/incidence of such outcomes before versus after surgery are show 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 mental health outcomes.

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 regard 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 health-related quality of life outcomes.

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 outcomes related to cognitive functioning.

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 outcomes related to exercise participation.

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 regard 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 study, Wagner et al. performed a nonparametric comparison between 38 medically disabled, patients with morbid obesity receiving Medicaid benefits who had undergone open RYGB and 16 nonoperative controls. They found that 37 percent of the bariatric group returned to work compared to 6 percent in the control group (P=0.02).[36]

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 regard 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 regard 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.[38]

In a 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.[32]

Irwin et al. compared postsurgical differences in warfarin doses in reference to the presurgical period between bariatric patients receiving RYGB or gastric banding and a control group of patients undergoing cholecystectomy or endoscopic retrograde cholangio-pancreatography (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 presurgical period for bariatric patients, while there was no difference over time for nonbariatric patients. For each time point, the decrease in warfarin dose in bariatric patients was significantly lower than in the nonbariatric patients.[56]

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.[56]

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 did not account for confounders or other prognostic factors associated with outcomes related to readmissions or rehospitalizations.

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 nonsurgical treatments or procedures, or to no treatment at all. The evidence base consists of nonrandomized studies. Many of these studies report data on more than one bariatric surgical intervention, but only a small fraction of them allow 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 13. 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 nonbariatric surgery/conventional treatment in regard to: (1) Mortality (2) Metabolic outcomes (3) Cardiovascular outcomes (4) Musculoskeletal outcomes (5) Warfarin dose after surgery (6) Respiratory outcomes (7) Renal function outcomes	High for (2), (3), (4), (5), (6) Low for (1), (7)	[Not rated]	Low for (4), (5) Moderate for (1), (2), (3), (6), (7)	Moderate for (1), (2), (3), (4), (5), (6), (7)	Moderate SoE for (1), (2), (3), (4), (5), (6), (7)	There are no randomized studies available in the Medicare-eligible population. The evidence-base consists of nonrandomized comparative studies. Use of inappropriate control groups limits applicability/generalizability. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
RYGB results in favorable outcomes compared to SG in regard to: (1) Postoperative complications (2) Metabolic outcomes (3) Polypharmacy (4) Cardiovascular outcomes (5) Renal function outcomes	Moderate for (1), (2), (3), (4) Low for (5)	[Not rated]	Low for (1), (2), (3), (4), Moderate for (5)	High for (1), (2), (3), (4), (5)	Moderate SoE for (1), (2), (3), (4) High SoE of (5)	There are no randomized studies available in the Medicare-eligible population. The evidence-base consists of nonrandomized comparative studies. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
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 nonrandomized comparative studies. Only one study addressed this question. Technical aspects of the surgical procedures may limit the feasibility of these surgeries across surgeons. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
RYGB results in favorable outcomes compared to LAGB in regard 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 nonrandomized comparative studies.

Conclusion statement	RoB (evidence-base)	Consistency	Precision	Directness and Applicability	Overall Rating	Comments
(3) Cardiovascular outcomes						*Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*
SG results in favorable outcomes compared to LAGB in regard 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 nonrandomized comparative studies. *Studies that were deemed as **insufficient** to make causal inferences about treatment effects do not contribute to SoE assessments.*

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 non-weight-loss outcomes.[32, 46]

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 compared 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).[46]

Leonetti et al. examined whether the effects on glucose levels and Hb1Ac of LSG relative to conventional treatment 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.[32]

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/m^2 and less than 30 kg/m^2.[36]

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 was 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).[145]

Ramos-Levi et al. examined the association between weight loss and diabetes remission after RYGB, BPD or SG. They found that patients with diabetes remission experienced higher percent weight loss compared to patients without remission (35.5+/- 8.1 vs. 30.2 +/-9.5, P=0.001), as well as higher percent excess weight loss (73.6+/-18.4 vs. 66.3+/-22.8, P=0.037).[146]

KQ 5.b.

We identified no studies that estimated the proportion of the effect of bariatric surgery on nonweight 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 83 studies, describing the spectrum of bariatric procedures and outcomes that have been studied in patients who are or 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. We did not identify any randomized controlled trials comparing these procedures in the Medicare-eligible population.

In the Medicare-eligible population, we did not identify any studies in patients undergoing bariatric endoscopic procedures. However, we found multiple studies evaluating 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.[3, 147, 148] Nevertheless, certain outcomes of primary interest to the Medicare population have not been studied extensively. These include health-related quality of life, hospital readmission after surgery, admission to skilled nursing facilities, and nutritional status. The same applies to bariatric procedures where evidence is limited or nonexistent 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 practice[149]). 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-eligible population. Even among the very few comparative nonrandomized studies, the majority were deemed to have at least 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 nonweight 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.

Based on the body of evidence pertaining to direct comparisons between different bariatric procedures, RYGB results in greater improvements in weight loss outcomes compared to SG up to four years after surgery (moderate SoE). Similarly, there is moderate SoE that bariatric surgery (regardless of procedure) reduces mortality and metabolic, cardiovascular, musculoskeletal, respiratory and renal function outcomes. In regard to specific procedures, the SoE is moderate to high for RYGB being more effective than SG in reducing postoperative complications and polypharmacy, and improving metabolic and cardiovascular outcomes. Similarly, there is moderate SoE that RYGB and SG each achieves better metabolic and cardiovascular outcomes compared to LAGB.

We acknowledge that substantial comparative evidence in younger patients exists. This evidence strongly suggests that bariatric surgery overall, as well as certain specific 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 regard to surgical

complications. Our conclusions should be viewed as complementary to this evidence rather than as disputing or replacing it. Nevertheless, evidence from studies in younger populations may not be directly generalizable to the Medicare-eligible population. The main reasons 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 with younger patients being able to lose more weight than older ones.[125] Although statistical methods for the transportability of treatment effects exist, a formal generalization of evidence from younger patients to the Medicare-eligible population requires access to individual-patient data and 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 (and should) 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. This kind of evidence transportability should be grounded in reasonable assumptions that younger and older patients with obesity are exchangeable to each other. Similar concerns hold when assessing evidence applicability and transportability from young nondisabled or non-ESRD patients with obesity to patients who in addition to obesity may also have a number of disabilities or ESRD.

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 nonweight 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.[150] 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. Multiple stakeholders, including the American College of Cardiology, the American Heart Association, the Obesity Society, have highlighted, in their clinical practice guidelines for the management of overweight and obesity in adults, the importance of at least 2 years of postsurgical follow-up time for establishing the effectiveness of bariatric surgery in regard to cardiovascular and other non-weight-loss outcomes.[57]

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. Secondarily, 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. Our findings of low to moderate strength of evidence regarding the effects of bariatric surgery on non-weight-loss outcomes agree with the conclusions of the American College of Cardiology, the American Heart Association, the Obesity Society as highlighted in their clinical practice guidelines for the management of overweight and obesity in adults.[57]

A total of 83 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).[151, 152]

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.[45] 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.[73, 74] 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.[75] 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 the surgeries themselves. Moreover, nonrandomized 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.[76, 77] This is because multiple biases relevant to observational studies can be overcome when a target trial is specified to guide the design and analysis of the observational studies.[77]

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.[77]

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, the estimation of accurate treatment effects even when a comparison group exists can be particularly problematic.[153, 154] Despite its easy and clinically relevant interpretation, percent 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.[153]

Pre- vs. post-surgery studies do not have an independent control group as each subject serves as their own control. Therefore, these studies have greater statistical power (since the independent control group confers additional variation) and subject-specific time-invariant confounders are eliminated.[58] 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 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- versus post-surgery studies, it is not possible to control for time-varying confounders.[58]

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. It should be acknowledged, however, that it is unlikely for a person to achieve weight loss of the magnitude reported in the eligible studies so rapidly without an effective intervention. 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 nondiabetic bariatric patients may develop diabetes after surgery. Thus the overall diabetes prevalence after surgery will still appear lower than before surgery.

Changes in the occurrence of the outcome before versus after the treatment cannot be completely attributed to the treatment, 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.[58] 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.[155] 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.[156, 157] 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 than 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).[158] Competing events are of particular concern when treating patients age 65 years and older or patients with multiple comorbidities, because these patients are more likely to experience a competing event that decreases the likelihood of treatment benefit.[159] 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 at younger ages. 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 internal and/or external validation limits the clinical utility of the existing predictive models for weight loss, which have not passed the initial phase of model development. Model validation is important for two reasons.[160] First, model performance is usually overestimated when only the training sample is used for evaluating a model.[161] To derive more accurate model parameters, validation of the model can be performed either using a subset of the original sample or a variety of statistical techniques.[151, 161] 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 external validation can be achieved using data that have not previously been used for model development, and which come from an independent population with similar distribution of clinical characteristics as the population in 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 the lack of a 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 also limited evidence on the extent to which the effects of bariatric surgery on nonweight outcomes are mediated though 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 nonweight outcomes, and association between weight loss and nonweight outcomes) were reported.

Future Research Recommendations

Since no randomized evidence is available for the effectiveness of different bariatric procedures (surgical or endoscopic) in Medicare-eligible beneficiaries with obesity, generating such evidence is critical for identifying 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.[59] 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 bariatric procedures in the Medicare eligible patients.

Given the lack of randomized trials, evidence also 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.[60-62] As very few studies are directly applicable to the Medicare population, existing research gaps in the comparative effectiveness of different bariatric surgical procedures can be addressed by analyzing claims data from Medicare beneficiaries.[162, 163] 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.[61, 62, 163] One example is the National Surgical Quality Improvement Program (NSQIP) by the American College of Surgeons.[164] 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 (MBSAQUIP), 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.[76, 165, 166] With recent statistical advances in the area of missing data,[167] it will be critical that high-quality observational studies and registries include longitudinal measurements and do not totally exclude patients with missing follow-up visits if they are otherwise eligible.

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.[168] 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 be used to externally validate existing models.[63] 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.[64] 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). Moreover, future studies should inform their outcomes by incorporating patient values and preferences which may guide the collection and analysis of patient-centered outcomes related to function and quality of life for patients undergoing bariatric surgery. Towards this end, an ongoing study funded by the Patient-Center Research Institute (PCORI; https://www.pcori.org/research-results/2015/comparing-benefits-and-harms-three-types-weight-loss-surgery-pcornet-bariatric) is expected to provide meaningful data upon its completion in the near future.[169]

The type of bariatric procedures covered by Medicare and other payers, and the conditions under which they are covered, will affect the populations analyzed in studies using routinely-collected health data. For example, gastric bypass, adjustable gastric banding, and duodenal switch currently are covered under Medicare's National Coverage Determination (NCD), while coverage of laparoscopic sleeve gastrectomy and revisional bariatric surgery are at the discretion of the local Medicare Administrative Contractors (MACs). By contrast, balloon devices, mini gastric bypass and several other similar procedures are excluded from coverage. Additionally, many public and private payers have criteria that limit access to bariatric surgery based on comorbidities with some requiring severe comorbidities to allow coverage and others being less restrictive. Because of these coverage restrictions, published studies using routinely-collected health data are scarce and it is likely that the clinical characteristics of patients in these studies will vary due to eligibility criteria determined by coverage type rather than by relevance to clinical practice. Therefore, generation of comprehensive real-world evidence regarding the effectiveness and safety of many bariatric procedures will require that patients' insurance covers the bariatric procedures and relevant services only in the context of a clinical study.

There are a large number of bariatric procedures (surgical and endoscopic), as well as a large number of short term 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 components that should be factored into the shared decisionmaking 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. 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 analysis[170] 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.[170]

Finally, more studies are needed to examine the mediating role of weight loss on the effect of bariatric surgeries on nonweight 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. As our systematic review of the available sparse evidence suggests, Medicare-eligible patients undergoing bariatric surgery achieve sustained weight loss for most types of bariatric surgical procedures. However, the strength of the available evidence is at best moderate and 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 about the extent to which the effects of bariatric surgery on nonweight 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, and the relative effectiveness of various surgical approaches, evidence from new randomized trials or high-quality comparative observational studies is needed.

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Abbreviations

AGB	Adjustable Gastric Banding
AHRQ	Agency for Healthcare Research and Quality
AIC	Akaike's Information Criterion
ASA	American Society of Anesthesiologists
AUC	Area Under the Receiver Operating Characteristic curve
BMI	Body Mass Index
CART	Classification And Regression Tree
BPD-DS	Biliopancreatic Diversion with Duodenal Switch
CI	Confidence Interval
CMS	Centers for Medicare & Medicaid Services
COPD	Chronic Obstructive Pulmonary Disease
DCG	Diagnostic Cost Group
EBMIL	Excess BMI Loss
eGFR	Estimated Glomerular Filtration Rate
EPC	Evidence-based Practice Center
EWL	Excess Weight Loss
FDA	Food and Drug Administration
GERD	Gastroesophageal Reflux Disease
GLP-1	Glucagon-Like-Peptide-1
HDL	High-Density Lipoprotein
HEI	Health Eating Index
HR	Hazard Ratio
HRQoL	Health-Related Quality of Life
LAGB	Laparoscopic Adjustable Gastric Banding
LASSO	Least Absolute Shrinkage And Selection Operator
LDL	Low-Density Lipoprotein
LL	Log-Likelihood
LRYGB	Laparoscopic Roux-En-Y Gastric Bypass
LSG	Laparoscopic Sleeve Gastrectomy
MAC	Medicare Administrative Contractor
MGB	Mini Gastric Bypass
MI	Myocardial Infarction
NA	Not Applicable
NAFLD	Nonalcoholic Fatty Liver Disease
NASH	Nonalcoholic Steatohepatitis
NCD	National Coverage Determination
NHANES	National Health and Nutrition Examination Survey
NR	Not Reported
OHAs	Oral Hypoglycemic Agents
OR	Odds Ratio
PMID	PubMed ID
PPV	Predictive Value Positive
PVN	Predictive Value Negative
RCT	Randomized Clinical Trial

RoB	Risk of Bias
ROBINS	Risk Of Bias In Nonrandomized Studies - of Interventions
RYGB	Roux-En-Y Gastric Bypass
SADS	Single Anastomosis Duodenal Switch
SD	Standard Deviation
SG	Sleeve Gastrectomy
SIP	Scientific Information Package
SoE	Strength of Evidence
SRDR	Systematic Review Data Repository
TEP	Technical Experts Panel
THA	Total Hip Arthroplasty
TKA	Total Knee Arthroplasty
VBG	Vertical Band Gastroplasty
WL	Weight Loss