



# Effective Health Care Program

## Bariatric Surgery and Nonsurgical Therapy in Adults With Metabolic Conditions and a Body Mass Index of 30.0 to 34.9 kg/m<sup>2</sup>

### Executive Summary

#### Background

Bariatric surgery, also known as weight-loss surgery, refers to surgical procedures usually performed on people who are morbidly obese for the purpose of losing weight and to treat, as well as prevent, obesity-related comorbidities. Bariatric surgery has evolved since its introduction in the 1950s, with some procedures that were popular initially (like jejunoileal bypass) having been abandoned because of unacceptable complication rates. The types of bariatric surgery that are most commonly performed now include laparoscopic adjustable gastric banding (LAGB); Roux-en-Y gastric bypass (RYGB); biliopancreatic diversion with duodenal switch (BPD); and sleeve gastrectomy (SG), also referred to as gastric sleeve. Newer procedures—gastric sleeve with ileal interposition, duodenal-jejunal bypass, and duodenal-jejunal exclusion—are being studied outside of the United States (one study in the United States was conducted in 2008, but the results were not published). The mechanism of weight loss and metabolic impact are under investigation, but they are not regularly performed in the United States currently. Thus, they are beyond the scope of this report.

#### Effective Health Care Program

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

The full report and this summary are available at [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).

Studies show that these procedures cause significant weight loss in morbidly obese patients. In addition, bariatric surgeries such as LAGB and RYGB in morbidly



obese patients have been found to be far more effective than conventional nonsurgical therapy at lowering blood sugar to improve diabetes in the short term. Improvement in diabetes has been demonstrated to start rapidly after bariatric surgery, especially for patients undergoing RYGB, before significant weight loss has occurred. The mechanism of postoperative metabolic improvements has not been fully elucidated and may in part be independent from weight loss, suggesting that bariatric surgery may improve metabolic comorbidities, even for patients who are not morbidly obese.

Bariatric surgery is an accepted practice for patients with a body mass index (BMI) of 40 kg/m<sup>2</sup> or greater, and for patients with a BMI of between 35 and 40 kg/m<sup>2</sup>, who have significant obesity-related comorbidities such as diabetes, hypertension, cardiovascular disease, dyslipidemia, obstructive sleep apnea, and degenerative arthritis. The National Institutes of Health (NIH) criteria state that patients should undergo medically supervised weight loss attempts before bariatric surgery.

In the past few years, bariatric surgery has been suggested as an option for patients with a lower BMI (at least 30 kg/m<sup>2</sup>, but less than 35 kg/m<sup>2</sup>) as a way to treat diabetes and other metabolic conditions. Given a lack of consensus regarding the minimum BMI requirement and uncertainties regarding the comparative effectiveness of different bariatric procedures, especially in the long term, a review of the relative risks and benefits of the various surgical and more conservative approaches to treatment of diabetes or impaired glucose tolerance (IGT) in patients whose BMI is between 30 and 35 kg/m<sup>2</sup> was suggested by a constituent group. The topic was refined by the Southern California Evidence-based Practice Center (EPC) in conjunction with Key Informants, including bariatric surgeons, researchers, consumers, and payers.

## Objectives

This systematic review aims to address the following Key Questions (KQs).

**KQ1.** What does the evidence show regarding the comparative effectiveness of bariatric surgery for treating adult patients with a BMI of 30.0 to 34.9 kg/m<sup>2</sup> and metabolic conditions, including diabetes? Are certain surgical procedures more effective than others (LAGB, RYGB, or SG)?

**KQ2.** What does the evidence show regarding the comparative effectiveness of bariatric surgery versus conventional nonsurgical therapies for treating adult patients with a BMI of 30.0 to 34.9 kg/m<sup>2</sup> and metabolic conditions?

**KQ3.** What are the potential short-term adverse effects and/or complications associated with bariatric surgery for treating adult patients with a BMI of 30.0 to 34.9 kg/m<sup>2</sup> who have metabolic conditions?

**KQ4.** Does the evidence show racial and demographic disparities with regard to potential benefits and harms associated with bariatric surgery for treating adult patients with a BMI of 30.0 to 34.9 kg/m<sup>2</sup> and metabolic conditions? What other patient factors (social support, counseling, preoperative weight loss, compliance with recommended treatment) are related to successful outcomes?

**KQ5.** What does the evidence show regarding long-term benefits and harms of bariatric surgery for treating adult patients with a BMI of 30.0 to 34.9 kg/m<sup>2</sup> and who have metabolic conditions? How do the long-term benefits and harms of bariatric surgery compare to short-term outcomes (within 1 year after surgery)?

## Analytic Framework

Figure A presents the analytic framework for this comparative effectiveness review (CER). Using data from controlled trials, cohort studies, and case series, we sought evidence of the benefits and harms of different types of bariatric surgeries and in treating targeted patients (those with diabetes or IGT and a BMI of  $\geq 30$  kg/m<sup>2</sup> and  $< 35$  kg/m<sup>2</sup>). The evidence for both short- and long-term outcomes was assessed. Planned comparisons included (1) among different surgical procedures such as RYGB, LAGB, SG, and BPD to answer KQ1; and (2) surgical procedures to conventional nonsurgical therapies (e.g., diet, exercise, and pharmaceuticals) to answer KQ2. Documented short- and long-term benefits and harms of surgical procedures were compared to answer KQ3 and KQ5.

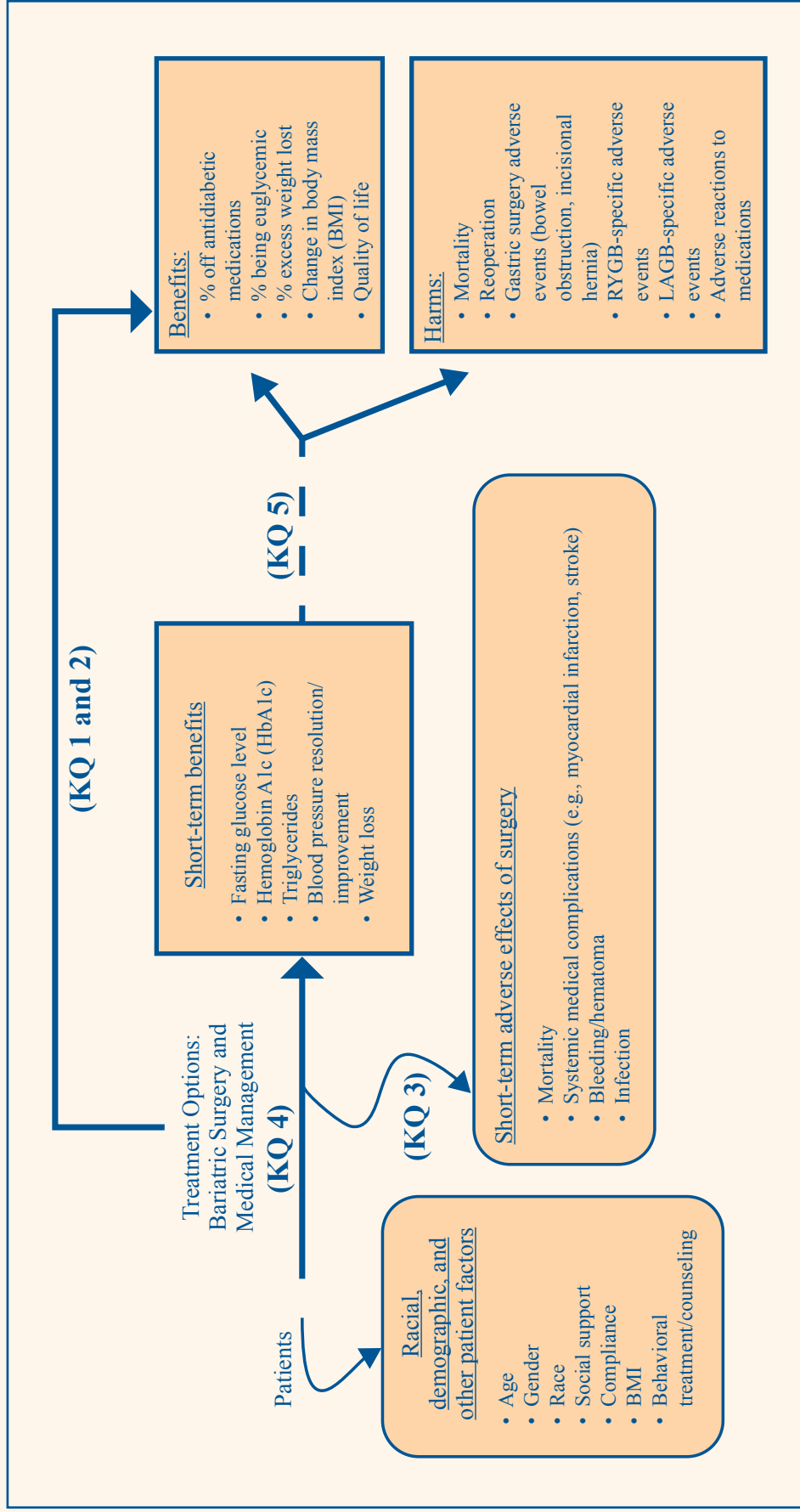
Benefits and harms for specific subpopulations (by gender, age, and race/ethnicity) and other patient factors (social support, counseling, preoperative weight loss, and compliance with recommended treatment) were examined and summarized to answer KQ4.

## Methods

### Input From Stakeholders

We searched the electronic databases PubMed<sup>®</sup>, Embase<sup>®</sup>, CINAHL (Cumulative Index to Nursing and Allied Health Literature), the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials (CENTRAL), and the Cochrane Database of Abstracts of Reviews of Effects (DARE) for studies addressing our

**Figure A. Analytic framework for evaluating the effectiveness and safety of alternative approaches to treatment of metabolic conditions in the patient population with BMI  $\geq 30 < 35$**



KQ = Key Question; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass

KQs. Other sources included Clinicaltrials.gov, references of included studies and relevant reviews, and personal files from projects with related topics. The original search was conducted in March 2010; electronic search updates were conducted monthly through March 2012. We used various search terms for each type of procedure and for nonsurgical interventions. Further details and surgery strategies are included in the full report. There were no limits on publication date or language.

We searched the literature for systematic reviews, case series, cohort, case control studies and controlled trials. To be included, studies had to report on one of the surgical procedures listed above or nonsurgical treatment, and had to include patients with a BMI of at least 30 kg/m<sup>2</sup> but less than 35 kg/m<sup>2</sup> with diabetes or IGT. The following studies were excluded: (1) studies that did not report any outcomes of efficacy, effectiveness, or safety/adverse events; (2) nonsurgical studies with less than 1 year followup; (3) nonsurgical studies already included in previous systematic reviews; and (4) studies with fewer than three subjects.

We note here that we are dealing with two concepts—weight and disorders of glucose metabolism—that are a continuum physiology, but in the KQs, are treated as dichotomous. In other words, we expect the risk of excess weight to be similar for a person with a BMI of 29.5 kg/m<sup>2</sup> and a person with a BMI of 31.5 kg/m<sup>2</sup>, yet our KQs deal with the latter and not the former. Indeed, the published literature does not always conform to the same threshold specified in the KQs. We judged that studies that included substantial numbers of patients within the threshold of our KQs, but also some outside the range, were still informative and were included. Thus, if a study included patients with a BMI of 29 kg/m<sup>2</sup>–37 kg/m<sup>2</sup>, we judged that it would be more relevant to the KQs to include rather than exclude, it. Similar decisions were made about the presence of IGT and the clinical diagnosis of diabetes.

We reviewed the studies retrieved from the various sources against our exclusion criteria. Items included specific surgical procedures or nonsurgical treatments, study design, sample size, and types of outcomes reported (i.e. metabolic, mortality, adverse events). Two reviewers, each trained in the critical analysis of scientific literature, independently reviewed each study and resolved disagreements by consensus. The lead investigator resolved any disagreements that remained after discussions between the reviewers. Results from controlled trials, case-control studies, cohort studies, and case series of surgical procedures were abstracted by researchers using Distiller<sup>®</sup> software (Evidence Partners, Ottawa, Canada).

Because of study heterogeneity, meta-analysis was not possible; thus, we summarized the data by procedure and intervention. Data abstracted included metabolic outcomes (glucose, blood pressure, lipids) and weight loss, mortality, and adverse events. Other details included setting; population characteristics (including sex, age, ethnicity, and comorbidities); eligibility and exclusion criteria; any cointerventions, including allowed medication; comparisons; and results for each outcome. Intent-to-treat results were recorded if available. For each study that provided sufficient information, we calculated the mean change from baseline to followup. A negative mean change indicated a decrease in outcome measure (e.g., BMI). We used these estimates to calculate a weighted mean change within surgery type and outcome.

The overall strength of evidence for intervention efficacy was assessed by using guidance suggested by the Agency for Healthcare Research and Quality (AHRQ) for its Effective Health Care Program. This method is based loosely on one developed by the GRADE working group, and classifies the grade of evidence according to the following criteria:

**High** = High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence on the estimate of effect.

**Moderate** = Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.

**Low** = Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.

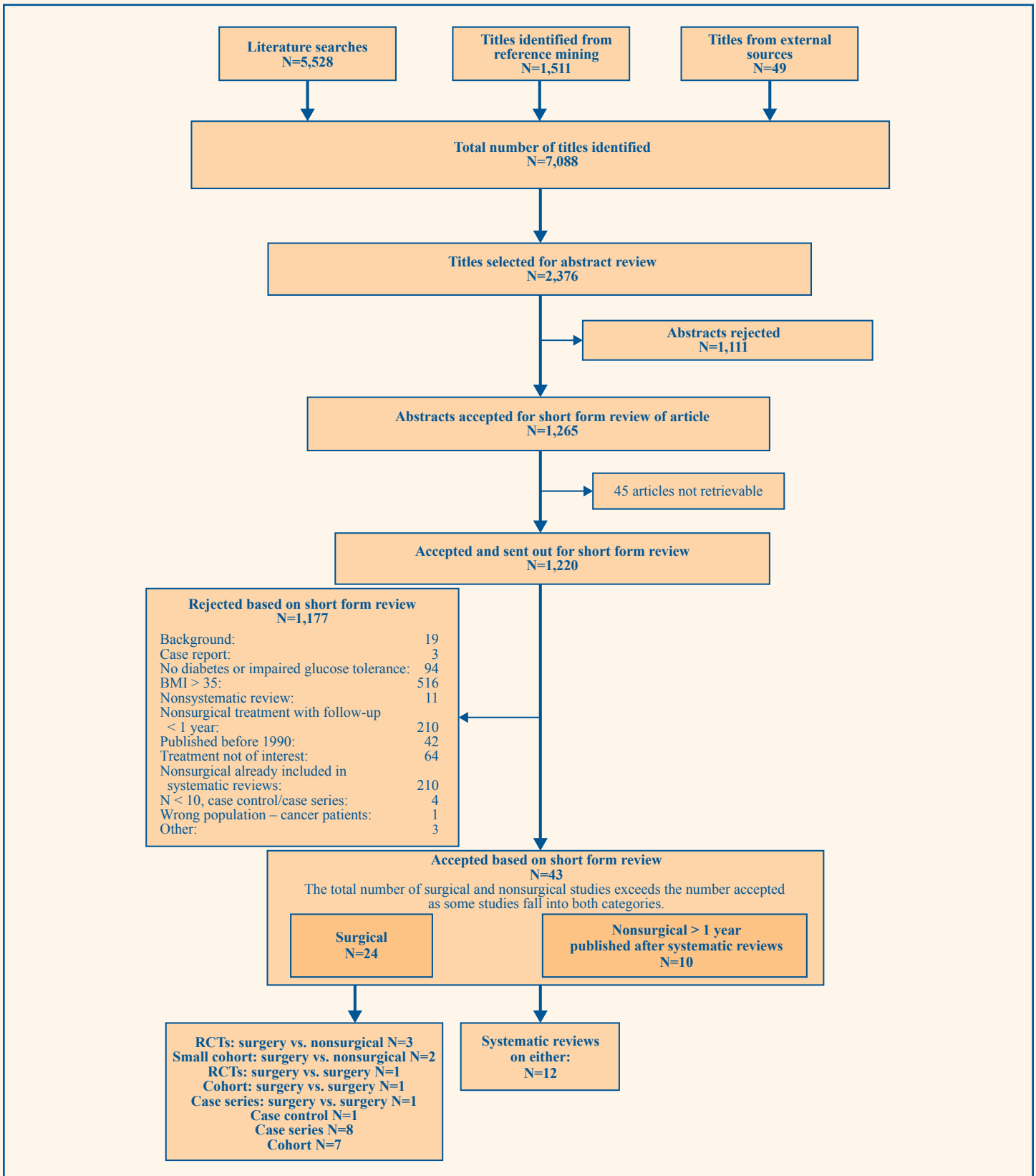
**Insufficient** = Evidence is either unavailable or does not permit a conclusion.

The evidence grade is based on four primary (required) domains and four optional domains. The required domains are risk of bias, consistency, directness, and precision; the additional domains are dose-response, plausible confounders that would decrease the observed effect, strength of association, and publication bias. For this review, global implicit judgment about “confidence” was used in the result.

## Results

Figure B displays the results of our literature search. We identified 7,088 titles through our electronic database searches, by reference mining, and by locating those

**Figure B. Study/literature flow diagram**



BMI = body mass index; RCT = randomized controlled trial

suggested by our Technical Expert Panel. We also reviewed scientific information packets received from device manufacturers. Our researchers selected 2,376 for further review; almost half were rejected upon abstract review. Of the 1,220 studies that underwent full-text review, we retained 24 surgical studies, 12 systematic reviews, and 10 nonsurgical studies. The most common reasons for exclusion of surgical studies were focus on patients outside the BMI range (516 studies) or that the study did not include patients with diabetes or IGT (94 studies). The most common reasons for excluding nonsurgical studies were followup of less than 1 year or inclusion in previous systematic reviews.

Of the 24 studies reporting bariatric surgery results in patients with diabetes or IGT and a BMI of at least 30 but less than 35 kg/m<sup>2</sup>, we found two head-to-head trials, one cohort study, and one case series comparing surgical procedures. We identified three controlled trials and two small cohort studies comparing surgery with nonsurgical intervention. (One of the trials contained two different surgical arms.) The remaining included studies were observational, with no comparison group. Six of the studies included only a portion of patients with diabetes or IGT; in the rest, all patients had one of these disorders.

Of the 24 surgery studies, there were 13 RYGB arms, 7 LAGB arms, 5 BPD arms, and 3 gastric sleeve arms. We also included 20 systematic reviews on diet, exercise, medication, or bariatric surgery in our target population. Table A presents a summary of our findings.

### Short-Term Outcomes

Based primarily on glucose control outcomes, there is moderate strength evidence of efficacy of bariatric surgery in treating diabetes in patients with a BMI of at least 30 but less than 35 kg/m<sup>2</sup> in the short term. At 1 year, surgery patients show much greater weight loss than usually seen in studies of diet, exercise, or other behavioral interventions. With the exception of GLP-1T agonists, diabetes medications do not cause significant weight loss. While both behavioral interventions and various medications lower HbA1c (glycosylated hemoglobin) levels significantly, the decreases reported in bariatric surgery patients at one year are greater. Improvements in glucose control outcomes have been reported as early as 1 month post-surgery. Several studies report improvement in hypertension and cholesterol at 1 year. We rated the overall evidence as moderate due to sparseness of data—three randomized controlled trials (RCTs) directly compared surgical with nonsurgical interventions, and two came from the same group of

researchers. Observational data, which start as low strength evidence, were upgraded due to consistency of results regarding BMI and blood sugar. Thus, the total body of evidence is considered moderate strength, based on moderate strength of evidence for BMI and glucose outcomes. Strength of evidence for cholesterol and blood pressure outcomes is low.

### Long-Term Outcomes

There are few long-term data on patients with diabetes or IGT in this weight class who have undergone bariatric surgery. We identified only two studies with followup of more than 2 years. One, a case series of LAGB patients in Italy, reported followup at 5 years for 29 of the 210 initial patients, for a followup rate of only 13.8 percent. Another very small Italian study followed seven BPD patients for at least 5 years. Thus, despite promising short-term outcomes reported, the evidence that bariatric surgery is an effective way to treat diabetes in patients with a BMI of at least 30 kg/m<sup>2</sup> but less than 35 kg/m<sup>2</sup> in the long term is insufficient. Strength of evidence is insufficient for all outcomes, including BMI, blood glucose, cholesterol, and hypertension. In contrast, behavior and medication interventions have been studied extensively for decades; several large, long-term RCTs have found improved HbA1c continues for 10 years. Several long-term trials and meta-analyses have reported clinically significant improvements in microvascular and macrovascular outcomes as a result of behavioral or medication interventions.

### Specific Bariatric Procedures

We found two head-to-head trials comparing bariatric procedures (one also had a medication-only group). An average-size trial (N=60) conducted in Taiwan compared RYGB with SG; the RYGB group had better weight and diabetes outcomes at 1 year postsurgery. A recent U.S. trial comparing these same procedures found similar results.

We also found two observational studies that compared procedures. One conducted in the United States compared RYGB with LAGB. This study was fairly large (N=235), and had an adequate followup rate (61.9% for RYGB, 69.2% for LAGB) at 6 to 12 months. Some patients were followed for 2 years. Weight loss was similar among groups; diabetes outcomes were generally better for RYGB patients. The other study, conducted in Germany, compared results for 12 BPD patients with 4 RYGB patients. Both groups lost a significant amount of weight. At 1 year, decrease in HbA1c was significantly greater in the BPD group.

**Table A. Summary of data on interventions and outcomes in patients with diabetes or impaired glucose tolerance**

	<b>Behavioral Changes (Data Almost Entirely From Systematic Reviews, RCTs)</b>	<b>Intervention Medications (Data Almost Entirely From Systematic Reviews, RCTs)</b>	<b>Bariatric Surgery (Data Primarily From Observational Studies)</b>
<b>Outcome</b> Weight loss at 1 year	2.8 kg for diet, exercise, behavioral vs. usual care	Weight gain from 1 to 5 kg with some drugs. 2.8 kg weight loss with GLP-1R agonists; no weight change with metformin	BMI loss of 5 to 7 kg/m <sup>2</sup> (about 15 to 20 kg for someone 5 feet 6 inches tall)
Weight loss at 2 years	2.7 kg for diet, exercise, behavioral vs. usual care	Data unavailable	BMI loss of 4 to 8 kg/m <sup>2</sup> (about 11 to 23 kg for someone 5 feet 6 inches tall)
Long-term weight loss (5 years and more)	1.7 kg for diet, exercise, behavioral vs. usual care at 5 years	Few data; the U.S. Diabetes Prevention Program Outcomes Study (DPPOS) found no significant change with metformin at 10 years	BMI loss of 5.7 kg/m <sup>2</sup> at 5 years, in one study of 29 LAGB patients
HbA1C, percentage of total hemoglobin, at 1 year	Decrease of 0.3 to 2.2 percentage points	Decrease of 0.5 to 1.0 percentage points	Decrease of 2.6 to 3.7 percentage points
HbA1C at 2 years	No significant change	Data unavailable	Decrease of 1.8 to 3.1 percentage points
HbA1C at 5 years and more	Few data; the U.S. Diabetes Prevention Program Outcomes Study (DPPOS) found HbA1C concentrations lower in behavioral group at 10 years (vs. placebo)	Few data; the U.S. Diabetes Prevention Program Outcomes Study (DPPOS) found HbA1C concentrations lower in metformin group at 10 years (vs. placebo)	Data unavailable
Other metabolic outcomes at 1 year	Diet improved fasting glucose (1.3%-36.6% reduction) and triglycerides (11.3%-58.9% reduction); the Spain PREDIMED study found Mediterranean diet reduced metabolic syndrome prevalence by 13.7% at 1 year; the Finnish Diabetes Prevention Study (DPS) found behavioral change reduced metabolic syndrome prevalence at 3.9 years (odds ratio: 0.62)	Most medications had minimal effects on systolic & diastolic blood pressure (< 5 mmHg change); metformin and second-generation sulfonylureas generally decreased LDL cholesterol levels	Mixed results, one RYGB and one BPD study reported slight increase in triglycerides at 1 year
Other metabolic outcomes at 5 years and more	Data unavailable	Data unavailable	Of 7 BPD patients followed, all had normal serum cholesterol and triglycerides

**Table A. Summary of data on interventions and outcomes in patients with diabetes or impaired glucose tolerance (continued)**

<b>Outcome</b>	<b>Behavioral Changes (Data Almost Entirely From Systematic Reviews, RCTs)</b>	<b>Intervention Medications (Data Almost Entirely From Systematic Reviews, RCTs)</b>	<b>Bariatric Surgery (Data Primarily From Observational Studies)</b>
Microvascular outcomes (renal disease, neuropathy, retinopathy, etc.)	Data unavailable	U.K. Prospective Diabetes Study (UKPDS) found patients taking sulfonylurea, insulin, or metformin had 24% risk reduction for microvascular disease at 10 years	Data unavailable
Macrovascular outcomes (cardiovascular disease, stroke, heart attack)	Few data; the China Da Qing Diabetes Prevention Study (CDQDPS) found no significant difference in first CVD event, CVD mortality and all-cause mortality between intervention and control group	Meta-analysis of 5 trials with 33,040 participants found that on an average A1C reduction of 0.9% there was a 19% reduction in non-fatal myocardial infarction and a 15% reduction on coronary heart disease, and no statistically significant effect on stroke or all-cause mortality	Data unavailable
Prevention of diabetes	Hazard ratio 0.51 for behavioral interventions vs. standard advice at 1 to 5 years; the U.S. Diabetes Prevention Program (DPP) found diabetes incidence in 10 years reduced by 34% by behavioral change vs. placebo, and the China Da Qing Diabetes Prevention Study (CDQDPS) found it was 43% lower in behavioral group over 20 years	Hazard ratio 0.70 for oral medications vs. control at 1 to 5 years; the U.S. Diabetes Prevention Program (DPP) found diabetes incidence in 10 years reduced by 18% in the metformin group vs. placebo	Data unavailable

BMI = body mass index; BPD = biliopancreatic diversion with duodenal switch; CVD = cardiovascular disease; LAGB = laparoscopic adjustable gastric banding; LDL = low-density lipoproteins; RCT = randomized controlled trial; RYGB = Roux-en-Y gastric bypass



Observational studies of surgical procedures without a comparison arm reported clinically meaningful decreases in BMI with all types of bariatric surgery at less than 1 year. Clinically meaningful diabetes outcomes were also reported at less than 1 year for all surgery types. At a year or more, weight loss was maintained or improved in all groups; RYGB patients had the greatest decrease in BMI.

Taking into consideration the entire body of evidence, we rate the strength of evidence of efficacy as moderate for RYGB, LAGB, and SG in treating diabetes and IGT in patients with a BMI of between 30 kg/m<sup>2</sup> and 35 kg/m<sup>2</sup> in the short term (up to 2 years), based primarily on glucose control outcomes. For BPD, both the number of studies and their sample sizes are much lower; thus the strength of evidence of efficacy is rated low. Evidence on comparative effectiveness of surgical procedures is insufficient.

### Adverse Events

The strength of evidence for short-term harms is low for all four surgical procedures. In the two RCTs comparing SG with RYGB, complications were minor, and rates were similar between groups. The surgical complications reported for RYGB and LAGB in observational studies were fairly consistent; they differ due to the nature of the procedures. Complications related to LABG include band slippage, tube problems, and band erosion, while those related to RYGB include stricture, ulcer, and on rare occasions, hemorrhage.

Studies were included in our mortality analyses only if they reported or mentioned either the number of deaths or lack of any deaths. Thus, 14 studies were included, which accounted for five LAGB arms, one gastric sleeve arm, nine RYGB arms, and one BPD arm. Only one death was reported—an LAGB patient with complications of a gastric perforation. Thus, the reported rate of mortality was 0.48 percent for LAGB and 0.0 percent for gastric sleeve, RYGB, and BPD.

The low strength of evidence reflects several limitations in the data. The majority of the adverse events data were submitted by surgeons, and thus subject to possible publication bias. Few studies were clear exactly when adverse events took place, and patients who were lost to followup had no adverse events data. In addition, definitions of complications varied from study to study.

We found no data on long-term adverse events of bariatric surgery in diabetes or IGT patients in our specific BMI range. Thus, strength of evidence for long-term adverse events is rated insufficient.

## Discussion

The literature on bariatric surgery for diabetes or IGT patients with BMI of at least 30 kg/m<sup>2</sup> and less than 35 kg/m<sup>2</sup> has many limitations. Most important, very few studies of this target population have long-term followup. Only two studies followed patients for more than 2 years; one has a followup rate of only 13.8 percent and the other includes only seven patients. Thus, we have almost no data on long-term efficacy and safety. No evidence was found on major clinical endpoints such as all-cause mortality, cardiovascular mortality or morbidity, or peripheral arterial disease. The studies of bariatric surgery in this population have measured only intermediate or surrogate endpoints regarding glucose control. While control of glucose is certainly important, the available evidence from the diabetes literature indicates it may be premature to assume that controlling glucose to normal or near normal levels completely mitigates the risk of microvascular and macrovascular events. Thus, claims of a “cure” for diabetes based on glucose control within 1 or 2 years require longer term data before they can be substantiated.

Randomized controlled trials are considered the highest level of medical evidence. We found three RCTs of surgery versus nonsurgical treatment (one of these also compared two procedures) and another RCT comparing surgical procedures. This was expected given the difficulty in conducting RCTs of surgery. Still, we identified only two observational studies comparing surgical procedures and two small cohort studies comparing surgery with nonsurgical approaches. The rest of our data came from studies with no comparison group and with data submitted primarily by the practicing surgeons. The sample sizes, regardless of methodological design, are far smaller than those of most trials of diet, exercise, and medications.

Applicability of this research to the larger treatment population of diabetes and IGT patients with BMI between 30.0 kg/m<sup>2</sup> and 34.9 kg/m<sup>2</sup> is important in interpreting the results. The participation rate, population characteristics, representativeness of the setting, and representativeness of the individuals are used to assess applicability. One RCT comparing surgery with nonsurgery was performed in the United States and included two of the more commonly performed procedures—RYGB and SG. However, it was of modest size and was conducted in an academic setting in a select group of patients with uncontrolled type II diabetes at baseline. Two RCTs of LAGB versus nonsurgical interventions conducted in Australia comprised primarily Caucasian patients. However, the RCT comparing LAGB with SG was conducted in Taiwan,

where diets and lifestyle may differ considerably from those of the West. One of the cohort studies comparing procedures was conducted in the United States, but only three of the remaining observational studies were conducted here. The others were conducted in Western Europe, South America, India, Asia, and Australia. Diet, behavior, and culture in many of these locations may differ dramatically from that in the United States. In addition, there may be biological or genetic differences. Thus, the results seen in studies in other countries may not be directly applicable to patients in the United States.

Data reported on adverse events also have several limitations. Most studies were not primarily designed to assess these outcomes and reflect surgeon or surgery team-reported events. There were only 20 instances in which 100 or more patients contributed data to a particular adverse event category; thus, the rate estimate for most adverse events is imprecise. Additionally, in 76 percent of instances, only a single study contributed data to a particular adverse event rate calculation, meaning the generalizability of the estimate is questionable. Followup times and rates were variable, and many studies did not state exactly when adverse events occurred, other than “within a year postsurgery.” As such, the rates of adverse events may be biased and lower than actual. Comparisons between procedure types are limited for the same reasons. Again, we found almost no long-term adverse events data for our target population.

Finally, although our literature-search procedures were extensive and included canvassing experts for studies we may have missed, the possibility of publication bias still exists. For all surgical procedures, there is the concern that published studies usually come from academic medical centers with high-performing surgical teams and careful patient selection. Outcomes for such patients may not reflect the outcomes achieved in the wider community. (The difference between complication rates seen in the major clinical trials of carotid endarterectomy and those observed in the general Medicare population is one well-known example of this phenomenon.) For bariatric surgery, there are media reports (Los Angeles Times) on several deaths following LAGB surgery. Whether there is any causal relationship between the surgery and the deaths has not yet been assessed in a peer-reviewed publication, so no conclusions can be drawn. Still, it illustrates the potential for there to exist adverse events and/or beneficial outcomes in as-yet-undescribed populations.

## Future Research

Future research should focus on long-term outcomes of bariatric surgery in U.S. patients with diabetes or IGT and a BMI of 30 kg/m<sup>2</sup> to 34.9 kg/m<sup>2</sup>. In this population, there is no evidence that bariatric surgery is effective in preventing the clinical consequences of diabetes—microvascular and macrovascular endpoints such as diabetic retinopathy, kidney failure, and myocardial infarction. Studies with followup of 5 to 10 years are needed.

We found one trial and one cohort study comparing procedures performed in the United States. The cohort study used the BOLD (Bariatric Outcomes Longitudinal Database), a resource created by the Surgical Review Corporation to monitor outcomes from the Bariatric Surgery Center of Excellence (BSCOE) program. As of June 2009, 235 patients with diabetes within our BMI range were in the BOLD database. The study we identified reported outcomes at 6 to 12 months. Outcomes at 12 to 24 months were reported for only a small number of patients (6.8 percent) presumably because that followup time had not expired for most of the patients. Continued followup of these patients and publication of findings will shed light on which, if any, bariatric procedures mitigate long-term sequelae of diabetes.

In addition, according to the U.S. clinical trials database (Clinicaltrials.gov), several bariatric surgery trials are being conducted in the target population. In addition to monitoring weight loss, these studies will frequently collect important metabolic data, including measures of blood sugar, cholesterol, triglycerides, and blood pressure. Long-term followup of the research subjects, if funded, could add to our knowledge base on the effects of bariatric surgery and cardiovascular morbidity and mortality. Collection and reporting of psychological and quality of life outcomes will also help inform prospective patients and providers.

## Glossary

**Bariatric surgery:** Surgery on the stomach and/or intestines to help a person lose weight.

**Biliopancreatic diversion with duodenal switch (BPD):** Surgery that involves removing 70 percent of the stomach, along with bypassing a significant proportion of small intestine.

**Body mass index (BMI):** An individual's weight, in kilograms, divided by his or her height, in meters squared. It is used to define normal weight, overweight, obesity, and morbid obesity.

**GLP-1 agonists:** Glucagon-like peptide-1 agonists, a class of diabetes drugs targeting the incretin system.

**HbA1c:** Glycosylated hemoglobin.

**Impaired glucose tolerance (IGT):** Prediabetic state of high blood sugar associated with insulin resistance.

**Laparoscopic adjustable gastric banding (LAGB):** A surgical weight-loss procedure that involves the placement of an adjustable belt around the upper portion of the stomach, restricting the size of the stomach and the amount of food it can hold.

**LDL (low-density lipoprotein) cholesterol:** Cholesterol that may collect in the walls of blood vessels, causing blockage.

**Metabolic condition:** A constellation of syndromes including impaired fasting glucose (prediabetes) and diabetes mellitus that increase the risk of cardiovascular disease.

**Roux-en-Y gastric bypass (RYGB):** A surgical weight-loss procedure that involves the creation of a small stomach pouch to restrict food intake and construction of bypasses of the duodenum and other segments of the small intestine to cause malabsorption (decreased ability to absorb nutrients from food). Often referred to as gastric bypass.

**Sleeve gastrectomy (SG):** A surgical weight-loss procedure in which the stomach is reduced to about 15 percent of its original size by surgical removal of a large portion of the stomach. There are variations on the sleeve gastrectomy that involve the addition of intestinal bypasses.

## References

Please refer to the reference list in the full report for documentation of statements contained in the Executive Summary.

## Addendum

As part of the preparation of a paper to appear in the *Journal of the American Medical Association (JAMA)*, we added to our analysis two additional elements:

1. We updated our literature search through September 2012. This resulted in including eight additional surgical observational studies (1-8 below).
2. We attempted to compare the weight loss and glucose control outcomes of bariatric surgery with nonsurgical therapy in the two RCTs that directly compared these in patients with diabetes for only those patients with a body mass index (BMI) of 30.0 to 34.9 kg/m<sup>2</sup>. The mean baseline BMI was 37.0 kg/m<sup>2</sup> in both RCTs. For the trial reported by Schauer and colleagues, we used the results of an analysis presented as supplemental material with their original publication. This analysis found no statistically significant evidence that the study outcomes differed in patients above and below the mean BMI of 37 kg/m<sup>2</sup>. For the trial reported by Dixon and colleagues, we obtained patient-level data from the authors, and compared weight loss and glucose outcomes in the 13 patients included in that trial that had a BMI of less than 35 kg/m<sup>2</sup>. There were statistically significantly better weight loss and glucose control outcomes in the patients treated with bariatric surgery compared to those treated nonsurgically.

These additions did not change our conclusions regarding the effectiveness and safety bariatric surgery in this population.

For further information, see:

Maggard-Gibbons M, Maglione M, Livhits M, et al. Bariatric surgery for weight loss and glycemic control in nonmorbidly obese adults with diabetes: a systematic review. *JAMA* 2013 June 5;309(21):2250-2261. DOI 10.1001/jama.2013.4851.

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## Full Report

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