HHS Public Access
Author manuscript
JAMA Surg. Author manuscript; available in PMC 2017 August 24.

Published in final edited form as:
JAMA Surg. 2014 December ; 149(12): 1323–1329. doi:10.1001/jamasurg.2014.2440.

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Long-term Outcomes of Bariatric Surgery: A National Institutes of Health Symposium

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Abstract

Importance—The clinical evidence base demonstrating bariatric surgery's health benefits is much larger than it was when the NIH last held a Consensus Panel in 1991. Still, it remains unclear whether ongoing studies will address critical questions about long-term complication rates and the sustainability of weight loss and comorbidity control.

Objective—The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Heart, Lung, and Blood Institute (NHLBI) convened a multidisciplinary workshop in May 2013 to summarize the current state of knowledge of bariatric surgery, review research findings on the long-term outcomes of bariatric surgery, and establish priorities for future research directions.

Evidence Review—The evidence presented at the workshop was selected by the planning committee for both its quality and duration of follow up. The data review emphasized RCTs and large observational studies with long-term follow up, with or without a control group.

Findings—Several small RCTs showed greater weight loss and T2DM remission compared to non-surgical treatments within the first 2 years of follow-up after bariatric surgery. Large, long-

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COMPETING INTERESTS: Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; Dr. Arterburn reports grants from National Institutes of Health, grants and non-financial support from Informed Medical Decisions Foundation, grants from Department of Veterans Affairs, and grants from Agency for Healthcare Research and Quality outside the submitted work. Dr. Courcoulas reports grants from NIH-NIDDK, grants from Covidien, grants from EndoGastric Solutions, grants from Nutrisystem, and advisory board and personal fees from J&J Ethicon Scientific outside the submitted work.

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term observational studies show durable (>5 years) weight loss, diabetes and lipid improvements with bariatric surgery. Still unclear are predictors of outcomes, long-term complications, long-term survival, micro- and macro-vascular events, mental health outcomes, and costs. The studies needed to address these knowledge gaps would be expensive and logistically difficult to perform.

Conclusions and Relevance—High-quality evidence shows that bariatric surgical procedures result in greater weight loss than non-surgical treatments and are more effective at inducing initial T2DM remission in obese patients. More information is needed about the long term durability of comorbidity control and complications after bariatric procedures and this evidence will most likely come from carefully designed observational studies.

Background

The worldwide practice of bariatric surgery was transformed following a 1991 National Institutes of Health (NIH) Consensus Conference. At that time early bariatric procedures, such as the jejuno-ileal bypass, had been found to have significant long-term risks, and the medical community had largely rejected the idea of surgical treatment for obesity. After reviewing the limited evidence that was available in 1991, the Consensus Panel concluded that the Roux-en-Y gastric bypass (RYGB) and vertical banded gastroplasty (VBG) procedures were safe and effective for patients with a body mass index (BMI) ≥40 kg/m^2 or with BMI ≥35 kg/m^2 when serious medical complications of obesity were present.[1] The consensus statement established a practice standard that was previously missing, helped to legitimize bariatric surgery as a surgical discipline, and resulted in a marked expansion of its use in clinical practice. Since that time, the clinical evidence base for bariatric surgery has grown tremendously. Post-operative mortality has declined, laparoscopic approaches for most procedures now dominate, and newer, less-invasive procedures have been introduced, including adjustable gastric band (AGB) and sleeve gastrectomy (SG).[2] Long-term outcomes are now available from observational studies, and recent randomized controlled trials have directly compared bariatric procedures to medical and lifestyle intervention for patients with type 2 diabetes (T2DM).[3–6] The improved evidence-base has generally established the short-term efficacy and safety of bariatric surgery for weight loss and T2DM remission; however, uncertainty remains about long-term complication rates and the sustainability of weight loss and comorbidity control. Although bariatric surgery is more widely accepted than in 1991, most patients continue to see these procedures as high risk,[7,8] providers are often reluctant to recommend bariatric surgery to their patients,[9] and many insurance plans still do not provide coverage for the procedures.[10–13]

In an effort to summarize the current state of knowledge of bariatric surgery, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Heart, Lung, and Blood Institute (NHLBI) convened a multidisciplinary workshop in May 2013 to review research findings on the long-term outcomes of bariatric surgery and to establish priorities for future research directions.[14] The workshop addressed three overarching questions: 1) what is the firmly-established evidence regarding the long-term outcomes of bariatric surgery? 2) what is not known about the long-term outcomes of bariatric surgery, and will the ongoing, currently-funded research studies address these knowledge gaps? and 3) what are the optimal and most feasible study designs to address the concerns about long-

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term outcomes? The discussions held at this recent NIDDK/NHLBI workshop are summarized in this report.

Summary of evidence: What do we know?

An overview of some recently published studies of long-term bariatric surgery outcomes and their limitations is provided in Table 1. Most publications reporting bariatric surgery long-term outcomes come from the Swedish Obese Subjects Study (SOS), initiated in 1987 as a non-randomized, matched intervention trial. 2010 subjects undergoing bariatric surgery were compared to a matched control group receiving usual care (n=2,037) with the primary endpoint of overall mortality and secondary outcomes including; myocardial infarction, stroke, other cardiovascular (CV) risk factors, and T2DM. [15–22] Obese Swedish patients electing to undergo surgery constituted the surgery group and those who declined comprised the control group, which were matched on 18 key variables that might affect prognosis. When the patients were recruited into the study (1987–2001), the most common bariatric procedure performed was VBG. RYGB, the most common procedure performed today, was only done in 13% of the SOS cohort.[15]

The SOS now has 15–20 years of follow up results for bariatric surgery, with results characterized by little loss to follow up for many study endpoints, an unusual phenomenon in weight loss studies. In the SOS study, bariatric surgery was associated with a 29% mortality reduction (Adjusted HR=0.71; 95% CI 0.54 to 0.92; P=0.01)[20] that was not correlated with extent of weight loss. Type 2 diabetes mellitus (T2DM) remission after 2 years was 72% (Odds Ratio=8.42; 95% CI 5.68 to 12.5; P<0.001) and 36% after 10 years (Odds Ratio=3.45; 95% CI 1.64 to 7.28; P=0.001).[15] Bariatric surgery was associated with fewer cardiovascular events (Adjusted HR=0.67; 95% CI 0.54 to 0.83; P<0.001) and other T2DM complications after more than 10 years follow up.[17,23] The SOS also found a reduced cancer incidence in women but not in men following bariatric surgery (Women HR=0.58, 95% CI 0.44–0.77, P=0.0001; Men hazard ratio (HR)=0.97, 95% confidence interval (CI) 0.62–1.52, P=0.90).[18] Bariatric surgery lowered medication costs from years 7 to 20 (mean annual drug cost surgery group $930 vs. $1123 control group, adjusted difference, −$228, 95% CI, −$335 to −$121, P<0.001) but hospital days and outpatient visits were greater in the surgery group in the first 6 postoperative years (years 2–6 mean annual hospital days for surgery patients 1.7 vs. 1.2 days for control patients, adjusted difference 0.5, 95% CI 0.2–0.7, P<0.001; years 2–6 mean annual non primary care outpatient visits surgery patients 1.3 vs. 1.1 control patients, adjusted difference 0.3, 95% CI 0.1–0.4, P=0.003).[16]

Although the SOS study has yielded important information about the long-term outcomes of bariatric surgery, most patients in SOS underwent procedures that are no longer performed today. Long term outcomes of a more contemporary operation, the RYGB, have been studied by Adams *et. al* in Utah.[3,24] In their first major study, they retrospectively compared the long-term survival of 7925 RYGB patients and 7925 weight-matched controls.[24] Baseline BMI was obtained from the medical records for the surgical patients and was estimated from self-reported height and weight for control patients using state driver's license data. At 7 years after surgery, RYGB was associated with a 40% reduction (HR=0.60; 95% CI 0.45–0.67; P<0.001) in all-cause mortality and 49% (HR=0.51; 95% CI 0.36–0.73; P<0.001) and

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92% (HR=0.08; 95% CI 0.01–0.47; P=0.005) compared with the control group, and reductions in cardiovascular and diabetes-related mortality.[24]

This same Utah group is performing an ongoing prospective analysis of a total of over 1,000 subjects, including RYGB cases and two non-randomized control groups of severely obese subjects, that examines the primary endpoints of weight loss, T2DM, hypertension, dyslipidemia, and health-related quality of life.[3] Six year outcomes show superior weight loss with RYGB, better control of co-morbid conditions, and greater improvements in quality of life compared to non-surgical treatment [at 6 years the surgical group lost 27.7% initial body weight 95% CI, 26.6%–28.9%; compared to 0.2% gain in control group 1 (surgery seekers) 95% CI, −1.1% to 1.4%; and 0% change in control group 2 (population-based control) 95% CI −1.2% to 1.2%).[3] All RYGB procedures in the Utah study were performed by a single group of surgeons, which limits this study's generalizability.

Observational studies are never definitive since potential confounding differences between groups cannot be completely eliminated. Proving the health impact of bariatric surgery would require long-term randomized, controlled trials (RCTs). Although RCT's would provide the most compelling evidence for the benefits and risks of bariatric surgery, they are difficult to perform. A recent systematic review and meta-analysis summarized all RCTs that have compared bariatric surgery with non-surgical treatments for obesity.[25] The review included eleven RCTs involving 796 participants with a BMI between 30 and 52 kg/m^2. These studies were on cohorts with T2DM with short term follow up and they provided evidence that bariatric procedures, including RYGB[4–6], LAGB[26,27] Biliopancreatic diversion (BPD)[5], and SG,[4] result in greater (1–2 years) weight loss (mean difference −26 kg; 95% CI: −31 to −21) and greater remission of T2DM [complete case analysis Relative Risk (RR) of T2DM remission: 22.1; 95% CI:3.2–154.3; conservative analysis RR: 5.3; 95% CI:1.8–15.8] compared to a variety of non-surgical treatment options.[4–6,26,27] An overview of the results and limitations of the largest of these RCTs is provided in Table 2. Longer-term data from RCTs is lacking.

In summary, workshop presentations of the available evidence from large, long-term observational studies and smaller, short-term RCTs revealed that all bariatric procedures result in greater weight loss than any conventional medical treatment, lifestyle intervention, or medically supervised weight loss program at both short and long-term (>5 years) follow up.[3,21,25] High quality evidence from RCTs also demonstrated the effectiveness of bariatric procedures for initial T2DM remission at 1–2 years after surgery. Furthermore observational studies suggest that bariatric surgery can reduce incident diabetes and cancer.[25] Finally, the physical-function components of quality of life are significantly improved after bariatric surgery and are likely related to the durability of weight loss, but no firm conclusion can be drawn about other domains of quality of life. [3,28,29]

What is not known about bariatric surgery outcomes?

Many aspects of bariatric surgical outcomes lack sufficient information to draw firm conclusions or help guide clinical recommendations. Major deficiencies in the knowledge about bariatric surgery outcomes are summarized in Table 3, below. Research studies

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addressing these gaps are needed to inform ongoing clinical and policy decisions regarding bariatric surgery. In addition, there is insufficient information regarding optimal dietary and nutritional management following bariatric procedures and a poor understanding of how to manage specific complications of bariatric operations (e.g. hypoglycemia, chronic nausea/vomiting, insufficient weight loss, decision making regarding candidates for revisional surgery).

What important studies are ongoing and what are their strengths and limitations for addressing key long-term outcomes?

Ongoing studies of bariatric surgery outcomes include prospective and retrospective observational studies and RCTs comparing contemporary procedures (RYGB, SG, and LAGB) to non-surgical care of severely obese patients.[30–36] The Longitudinal Assessment of Bariatric Surgery study (LABS) and its sub-studies are designed to address key long-term outcomes of bariatric surgery with a planned follow-up of at least 5 years.[37] The LABS study has prospectively enrolled 2,427 severely obese patients who underwent bariatric surgery (1,716 RYGB, 602 LAGB, and 58 SG) between 2004 and 2009. These participants are evaluated at baseline and annually with standardized measures by trained personnel to address important questions about the comparative efficacy and safety of surgical procedures as well as the durability of weight loss and health improvements. Three year results show substantial weight loss with most of the weight change occurring in the first year and significant variability in the amount of weight loss, as well as in diabetes, blood pressure, and lipid outcomes at three years.[38] A separate Teen-LABS cohort study is examining the efficacy and safety of bariatric procedures (161 RYGB, 14 LAGB, 67 SG) among 242 adolescents,[39] and 30-day safety results have been published.[40] The primary limitation of the LABS studies is the lack of a non-surgical control cohort, which precludes determining whether bariatric surgery is more effective than usual or intensive medical care and/or lifestyle intervention for improving long-term health and costs of care. Also, the LABS studies include very few SG procedures. This operation now makes up a growing fraction of all bariatric surgical procedures performed in the United States, but outcomes are still incompletely understood.[41,42]

There are a number of other ongoing long-term outcomes studies that will yield results in the future (Table 1). These include the previously described Utah Obesity Study;[3] the large, prospective Michigan Bariatric Surgery Collaborative,[43] a retrospective study of surgical subjects and matched nonsurgical control in the Veterans Affairs System;[44,45] and a retrospective study of long-term T2DM outcomes in the HMO Research Network.[46] Each of these observational studies will answer important questions about long-term outcomes in defined populations, but these studies are not randomized and lack a comparison arm receiving intensive medical care or lifestyle intervention.

During the past 5 years, several small size RCTs of bariatric surgery compared with non-surgical care were initiated.[30–36] Most of these are investigating the effect of bariatric surgery on T2DM. The main strengths of these studies are their random treatment allocation, which reduces confounding bias, and their inclusion of a control group. Individually, the

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trials are small but, in aggregate, have appreciable numbers of patients. Seven RCTs currently funded by the NIH include ~450 randomized subjects, but the trials are not entirely comparable since the control groups treatments are not uniform across studies. Several other non-NIH funded, U.S.-based RCTs include an additional ~400 randomized subjects. There are 13 ongoing international RCTs with an anticipated enrollment of nearly 2000 patients. These RCTs will provide more definitive information about the comparative efficacy and safety of bariatric procedures as compared to usual or intensive medical care and/or lifestyle intervention. The trials mostly plan for short term follow up, especially among patients with T2DM having mild to moderate obesity (BMI between 30 and 40 kg/m^2). Few of these RCTs are planning for follow-up of 5 years or longer. This is unfortunate, as knowledge about the short-term outcomes in low BMI patients are limited and there are major unanswered questions about long-term outcomes as well.

How can existing studies be leveraged to address deficiencies in the knowledge base for bariatric surgery outcomes?

Although RCTs could provide definitive evidence for the efficacy and safety of bariatric procedures, a number of challenges exist regarding the feasibility of large, long-term, multi-center RCTs of bariatric surgery compared with non-surgical treatment. The sample sizes needed to address many of the outstanding questions regarding "hard endpoints," such as mortality, CV events, and cancer outcomes, can exceed 5,000 patients and would require many years of follow-up to achieve a sufficient number of events. Projecting from the long-term SOS study mortality results, a massive prospective RCT would be required to unequivocally demonstrate improved survival attributable to bariatric surgery. In the SOS, 4,047 patients and 13 years of follow-up were needed to demonstrate a statistically significance difference in survival. Currently ongoing and recent RCTs have demonstrated that it is both time/labor-intensive and expensive to recruit and retain participants. Recently conducted RCTs have needed to interview as many as 10-to-50 potentially-eligible patients for every one enrolled. To obtain reliable outcomes information, long-term retention (5–10 years or greater) of most of the patients is essential, but has proven an elusive goal for most weight-loss studies. Participant retention requires multi-faceted strategies and significant financial resources. Given the long durations of follow-up needed, rapid advances in bariatric techniques could make the examined procedures obsolete before the studies are concluded – as occurred with VBG in the SOS. Finally, funding for the surgical procedures remains a major problem for conducting bariatric surgery RCTs, since federal research funding agencies do not, in general, pay for surgical care and payers are often unwilling to fund research. Despite these challenges, a multi-site, multi-funder collaborative effort could be one way to assemble the necessary resources to conduct a large RCT of bariatric surgery.

An alternative to a large, RCT is a pooled analysis of ongoing, smaller RCTs. If outcomes data from these studies could be combined and standardized follow-up protocols incorporated, they could answer important questions regarding the durability of weight loss, T2DM remission and improvements in other comorbidities (hypertension, dyslipidemia) among patients with T2DM and mild to moderate obesity. This sort of study could yield robust information on the outcomes of bariatric surgery compared to non-surgical

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treatments. Given the sample size of currently active RCTs, a pooled cohort remains unlikely to adequately address some long-term bariatric surgery outcomes, such as survival, incident CV disease, and cancer.

Given the challenges of conducting large, long-term RCTs of bariatric surgery, continued investments in high quality, carefully designed observational studies should be considered. These studies will help to answer questions about the long-term efficacy and safety of surgical procedures and the durability of weight loss and health improvements. Typically, these studies lack an intensively treated control group. This could possibly be remedied by rigorous matching of surgical patients to other large cohorts previously receiving intensive lifestyle intervention for obesity (e.g., Look AHEAD, Diabetes Prevention Program). Alternatively, creation of new prospective observational usual-care cohorts with long-term follow-up using well-defined electronic medical record (EMR) populations could provide reasonable comparison populations. Existing observational studies also include very few SG patients, which is important, since this operation is increasingly popular. Long-term outcomes of SG as well as other evolving bariatric surgical procedures might be effectively studied by creation of prospective EMR populations.

Perhaps the most cost-efficient way to examine the long-term outcomes of bariatric surgery is to conduct additional analyses of large existing databases of patients whose clinical information is accessible by EMR. Standardized, prospective surgical registries should also be developed to follow-up bariatric patients in settings with high-quality EMR information. Although these types of studies have many potential biases owing to their observational designs and reliance on data collected in routine clinical care,[47] prior EMR-based studies have yielded important findings, and additional studies could address key questions in many areas, including survival, cancer incidence, comparative effectiveness of bariatric procedures, as well as the heterogeneity of treatment effects in subpopulations of severely obese patients, such as racial and ethnic minority groups.

Bariatric surgery and its short-term outcomes have greatly improved since the last NIH conference in 1991. Nevertheless, questions remain about the long-term outcomes of these procedures. The available evidence clearly shows that bariatric surgical procedures result in greater weight loss than non-surgical treatment. Bariatric surgery more effectively induces short-term T2DM remission than non-surgical treatments for obese patients. More knowledge is needed regarding the long term sustainability of surgically-induced weight loss and subsequent improvement in obesity-related comorbid disease. Similarly, more information is needed regarding the long term safety and complication profiles for these operations. Previous investments in bariatric surgery research provided findings important to the understanding of this very effective treatment for obesity. More research is needed, most likely through carefully designed observational studies, to more fully understand the entire spectrum of long term outcomes from bariatric surgery.

Acknowledgments

Dana Andersen, MD, Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD and Karen Teff, MD, Division of Diabetes,

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Table 1

Examples of recent long-term studies of bariatric surgery outcomes and their limitations

Study/Lead Author	Study Design	Populations and Procedures	Follow-up Duration	Published Outcomes	Limitations
Swedish Obese Subjects Study/ Sjostrom[15,17,18,20,22]	Prospective observational with matched controls	2010 surgical cases (13% RYGB; 19% banding; 68% VBG) and 2037 matched controls	10 to 20 years depending on the report	Surgery was associated with greater weight loss at 2 years (−23% vs. 0%) and 20 years (−18% vs. −1%)[17]; Lower overall mortality (HR: 0.71; P=0.001)[20]; Lower incidence of T2DM (HR: 0.17; P<0.001)[22], myocardial infarction (HR: 0.71; P=0.02)[17], stroke (HR: 0.66; P=0.008)[17], and cancer (in women only; HR: 0.58; P=0.0008)[18]; and greater remission of T2DM after 2 years [OR for remission: 8.4; P<0.001] and 10 years (OR: 3.5; P<0.001).[15]	Not randomized; includes mostly procedures (87%) that are no longer in use today; involves patients from a single country with little racial/ethnic diversity
Utah Mortality Study/Adams[24]	Retrospective observational with matched controls	7,925 RYGB cases and 7,925 weight-matched controls	Mean 7.1 years	40% reduction in all-cause mortality (HR: 0.60; P<0.001) and a 49% and 92% reduction in CV mortality (HR: 0.51; P<0.001) and T2DM mortality (HR: 0.08; P=0.005)	Not randomized; matching based on self-reported height and weight from drivers-license database; includes only RYGB procedures; patients from a single state
Utah Obesity Study/Adams[3]	Prospective observational with matched controls	400 RYGB cases; 400 bariatric surgery seekers that did not undergo operation (control 1); 400 population-based matched controls (control 2)	6 years	RYGB group lost 27.7% body weight compared to 0.2% weight gain in control group 1, and 0% change in control group 2. T2DM remission in 62% of RYGB patients and only 8% and 6% in each of the control groups (P<0.001), while incident T2DM was observed in 2% of RYGB patients but 17%, 15% of the control groups at 6 years (P<0.001). Surgery associated with greater improvements in blood pressure, cholesterol, and quality of life (P<0.01).	Not randomized; includes only RYGB procedures; patients from a single state
Department of Veterans Affairs/ Maciejewski[44,45]	Retrospective observational with matched controls	847 surgical cases and 847 matched controls	6.7 years	In unadjusted analyses, surgery was associated with reduced mortality (HR: 0.64; 95% CI: 0.51–0.80).[45] After propensity-matching patients, bariatric surgery was no longer significantly associated with reduced mortality in unadjusted (HR: 0.83; 95% CI, 0.61–1.14) and time-adjusted (HR: 0.94; 95% CI, 0.64–1.39) Cox regressions.[45] Surgery was also not significantly associated with	Not randomized; includes older (mean age 55), primarily male (74%) veterans; mostly RYGB procedures

Study/Lead Author	Study Design	Populations and Procedures	Follow-up Duration	Published Outcomes	Limitations
				lower health expenditures 3 years after the procedure.[44]	
Longitudinal Assessment of Bariatric Surgery/LABS Consortium[38]	Prospective observational	2,458 surgical cases (70.7% RYGB; 24.8% AGB; 5% other procedures)	3 years currently (plan for 5 years)	Median percent weight loss 31.5% for RYGB and 15.9% for AGB; T2DM remission in 67.5% of RYGB cases and 28.6% for AGB; Dyslipidemia remission in 61.9% RYGB and 27.1% AGB; HTN remission in 38.2% RYGB and 17.4% AGB. Other procedures not reported	Not randomized; lacks non-surgical control population; primarily RYGB procedures; in-person weight measures available on 66% of RYGB cases and 76% of LAGB cases
HMO Research Network/Arterburn[46]	Retrospective observational	4,434 RYGB cases with T2DM	Median 3.1 years	68 % (95 % CI: 66 to 70 %) experienced an initial T2DM remission within 5 years after RYGB. Among these, 35.1 % (95 % CI: 32 to 38 %) redeveloped T2DM within 5 years. The median duration of T2DM remission was 8.3 years.	Not randomized; lacks non-surgical control population; only RYGB procedures
Michigan Bariatric Surgery Collaborative/Birkmeyer[43]	Prospective observational	Varies depending on publication; 8,847 to 35,477	Varies depending on publication; 30-days to 3 years	Complication rates for SG (6.3%) were significantly lower than for RYGB (10.0%, P < 0.0001) but higher than AGB (2.4%, P < 0.0001). Excess body weight loss at 1 year was 13% lower for SG (60%) than for RYGB (69%, P < 0.0001), but was 77% higher for SG than for LAGB (34%, P < 0.0001).	Not randomized; lacks non-surgical control; patients from a single state

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Table 2

Recently Published Randomized Control Trials Comparing Bariatric Surgery to Non-Surgical Treatment of Obesity and Type 2 Diabetes

Study/Lead Author	Study Design	Populations and Procedures	Follow-up Duration	Outcomes	Limitations
Stampede I Trial/Schauer[4]	12-month, 3-arm, unblinded RCT at a single center	150 subjects, BMI 27–43, diagnosis of T2DM (A1c > 7.0%); Tx arms: medical therapy alone vs. medical therapy plus RYGB or sleeve gastrectomy	12 months	93% retention. Primary endpoint A1c ≤6.0% achieved by 12% medical group, 42% RYGB and 37% sleeve; EWL 13%, 88%, and 81% respectively; RYGB achieved endpoint with no medications; medical group increased medications; Adverse events requiring hospitalizations occurred in 9% medical, 22% RYGB and 8% sleeve.	Single center
Mingrone[5]	24-month, 3-arm, unblinded RCT at a single center	60 subjects, BMI > 35, T2DM duration ≥5 years, A1c ≥ 7.0%; Tx arms: conventional medical therapy, RYBG, open BPD	24 months	93% retention. Primary endpoint FPG <100 mg/dL and A1c <6.5% without medication. Achieved by 75% RYGB and 95% BPD; mean A1c 7.69%, 6.35%, 4.95% in medical, RYGB, and BPD groups, respectively; all surgical patients discontinued medications within 15 days surgery; 4 adverse events	Single center; diabetes remission in medical group not a goal, medical group less well characterized
The Diabetes Surgery Study/Ikramuddin[6]	12-month, 2-arm unblinded RCT at 4 teaching hospitals in US and Taiwan	120 subjects, A1c ≥8.0%, BMI 30.0–39.9, C peptide >1.0 ng/mL, T2DM duration ≥ 6 mos.; Tx arms: lifestyle-intensive medical management intervention and medical management plus RYGB	12 months	95% retention. Primary endpoint A1c <7.0%, LDL < 100 mg/dL, SBP< 130 mm/Hg. Achieved by 49% RYGB and 19% medical subjects; RYGB subjects required 3.0 less medications and lost 26.1% initial body weight vs. 7.9% in the medical group; 22 serious adverse events in RYGB	High complication rate; composite outcome driven primarily by T2DM remission
Dixon[26]	24- month, 2-arm, unblinded RCT at a single site	60 subjects, BMI > 30 and < 40, T2DM diagnosed < 2 years, Tx arms: Conventional T2DM therapy vs. LAGB with conventional T2DM care	24 months	92% retention; Primary endpoints FPG < 126 mg/dL and A1c < 6.2% without medication; secondary measures weight and components of metabolic syndrome; T2DM remission achieved by 73% surgical and 13% conventional-therapy. 20.7% vs. 1.7% weight loss in surgical vs. conventional groups; no serious complications	Recent T2DM diagnosis
O'Brien[27]	24-month, 2-arm, unblinded RCT at a single site	80 subjects BMI 30–35; Tx arms: pharmacotherapy/lifestyle (nonsurgical) and LAGB	24 months	98% LAGB retention, 83% nonsurgical retention; Primary end point weight loss. 21.6% initial weight lost and 87.2% excess weight lost in LAGB; 5.5% initial weight lost and 21.8% excess weight lost in nonsurgical. Metabolic syndrome (defined by the Adult Treatment Panel III criteria present initially in 15 (38%) subjects in each group, at 24 mos. present in 8 nonsurgical and 1 surgical subject	Less focus on T2DM

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Table 3

Deficiencies in Knowledge of Long-Term Bariatric Surgery Outcomes

Area of Knowledge Gap	Issues, Problems	Potential Study Designs
Surgical complications - Incidence	Standards for completeness of follow-up and management of missing data are needed.	Comparative safety of surgical procedures; analyses of EMR databases
Predictors of surgical outcomes	Very little data available to inform which patient should undergo which procedure	Comparative outcomes of surgical procedures; analyses of EMR databases
Overall mortality/survival	Data from observational trials only	Long term observational and RCTs; analyses of EMR databases
T2DM remission	Little data on durability of remission	Long term observational and RCTs; analyses of EMR databases
T2DM micro vascular complications	No data on long-term microvascular disease	Long term observational and RCTs; analyses of EMR databases
Cardiovascular events (stroke, MI)	Data from two observational studies, only	Long term observational and RCTs; analyses of EMR databases
Mental Health outcomes, including suicidality, alcohol, substance abuse, other risk-taking behaviors	Comprehensive, long term data lacking for most mental health outcomes	Long term studies with focus on mental health outcomes; analyses of EMR databases
Cancer	Data from two observational studies, only	Long term studies with accurate cancer incidence; analyses of EMR databases
Reproductive outcomes	Very little data available	Short and longer term observational studies; analyses of EMR databases
Cost and health care use	Lack of data with standard reporting of cost and use outcomes	Short and longer term data with cost and health care use; analyses of EMR databases outcomes in surgical vs. control groups