

Obesity and Diabetes: Evaluating the Bariatric Surgery Option

A review of available literature

This white paper has been prepared by Ethicon US, LLC, and has not been subject to peer review.

Bariatric surgery is used in the treatment of qualifying obese adult patients for significant long-term weight loss. Individual results following bariatric surgery may vary. Bariatric surgery may be appropriate for some patients and not for others, depending on their specific weight, age, and medical history. Patients and doctors should review all available information on non-surgical and surgical options in order to make an informed treatment decision.

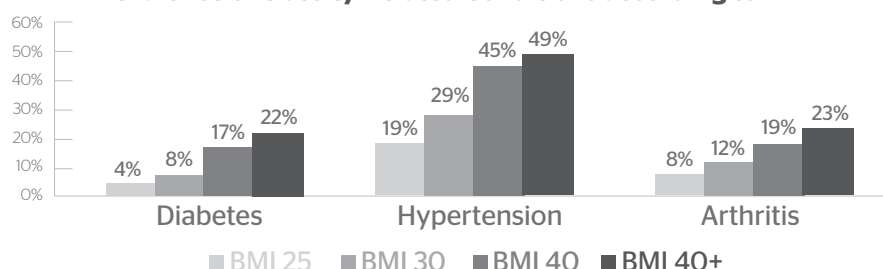
ETHICON manufactures and markets general surgical instruments used in bariatric surgery. The potential benefits discussed are associated with the patient's weight loss and other metabolic effects following bariatric surgery, not with the use of the instruments. ETHICON is offering this information in good faith as an overview to published literature in this area and a starting point for further research. It is not intended to constitute medical advice or recommendations.

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Introduction

Obesity, a chronic disease of substantial public health concern in the United States, is now being classified as an epidemic.¹ More than one third of the American adult population, 75 million adults, is classified as having obesity, with 15 million people classified as having severe obesity (a body mass index (BMI) of ≥ 40 kg/m²).² Often, individuals living with obesity suffer from obesity-related health conditions such as type 2 diabetes (T2DM), hypertension, hyperlipidemia, sleep apnea and arthritis.³ There are over 40 known obesity-related conditions.³ This is particularly problematic because when BMI increases so does the prevalence of obesity-related conditions.⁴ As a result, patients with severe obesity often experience diminished quality of life and increased mortality.^{4,5}

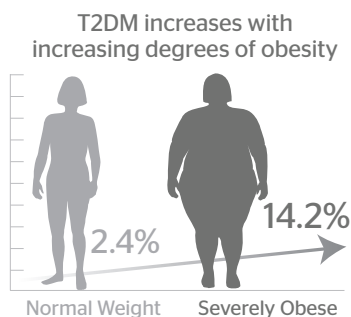
Prevalence of Obesity-Related Conditions according to BMI



Data source: Stommel M, et al. Obesity. 2010;18(9):1821-1826.

The Link between Obesity and Diabetes

Evidence has demonstrated that obesity is a major independent risk factor for the development of diabetes.⁶ As abdominal fat mass, waist circumference, and waist-to-hip circumference ratio increase, so does the risk for developing type 2 diabetes mellitus (T2DM).⁷ More than 90% of individuals with T2DM also are overweight.⁸ The risk for developing T2DM begins at a BMI as low as 22 kg/m².⁹ The relative risk of developing T2DM increases linearly by approximately 25% for each additional unit of BMI.^{8,9} Adults aged 35-59 with a BMI between 40 and 50 kg/m² are 22.5 times more likely to die from T2DM than those with a BMI of 22.5-25 kg/m².¹⁰



According to a National Health and Nutrition Examination Survey (NHANES; n=4,205) taken between 1999 and 2004, the prevalence of diabetes increases with increasing degrees of obesity. 14.2% of individuals with BMI greater than 40 kg/m² had T2DM, while in normal weight individuals, diabetes presented in only 2.4%.¹¹

Of the portion of patients who have obesity, approximately 15% have T2DM and experience insulin resistance.¹² A possible physiological cause of insulin resistance is a decrease in the cytokine adiponectin in individuals with obesity. Obesity often leads to a decrease of adiponectin release from adipose tissue, which potentially increases insulin resistance, contributing to the risk for development of T2DM.¹³ For patients with obesity, the body may not be able to respond appropriately to normal or even high circulating levels of insulin, resulting in increased T2DM risk in these patients. Excess adipose tissue derives free fatty acids, which can weaken the body's sensitivity to insulin at high levels. Excess free fatty acids impair the function of β -cells in the pancreas, which are responsible for the secretion of insulin.¹³ This combination prevents the body from using insulin correctly, decreasing insulin-mediated glucose uptake in peripheral tissues.¹⁴

The Bariatric Surgery Treatment Option for Obesity

Traditional approaches to weight loss, including changes in diet and physical activity, are important for a healthy lifestyle. However, a landmark Swedish study found that on average, a 200-pound patient fighting obesity with diet and exercise alone would only be able to achieve a sustained weight loss of 4 pounds over 20 years.¹⁵ Weight loss resulting from behavioral interventions generally leads to a

“starvation response”.¹⁵ The body seeks to defend its body weight by increasing appetite while lowering the metabolism.¹⁵ This limits weight loss and promotes weight regain.¹⁵

Bariatric surgery helps to reset the body’s ability to effectively manage weight by altering the complex relationship the body has with food and its metabolism. New research indicates that with procedures that alter the stomach or intestine, surgery has metabolic and hormonal impacts that enable the body to regulate itself down to a lower set point for body fat. Following bariatric procedures such as sleeve gastrectomy and gastric bypass, the digestive tract is altered in a way that decreases appetite due to modification of gastrointestinal (GI) hormone levels including ghrelin, glucagon-like peptide-1, peptide YY, cholecystokinin, amylin, leptin, insulin, and adiponectin.¹⁶ Many patients experience a decrease in hunger, increased satiety, and even healthier food preferences.¹⁷

Bariatric surgery is the most effective long-term treatment option for qualifying patients with obesity. It has been shown to improve associated conditions through weight loss, or in some cases such as T2DM, through metabolic processes that can complement or replace the need for other treatments.¹⁸ According to America Heart Association Scientific Statement from 2011, “it is clear that obesity surgery today offers the only effective long-term treatment option for the severely obese patient.”¹⁷ Bariatric surgery has been shown to provide the greatest amount of excess weight loss with greater than 45% one year post surgery compared to 10% or less for lifestyle and pharmacological treatments.^{19,20,21} Obesity-related health conditions have been resolved in up to 80% of patients.²² Approximately 179,000 bariatric procedures were performed in 2014 in the US.²³

A comparison of weight loss between obesity treatment options		
Treatment	Average Weight Loss at 3 years	Average Weight Loss at 5 years
Diet and Exercise	-0.1% ²⁴	-1.6% ²⁴
Drug Therapy	11.0% ²⁵	Not enough data
Surgery	Excess Weight Loss at 3 years	Excess Weight Loss at 5 years
Gastric Bypass	71.2% ²⁶	60.5% ²⁸
Sleeve Gastrectomy	66.0% ²⁷	49.0% ²⁸
Gastric Band	55.2% ²⁶	29.5% ²⁸

Percent average weight loss = % of total body weight lost as a result of treatment
Percent excess weight loss= % of body weight in excess of the ideal body weight that is lost as a result of treatment

T2DM Condition Improvements post Bariatric Surgery

For most patients with severe obesity, bariatric surgery produces excess weight loss of +25% at 5 years.²⁸ Bariatric surgery is an effective intervention for severe obesity and may reduce the risk for diabetes.²⁹ Both the American Heart Association (AHA) and the American Association of Diabetes (ADA) have published statements in support of bariatric surgery as a treatment option for T2DM. The AHA said that - “The most clinically relevant impact of surgically induced weight loss compared to medically induced weight loss on diabetes mellitus, is the ability of the former to completely reverse established diabetes mellitus in a large percentage of subjects.”¹⁷ The ADA also supports bariatric surgery as a possible diabetes treatment option stating that “Bariatric surgery should be considered for adults with BMI ≥ 35 kg/m2 and Type 2 Diabetes, especially if the diabetes is difficult to control with lifestyle and pharmacologic therapy.”³⁰

Since weight gain may be caused by some diabetic medications and insulin therapy, management of diabetes can be particularly challenging in patients with obesity, as metabolic control becomes further impaired.³¹ Ethicon sponsored a Cleveland Clinic randomized clinical trial study named the Surgical Therapy and Medications Potentially Eradicate Diabetes Efficiently study (STAMPEDE, n=150), which showed that uncontrolled diabetes in patients (40% of whom were on insulin) who are overweight or have obesity was managed more effectively with intensive medical therapy plus Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) surgeries, than with intensive medical treatment alone. “Control” of diabetes for this study was defined as HbA1c <6. Patients who underwent both medical therapy and either RYGB or SG had greater weight loss than patients who received only intensive medical therapy, including lifestyle counseling, weight management, frequent home glucose monitoring, and the use of newer drug therapies (e.g., incretin analogues) approved by the Food and Drug Administration. Findings indicated that at three years post-surgery with medical therapy, more patients achieved the glycemic target of HbA1c<6.0% (38% of RYGB patients; 24% of SG patients) than did patients with medical therapy alone (5%).³² Furthermore, half of the patients in the RYGB plus medical therapy group (58%) and a third of patients in the SG plus medical therapy group (33%) achieved glycemic control (HbA1c<7.0%) without the need for any diabetes medications 3 years post-surgery.³²

Compared with the reduction observed in the medical therapy alone group (6.0 mg·dL⁻¹), reductions in the median levels of fasting plasma glucose were significantly lower in patients undergoing medical therapy plus either RYGB (85.5 mg·dL⁻¹) or SG (46.0 mg·dL⁻¹) procedures.³² These improved health outcomes were accomplished with a concurrent, significant improvement in quality of life with improved scores on the validated SF-36 psychometric tool. Other outcomes, such as decreased weight, waist circumference, HbA1C, fat mass, lean mass, blood pressure, and triglyceride levels, as well as increased high-density lipoprotein cholesterol were also seen in patients undergoing medical therapy plus either RYGB or SG.³³ Since the publication of STAMPEDE, the dramatic impact of bariatric surgery on T2DM has been documented in numerous other randomized trials.³⁴

**Cleveland Clinic STAMPEDE Results as reported in the
New England Journal of Medicine - May, 2014³²**

	RYGB	SG	Control
HgA1c<6.0% 3 years post op	38%	24%	5%
HgA1c<6.0% 3 years post op without diabetes meds	35.5%	24.5%	0%
HgA1c<7.0% 5 years post op	58%	33%	9%
Reductions in median fasting plasma glucose	85.5 mg dL	46.0 mg dL	6.0 mg dL

Of note, all options included intensive medical therapy. The control group included ONLY intensive medical therapy.

Additional studies have shown that 12 months after bariatric surgery, patients demonstrated resolved (78.1%)³⁵ or improved (86.6%) diabetes and other obesity-related conditions,³⁶ and medication use for T2DM was reduced by 75%. In a retrospective matched cohort analysis from 2015, at 5 years post-surgery, insulin usage was reduced by 26% of surgical patients compared to only 9% of patients that did not have surgery.³⁷

Retrospective Matched Cohort Analysis of T2DM patients with and without bariatric surgery - 2015

	With Surgery	Without Surgery
Insulin Usage	Reduced by 26%	Reduced by 9%

In 2013 the British Medical Journal reported on "Bariatric Surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomized

controlled trials". This report included 11 studies, 796 patients with a BMI between 27-53. The results were that surgery was found to be superior to medical treatment in terms of weight loss, HbA1C control, T2DM remission, Triglycerides, HDL, remission of metabolic syndrome, quality of life measures and medication reduction with no difference in blood pressure or LDL. Furthermore there were no cardiovascular events or death after surgery.¹⁸

Diabetes control in obese patients can be facilitated by bariatric surgery. The probability of achieving T2DM remission post bariatric surgery is related to the disease severity (time since diagnosis and/or insulin use) at the time of surgery and bariatric procedure performed. Tools for predicting probability of remission have been developed, the DiaRem score and ABCD score. T2DM remission can be related to the bariatric procedure performed. The procedures that have been shown to have a greater metabolic response, namely the biliopancreatic diversion and duodenal switch, offer a higher probability of T2DM remission but also a higher probability of medically important nutritional deficiencies following the procedure.³⁸ Gastric bypass provides less nutritional risk long term³⁸ and has been shown to induce T2DM control even in patients requiring insulin pre-surgery.³⁹ Procedures which induce weight loss without realignment of the small bowel, such as sleeve gastrectomy and gastric banding, can also facilitate diabetes control and remission, but to a lesser degree than the metabolic procedures, and are most effective early in the disease process.⁴⁰ With excess weight loss ranging from 23% for laparoscopic adjustable gastric banding to up to 95% for biliopancreatic diversion with duodenal switch there is wide variation on the effect of bariatric procedures to T2DM remission.³⁸ In some patients, early remission of diabetes may occur within days after surgery and before major weight loss has been achieved.³⁸

**T2DM Elimination of Medications comparing
surgical and non-surgical**

	No longer needed	Substantially reduced
Gastric bypass	84%	93%

"Residual hyperglycemia is easier to manage following bariatric surgery. It can therefore be argued that bariatric surgery for the severely obese with Type 2 diabetes should be considered early as an option for eligible patients, rather than being held back as a last resort." (International Diabetes Foundation).⁴¹

Bariatric surgery may also reduce the risk for diabetes in patients with pre-diabetes. According to the Swedish Obesity Study (SOS), in subjects without diabetes at baseline, the risk of developing T2DM was reduced by 96% two years post-surgery and by 78% fifteen years post-surgery.⁴² Bariatric surgery has been effective for the treatment of uncontrolled diabetes, as well as lowering the risk for T2DM.⁴³

Cost Effectiveness of Bariatric Surgery

Following bariatric surgery, patients may have substantially lower costs associated with reduced medications and a reduced interaction with all levels of the healthcare system as their obesity-related conditions improve.⁴⁴ In a study on patients with T2DM, there was an 88% cost savings for T2DM medications at 12 months following gastric bypass⁴⁵ and 80%-99.7% cost savings following sleeve gastrectomy.⁴⁶ The average T2DM medication usage dropped by half in 12 months.⁴⁷

The cost of surgery may begin to be recouped within the first four years, and related cost savings for antidiabetic, antihypertensive and dyslipidemia agents continue through six years.⁴⁸ According to the American Journal of Managed Care (AJMC), a peer-reviewed journal on health outcomes research, health insurers recover their costs for bariatric surgery in about two years for laparoscopic surgery and in about four years for open surgery.⁴⁹ The analysis covered six months of pre-surgical evaluation and care, the surgery itself, and up to five years of post-surgical care. Bariatric surgery appears to be a clinically effective and cost-effective intervention for moderately to severely obese people compared with non-surgical interventions.

Bariatric Surgery Risks

All surgeries have risks, such as adverse reactions to medications, problems with anesthesia, problems breathing, bleeding, blood clots, inadvertent injury to nearby organs and blood vessels, even death. According to outcomes data from Bariatric Surgery Centers of Excellence, bariatric surgery has an overall mortality of about 0.1%,⁵⁰ which is less than cholecystectomy (0.7%)⁵¹ and hip replacement (0.93%)⁵² surgeries. The success of bariatric surgery is highly correlated with the experience of both the surgeon and the health center.

The overall likelihood of bariatric surgery major complications is 4.3%.⁵³ The risk for serious complications depends on the type of bariatric surgery, the patient’s medical condition, and age, as well as the surgeon’s and anesthesiologist’s experience. General risks associated with bariatric surgery include a failure to lose weight, nutritional or vitamin deficiencies, inflammation of the gallbladder, gallstones, dilated pouch, dysphagia, GERD, incisional hernia, malnutrition, and weight regain. Bariatric surgery may also cause changes to the autonomic nervous system, specifically to the processes that regulate energy balance and metabolic function. While these changes may help to sustain a lower weight set point, they also could induce changes to circulating bile acids, distribution of bacteria in the gut microbiota, and altered vagal and sympathetic neural activity.^{54,55}

Each type of bariatric surgery is associated with its own risks. Risks related to gastric bypass may include nutrient deficiency, anastomotic stenosis, leak or fistula, marginal ulcer/gastritis and stenosis, bowel injury or obstruction, nausea/vomiting, internal/incisional hernia, and pouch dilation.⁵⁶ Sleeve gastrectomy may be associated with gastric leak, intra-abdominal abscess, pulmonary embolism, delayed gastric emptying, splenic injury, stricture, and late choledocholithiasis.⁵⁷ Gastric banding risks can include gastric perforation, port rotation or leak, band or port-site infection, band obstruction, malposition, nausea/vomiting, and band erosion.⁵⁶

Identifying a Candidate for Bariatric Surgery

Bariatric surgery can be considered for weight reduction in patient that are 18 years of older with a BMI of >40 or ≥35 with an obesity related condition. Bariatric surgery is a viable alternative when diet exercise and other behavioral interventions are not effective. Bariatric surgery has been shown to produce +25% weight loss at 5 years.²⁸ Bariatric surgery can be considered for patient with obesity that are already diagnosed with T2DM, that are pre-diabetic or that have a high risk for diabetes.³⁰

Since bariatric surgery is a life changing event it is important to ensure patients are well informed, motivated and cognizant of the operative risk. It is also important to advise patients on the need for long term follow up. Clinical evidence suggests that the overall risks of severe obesity often outweigh the risks for bariatric surgery.⁵⁸ Bariatric surgery results may vary and surgery may or may not be

Mortality Rate for Surgical Procedures		
Bariatric Surgery	Cholecystectomy	Hip Replacement
0.1% ⁵⁰	0.7% ⁵¹	0.93% ⁵²

appropriate for particular patients depending on their specific age, weight and medical history. Patients and doctors should review all available medical information on surgical and non-surgical options in order to make an informed decision.

How to Refer Patients

After discussing a patient's candidacy for surgery, it is important to emphasize behavioral and psychological readiness for the procedure, discuss potential benefits and possible complications, manage post-operative expectations, as well as emphasize the long-term responsibilities associated with bariatric surgery. Patients should be encouraged to check with their current health insurance plan to determine specific requirements for surgery and proactively provide them with the necessary documentation that will be required for their surgical consultation. These documents may include weight loss attempts, medical records, and a pre-surgery health evaluation.

Additional Resources

Online resources are available at ethicon.com/obesity, or ASMBS.com for those healthcare professionals interested in learning more about bariatric surgery or realize.com for patients who are interested in attending a local informational bariatric surgery seminar or finding a surgeon for a consultation.

Patients can receive more information and answers to common questions about obesity and bariatric surgery by calling: Ethicon's Call Center at **1 (855) 273-2549**.

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