HHS Public Access

Author manuscript

Curr Diab Rep. Author manuscript; available in PMC 2020 September 29.

Published in final edited form as:

Curr Diab Rep. ; 19(12): 156. doi:10.1007/s11892-019-1269-4.

Bariatric Surgery in the Treatment of Type 2 Diabetes

Alison H. Affinati[1], **Nazanene H. Esfandiari**[1], **Elif A. Oral**[1], **Andrew T. Kraftson**[1]

[1]Division of Metabolism, Endocrinology and Diabetes (MEND), Department of Internal Medicine, Michigan Medicine, University of Michigan, 24 Frank Lloyd Wright Drive, Lobby G, Suite 1500, Ann Arbor, MI 48106-0482, USA

Abstract

Purpose of Review—We seek to characterize the impact of bariatric surgery on diabetes mellitus by recalling its history, examining the clinical data, exploring the putative mechanisms of action, and anticipating its future.

Recent Findings—Results of clinical trials reveal that bariatric surgery induces remission of diabetes in 33–90% of individuals at 1-year post-treatment versus 0–39% of medically managed. Remission rates decrease over time but remain higher in surgically treated individuals. Investigations have revealed numerous actions of surgery including effects on intestinal physiology, neuronal signaling, incretin hormone secretion, bile acid metabolism, and microbiome changes.

Summary—Bariatric surgery improves control of diabetes through both weight-dependent and weight-independent actions. These various mechanisms help explain the difference between individuals treated surgically vs. medically. They also explain differing effects of various bariatric surgery procedure types. Understanding how surgery affects diabetes will help optimize utilization of the therapy for both disease prevention and treatment.

Keywords

Bariatric surgery; Metabolic surgery; Diabetes mellitus; Diabetes remission; Obesity

Introduction

"Diabesity" was coined in 1973 to emphasize the pathophysiologic interconnection between the diseases of type 2 diabetes and obesity [1, 2]. Since that time, the acceleration of diabesity's impact on health and economics has led Dr. Paul Zimmet to state that it "is likely to be the biggest epidemic in human history" [3]. Worldwide, 650 million individuals have the disease of obesity and over 400 million individuals have diabetes [4, 5]. The impact of these diseases on morbidity, mortality, quality of life, and healthcare costs have been well-

Andrew T. Kraftson, andrewkr@med.umich.edu.

This article is part of the Topical Collection on *Therapies and New Technologies in the Treatment of Diabetes*

Conflict of Interest Alison H. Affinati, Nazanene H. Esfandiari, and Andrew T. Kraftson declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (include name of committee + reference number) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

described [6]. Treating individuals with diabetes and obesity results in health improvements and long-term reductions in healthcare costs [7–9]. Unfortunately, significant health improvements can be difficult to attain and/or maintain even with the best available dietary, behavioral, and medication therapies available [2]. As an illustration of this point, the results of a study examining the 2012 claims data from the 50 largest metropolitan areas in the USA revealed that 44% of insured patients diagnosed with diabetes and receiving medication therapy were classified as having “uncontrolled” diabetes [10]. Similarly, conventional, lifestyle-focused weight management strategies face challenges in terms of degree of weight loss, weight maintenance, and attrition [11, 12]. Furthermore, individuals with both obesity and diabetes tend to lose less weight and have more difficulty maintaining a reduced-weight state when compared to individuals without diabetes [13, 14]. As such, there has been a pressing need for therapeutic options beyond the traditional medical tools. Bariatric surgery has emerged as the most effective treatment for weight loss and maintenance. Unsurprisingly, it is also being recognized as a highly effective treatment for type 2 diabetes [15]. Interestingly, the mechanisms by which surgery impacts glucose homeostasis are much more extensive than originally expected and continue to be elucidated. In this review, we will describe the clinical problem, the impact of bariatric surgery on diabetes, the physiologic mechanisms for the glycemic effects of surgery, and emerging policy discussions.

Obesity and Diabetes

The connection between obesity and type 2 diabetes has long been recognized [1]. Observationally, the rise in incidence and prevalence of diabetes has mirrored the rise in obesity prevalence rates [16, 17]. However, even though 90% of individuals with type 2 diabetes are obese, a substantially smaller fraction of individuals with obesity develop diabetes [4]. Yet, obesity is thought to be the strongest risk factor for development of type 2 diabetes [18]. This observation can be explained through an understanding of the biology of these diseases. Obesity is associated with various pathophysiologic changes that increase insulin resistance [19]. Despite the increase in insulin demand and decrease in insulin sensitivity, the pancreas can normally compensate by increasing insulin production to maintain glucose homeostasis. In contrast, when an individual with the genetic predisposition for type 2 diabetes is exposed to obesogenic environmental factors (increased fat/carbohydrate/caloric intake; decreased physical activity), pancreatic beta-cell dysfunction, altered adipose tissue function, and weight gain can occur [20]. The combination of progressively declining insulin production capacity and rising insulin resistance results in the inability of the body to maintain euglycemia. Eventually, this can be detected as impaired glucose tolerance and, later, clinical type 2 diabetes [19, 21]. Given the intersection between these processes, weight reduction has been the foundational treatment recommendation for individuals diagnosed with both obesity and diabetes [22]. Unfortunately, conventional methods to facilitate weight loss are unsuccessful for the majority of individuals [2]. Furthermore, many anti-diabetes medications such as insulin, sulfonylureas, meglitinides, and thiazolidinediones are associated with weight gain [23, 24]. Consequently, many individuals with diabetes remain in a vicious cycle where treatments for hyperglycemia can complicate long-term care by exacerbating obesity. Fortunately, weight-

negative anti-diabetes treatment options such as glucagon-like peptide-1 receptor agonists (GLP-1 RA) and sodium glucose transporter-2 inhibitors have become available [25]. Yet, the magnitude of the weight loss seen with use of these medications is often insufficient to address severe obesity [26, 27].

After years of observing that shortened guts were associated with weight loss, surgeons in the 1950s started to develop surgical procedures to treat obesity [15]. Over the ensuing decades, surgical options have evolved in pursuit of the goal of optimizing both safety and efficacy. The types of bariatric surgery are reviewed in Table 1 [28–30].

As of 2019, the most commonly performed surgeries are sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), laparoscopic adjustable gastric band (LAGB), and biliopancreatic diversion with duodenal switch (BPD/DS) [28]. As the techniques have changed and matured, the understanding of the mechanisms by which surgery facilitates weight loss and maintenance of a reduced-weight state has also evolved. At first, weight loss was thought to occur primarily through caloric restriction and/or malabsorption and surgical procedures were categorized based on these presumed mechanisms of action. It is now recognized that most of the current, commonly performed surgeries improve both obesity and its comorbidities (including type 2 diabetes) through pleiotropic effects on intestinal physiology, transcriptional programs in intestinal differentiation programs, neuronal signaling, incretin hormone secretion, bile acid metabolism, lipid regulation, microbiome changes, and glucose homeostasis. For this reason, many prefer to describe these procedures as types of “metabolic surgery” [31, 32]. These observations have led to intensified efforts to assess the impact of surgery on type 2 diabetes and better understand the mechanisms behind its effects.

Impact of Surgery on Type 2 Diabetes

Given the long-recognized association of type 2 diabetes and obesity, it was expected that glycemic control would improve as a result of surgically facilitated weight loss. However, the surprising observation of immediate, post-surgical glycemic improvement suggested short-term mechanisms of action that were distinct from (but complementary to) long-term mechanisms. These provocative anecdotal accounts and ensuing case reports paved the way for several cohort studies published in the 1980s that helped explore the impact of bariatric surgery on type 2 diabetes in both the short and long term. For example, one study of insulin-treated patients with type 2 diabetes recorded an improvement in glycated hemoglobin (HbA1c) from 11.8 to 7.9% following gastric bypass surgery and another study noted 139 of 141 patients were able to discontinue anti-diabetes medications by 4-month post-surgery [33, 34].

These early studies stimulated efforts to quantify the impact of bariatric surgery on type 2 diabetes. Consequently, metrics were needed as part of the assessment process. The chief metric that has emerged is the rate of inducing “diabetes remission.” Unfortunately, there has not been consensus on the definition of the term and the ensuing variations complicate review of the data. For example, some early cohort studies defined remission as medication-free euglycemia (i.e., normal range fasting blood sugar and/or HbA1c) while others allowed for continued monotherapy with metformin [35–37]. In 2009, the American Diabetes

Association (ADA) published a consensus statement defining complete diabetes remission as demonstrating normal fasting blood glucose levels and/or HbA1c without the use of anti-diabetes medications for at least 1 year. Partial remission was defined as HbA1c < 6.5% and fasting blood glucose less than 126 mg/dL without medications for 1 year [38]. Since then, many of recent studies have used similar definitions [39–42•]. Of note, at the time of manuscript submission, the upcoming revised ADA consensus statement on diabetes remission was still under development.

Regardless of the definitions used, clinical studies have repeatedly demonstrated the significant ability of surgery to improve glucose homeostasis and induce remission. Several large cohort studies comparing bariatric surgery to conventional obesity management have confirmed that bariatric surgery patients are able to achieve diabetes remission more frequently than those who use conventional obesity therapy alone [35–37, 43•, 44•]. For example, in the Swedish Obesity Study (SOS), of 343 patients that underwent bariatric surgery (VBG, LAGB, and RYGB), 72.4% achieved diabetes remission at 2 years, compared to only 16.4% of control patients [35]. Similarly, in a 2019 study that included 1111 patients with diabetes who underwent RYGB, 74% of patients had diabetes remission at 1 year [44•].

While cohort studies provide evidence that bariatric surgery can induce diabetes remission, they may be confounded by factors inherent to the patients that choose bariatric surgery over medical therapy. Additionally, some cohort studies use conventional obesity therapy, which may not include a rigorous, validated weight loss program as the control group [35, 44•], leading to under-estimation of the effectiveness of medical therapy and inflation of the efficacy of bariatric surgery. To address these concerns and improve scientific understanding, randomized controlled trials (RCTs) were conducted. These have been designed to compare the effectiveness of bariatric surgery and lifestyle/medical management to induce diabetes remission. The results of significant trials (cohort and RCT) are summarized in Table 2.

As seen by the studies summarized, there is a wide range of remission rates reported after surgical therapy. The heterogeneity is likely due to the diversity of surgical procedures included, the varied populations studied, and the different definitions of diabetes remission used. Additionally, studies can vary with respect to reporting cumulative remission (counted as any individual who ever achieved remission) and/or prevalent remission (counted as only individuals who were in remission at the time of measurement). Furthermore, some studies correct for attrition while others do not [54]. Despite this variability, the RCTs consistently demonstrate that bariatric surgery has a superior diabetes remission rate when compared to medical therapy. For example, after 1 year of treatment, diabetes remits in a substantial proportion (33–90%) of surgically managed individuals but only in a small minority (0–39%) of medically managed individuals (Table 2). As further evidence of this, a meta-analysis of clinical trials available through 2013 (with follow-up ranging from 40 weeks to 2 years) concluded that the relative risk of attaining diabetes remission was at least 5 times higher in surgically treated individuals versus non-surgical groups and possibly as much as 22 times higher [55].

Diabetes and Bariatric Surgery: Mechanisms

As the results of the numerous clinical studies have accumulated, many clinical and scientific questions have arisen. The most fundamental of these is: why does diabetes improve after surgery? In keeping with expectations, some degree of glycemic improvement after bariatric surgery is associated with weight loss. Indeed, 75% of patients who did not achieve diabetes remission had weight regain [47]. Insulin sensitivity, a crucial component of diabetes pathogenesis, improves in patients following bariatric surgery to a similar degree as in patients who have lost an equivalent amount of weight using caloric restriction [57, 59, 61]. The weight-dependence of improved insulin sensitivity is further supported in studies comparing SG and RYGB, which have differing effects on gut physiology. In patients that achieved 20% weight loss, both SG patients and RYGB patients achieved similar improvements in insulin sensitivity [62].

Somewhat less expected has been the discovery that the microbiome may contribute to improvement in glucose homeostasis following bariatric surgery. While it is unclear if changes in the gut microbiome cause metabolic improvement, or occur because of metabolic improvement, the gut microbiome is markedly altered following bariatric surgery with increased microbiome diversity within 3 months [63–66] in both RYGB and VBG. In rodents, fecal transplant from either mice or humans that have undergone RYGB into germ-free rats fed a high-fat diet results in weight loss and improvement in glycemic parameters, suggesting that, regardless of what causes the microbiome to change, the post-RYGB microbiome improves glycemic control [67, 68].

A striking feature of bariatric surgery is the rapid improvement in glycemic control that precedes weight loss. In some of the earliest case reports, authors remarked that some patients were insulin-free at the time of discharge despite having pre-surgical insulin requirements of hundreds of units [34]. What are the mechanisms that drive these rapid, weight-independent improvements in glucose homeostasis? The answer to this question is rather complex but starts with alterations in gut hormones which are worth reviewing here.

Glucagon-like peptide 1 (GLP-1) is a gut hormone secreted from intestinal neuroendocrine L cells which induces the “incretin effect” of increasing insulin secretion and glucose clearance in response to oral glucose. Following bariatric surgery, post-prandial GLP-1 levels are increased, leading to improved beta-cell glucose sensitivity and lower post-prandial blood glucose [69–72]. In mice lacking the GLP-1 receptor (GLP-1R KO mice), continued improvements in glucose homeostasis following SG and RYGB are observed [73–75], as occurs in patients treated with a GLP-1 receptor antagonist following bariatric surgery [76].

Other gut hormones that may contribute to improved glucose homeostasis include PYY and oxyntomodulin, both of which are increased following bariatric surgery. Indeed, a recent clinical trial of subcutaneous GLP-1, PYY, and oxyntomodulin combination therapy for 4 weeks demonstrated improved post-prandial glycemic control similar to that of RYGB patients [77].

As practice patterns evolved and as SG has superseded RYGB as the most commonly performed bariatric surgery [28], most recent studies have focused on comparisons between these two procedures. Based on these studies, it appears that patients who undergo “more” rearrangement of their GI tract have a small, but reproducible, improvement in long-term glycemic control compared to patients undergoing less drastic procedures. This is demonstrated by a recent meta-analysis that reviewed 16 RCTs comparing glycemic outcomes in patients who underwent SG versus RYGB and found that patients who underwent RYGB had lower fasting blood sugar and lower A1c at 3 years following surgery [78•]. In further support of this hypothesis, the lowest remission rate is reported for LAGB, which does not alter the gut anatomy, with a 1-year diabetes remission rate of 33% [79].

Why do some procedure types affect glycemic control more than others? Historically, two competing (but not mutually exclusive) hypotheses have emerged to explain how gut rearrangement leads to improvements in glycemic control: the hindgut hypothesis and the foregut-exclusion hypothesis.

The hindgut hypothesis states that bypassing the proximal small bowel causes rapid transit of nutrients into the distal bowel, increasing secretion of gut hormones such as GLP-1 and PYY. This is supported by rodent studies in which anastomosing the ileum to the proximal bowel increases gut transit time [80], while post-surgical GLP-1 levels are higher in rats that underwent RYGB than in those that underwent SG [81].

The foregut-exclusion hypothesis posits that exclusion of nutrients from the duodenum and proximal jejunum decreases secretion of an as-yet unidentified signal that increases insulin resistance. This hypothesis has been tested in rodent studies as well. Rats received either duodenojejunal bypass, which completely excludes nutrients from the duodenum and proximal jejunum, or gastrojejunostomy, in which nutrients are able to rapidly reach the distal jejunum, but still have access to the duodenum. Rats that underwent duodenal-jejunal bypass had a significant improvement in their glucose tolerance, while the gastrojejunostomy rats did not, leading to the proposal of “anti-incretin” factors secreted from the duodenum [82]. Based on these findings, less invasive metabolic surgeries are now under investigation that simply ablates the duodenal mucosa, known as duodenal mucosal resurfacing [83].

Another metabolic pathway that is altered following rearrangement of the gut is bile acid signaling. Serum bile acid concentrations and composition change following RYGB and SG, but not following LAGB. Bile acids act as hormones that bind to the hormone receptor FXR and lead to improvements in glucose tolerance [84–89]. In rodent studies, improvements in glucose tolerance following VSG are reduced in mice lacking FXR or its binding partner TGR5 [88, 89]. However, pharmacologic studies in rodents have also shown that both inhibition and activation of FXR result in improved metabolic phenotypes accompanied by weight loss, thus the specific effect of activating FXR-signaling is unclear.

Failure to Achieve Diabetes Remission and Relapse of Diabetes

While bariatric surgery clearly demonstrates a high ability to induce remission of type 2 diabetes, the clinical trial data also reveal that remission is not attained in all individuals.

Understanding the factors that predict glycemic response to surgery is critical in determining which patients are most likely to achieve diabetes remission. Several studies have addressed this question and the factors that are most associated with diabetes remission include shorter duration of diabetes prior to surgery (< 4 years), higher C-peptide, younger age, and use of only oral agents or diet to control diabetes [90–93]. While these collective data demonstrate the short-term efficacy of bariatric surgery, the durability of diabetes remission remains a pressing clinical question. Even though the majority of individuals will have long-term improvements in diabetes metrics (i.e., HbA1c < 7%, reduction in anti-diabetes medications, and reduction in complication rates), sustained remission is experienced by only a minority. Studies evaluating long-term outcomes have demonstrated an almost 50% relapse rate for patients who achieve diabetes remission [39, 44•, 47, 48, 50]. For example, 15-year follow-up data from the SOS revealed that rates of diabetes remission (defined as blood glucose levels under 110 mg/dL without anti-diabetes medication use) drop from 72.4% at 2 years post-surgery to 38.1% at 10 years and further to 30.4% at 15 years [60]. This is replicated in RCTs, as well. In a 2015 study conducted by Mingrone and colleagues in which individuals were randomized to medical therapy ($n = 20$), RYGB ($n = 20$), or BPD ($n = 20$), ADA partial remission was achieved at 2 years in 0, 75%, and 95% of individuals in these respective groups. By 5 years, the rates were 0, 37%, and 63% [47]. The factors that predict remission also contribute to achieving sustained remission. Predictors of relapse include insulin use and a longer duration of diabetes prior to surgery, with an HR of 1.13 for every additional prior year of having a diabetes diagnosis [39].

Impact of Bariatric Surgeryon Diabetes-Related Complications and Prevention

While diabetes remission rates are an important metric for assessing bariatric surgery's impact on type 2 diabetes, health benefits are not exclusively conferred to individuals attaining remission. Multiple cohort studies and RCTs demonstrate that patients who undergo bariatric surgery experience a significant reduction in the use of both oral anti-diabetic medications and insulin. In one study, there was an 87% reduction in oral medication use and a 79% reduction in patients who continue to require insulin [36, 41, 47, 49•]. Our own data from a real world setting suggest 68.7% vs 56.0% reduction in diabetes medication usage after GB versus SG [52•]. Moreover, the years spent in good control are known to have a legacy effect for the subsequent decade in terms of fewer diabetes complications. Therefore, it is not surprising that bariatric surgery is also associated with a decreased incidence rate of both diabetes-related microvascular and macrovascular complications and decreased mortality. In the 15-year follow-up of the SOS, microvascular complications were 20.6 per 1000 person-years in the surgical patients as compared to 41.8 per 1000 person-years in controls (HR of 0.44 for the surgical patients). Additionally, macrovascular complications were also lower in the surgical group (31.7 per 1000 person-years) as compared to the control group (44.2 per 1000 person-years) with an HR of 0.68 for surgical patients. Perhaps most importantly, this study and several others have also shown decreased long-term mortality in surgical patients [60, 94, 95].

Studies have also examined the effect of bariatric surgery on prevention of diabetes development. In the SOS trial, bariatric surgery reduced the risk of developing diabetes by 96% at 2 years post-intervention and 78% at 15 years [60, 96]. Given the data on complications and prevention, bariatric surgery is being recognized as a valuable tool for disease and complication prevention, not just treatment [97].

Bariatric Surgery: Diabetes Treatment Guidelines

Globally, consideration for bariatric surgery generally occurs for individuals that meet the 1991 National Institutes of Health (NIH) criteria [98]. Qualifying individuals must have a body mass index (BMI) ≥ 40 kg/m^2 or BMI ≥ 35 with a serious weight-related comorbid health condition (such as diabetes). Yet, studies such as the STAMPEDE trial have included participants with lower BMIs than the NIH criteria and provided evidence of benefit for these patients [49•].

Based on the growing body of evidence and the expanded understanding of the mechanisms of actions of metabolic surgeries, there has been a growing movement to expand the eligibility criteria for surgery. In 2016, the 2nd Diabetes Surgery Summit (DSS-II) was convened which led to a consensus statement for the use of surgery as a primary treatment method for type 2 diabetes. A joint statement of the partner societies (including the ADA, the International Diabetes Federation, Diabetes UK, the Chinese Diabetes Society, and Diabetes India) was released and called for bariatric surgery to be “considered in patients with class I obesity (BMI 30.0–34.9) and inadequately controlled hyperglycemia despite optimal medical treatment by either oral or injectable medications (including insulin)” [99]. This statement falls short of acknowledging the racial and ethnic differences of adiposity and the resulting metabolic complications across populations of the world. It will be interesting to see if the improved understanding of these differences will lead to recommendations for surgical interventions at lower adiposity ranges in populations where metabolic consequences of increased adiposity are noted at much lower BMI levels.

Conclusion

Diabetes and obesity pose individual and global health challenges to a scale that is unprecedented. While many conventional medical therapeutic options are available, they are not universally effective due to myriad physiological, behavioral, and financial barriers. Bariatric surgery has emerged as the single most effective treatment option for type 2 diabetes and obesity. It must be acknowledged that surgery does not address the fundamental problem of overabundance of energy availability. Yet, though not a panacea for the environmental challenges, or a cure for these diseases, surgery significantly decreases their burden through weight-dependent and weight-independent mechanisms. Furthermore, elucidating these mechanisms improves the understanding of the diseases, themselves. Consequently, bariatric surgery serves as both an illuminating scientific model and an effective treatment tool to address the diabesity crisis.

Funding Information

Alison H. Affinati reports a grant from NIDDK (F32 DK122660).

Elif A. Oral reports grants from Gi Dynamics; grants, personal fees, and non-financial support from Aegerion Pharmaceuticals; grants and personal fees from Akcea Therapeutics; grants from Ionis Pharmaceuticals; grants and personal fees from Regeneron Pharmaceuticals; and grants from Gemphire Therapeutics. In addition, Dr. Oral has a patent issue on an Intragastric device.

References

Papers of particular interest, published recently, have been highlighted as:

• Of importance

•• Of major importance

1. Sims EA, Danforth E, Horton ES, Bray GA, Glennon JA, Salans LB. Endocrine and metabolic effects of experimental obesity in man. Recent Prog Horm Res. 1973;29:457–96. [PubMed: 4750591]
2. Pappachan JM, Viswanath AK. Medical management of diabesity: do we have realistic targets? Curr Diab Rep. 2017;17(1):4. [PubMed: 28101792]
3. Zimmet PZ. Diabetes and its drivers: the largest epidemic in human history? Clin Diabetes Endocrinol. 2017;3(1):1. [PubMed: 28702255]
4. Diabetes [Internet]. [cited 2019 Jun 19]. Available from: https://www.who.int/news-room/fact-sheets/detail/diabetes
5. Obesity and overweight [Internet]. [cited 2019 Jun 19]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
6. Foster D, Sanchez-Collins S, Cheskin LJ. Erratum: multidisciplinary team-based obesity treatment in patients with diabetes: current practices and the state of the science. Diabetes Spectrum 2017;30: 244–249 (DOI: 10.2337/ds17-0045). [PubMed: 29151714] Diabetes Spectr. 2018;31(1):119.
7. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998 9 12;352(9131):854–65. [PubMed: 9742977]
8. Wing RR, Reboussin D, Lewis CE, Look AHEAD Research group. Intensive lifestyle intervention in type 2 diabetes. N Engl J Med. 2013;369(24):2358–9. [PubMed: 24328474]
9. Rothberg AE, McEwen LN, Fraser T, Burant CF, Herman WH. The impact of a managed care obesity intervention on clinical outcomes and costs: a prospective observational study. Obesity (Silver Spring). 2013;21(11):2157–62. [PubMed: 24136667]
10. Yang W, Dall TM, Tan E, Byrne E, Iacobucci W, Chakrabarti R, et al. Diabetes diagnosis and management among insured adults across metropolitan areas in the U.S. Prev Med Rep. 2018;10: 227–33. [PubMed: 29868373]
11. Miller WC, Koceja DM, Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. Int J Obes Relat Metab Disord. 1997;21(10): 941–7. [PubMed: 9347414]
12. Ayyad C, Andersen T. Long-term efficacy of dietary treatment of obesity: a systematic review of studies published between 1931 and 1999. Obes Rev. 2000;1(2):113–9. [PubMed: 12119984]
13. Wing RR, Marcus MD, Epstein LH, Salata R. Type II diabetic subjects lose less weight than their overweight nondiabetic spouses. Diabetes Care. 1987;10(5):563–6. [PubMed: 3677974]
14. Guare JC, Wing RR, Grant A. Comparison of obese NIDDM and nondiabetic women: short- and long-term weight loss. Obes Res. 1995;3(4):329–35. [PubMed: 8521149]
15. Celio AC, Pories WJ. A history of bariatric surgery: the maturation of a medical discipline. Surg Clin North Am. 2016;96(4):655–67. [PubMed: 27473793]
16. Colditz GA, Willett WC, Rotnitzky A, Manson JE. Weight gain as a risk factor for clinical diabetes mellitus in women. Ann Intern Med. 1995;122(7):481–6. [PubMed: 7872581]
17. Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care. 1994;17(9):961–9. [PubMed: 7988316]

18. GBD 2013 Risk Factors Collaborators, Forouzanfar MH, Alexander L, Anderson HR, Bachman VF, Biryukov S, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;386(10010):2287–323. [PubMed: 26364544]
19. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444(7121): 840–6. [PubMed: 17167471]
20. Reilly SM, Saltiel AR. Adapting to obesity with adipose tissue inflammation. Nat Rev Endocrinol. 2017;13(11):633–43. [PubMed: 28799554]
21. Almind K, Doria A, Kahn CR. Putting the genes for type II diabetes on the map. Nat Med. 2001;7(3):277–9. [PubMed: 11231616]
22. American Diabetes Association. 5. Lifestyle management: *Standards of Medical Care in Diabetes —2019*. Dia Care. 2019 1;42(Supplement 1):S46–60.
23. UK Prospective Diabetes Study 7: response of fasting plasma glucose to diet therapy in newly presenting type II diabetic patients, UKPDS Group. Metab Clin Exp. 1990 9;39(9):905–12. [PubMed: 2392060]
24. Pi-Sunyer FX. Weight loss in type 2 diabetic patients. Diabetes Care. 2005;28(6):1526–7. [PubMed: 15920086]
25. Joy SV, Rodgers PT, Scates AC. Incretin mimetics as emerging treatments for type 2 diabetes. Ann Pharmacother. 2005;39(1): 110–8. [PubMed: 15562141]
26. Rose F, Bloom S, Tan T. Novel approaches to anti-obesity drug discovery with gut hormones over the past 10 years. Expert Opin Drug Discovery. 2019;29:1–9.
27. Cai X, Yang W, Gao X, Chen Y, Zhou L, Zhang S, et al. The association between the dosage of SGLT2 inhibitor and weight reduction in type 2 diabetes patients: a meta-analysis: SGLT2 inhibitor dosage and weight reduction. Obesity. 2018;26(1):70–80. [PubMed: 29165885]
28. Story of Obesity Surgery [Internet]. American Society for Metabolic and Bariatric Surgery. 2004 [cited 2019 Jun 19]. Available from: https://asmbs.org/resources/story-of-obesity-surgery
29. Faria GR. A brief history of bariatric surgery: porto biomedical. Journal. 2017;2(3):90–2.
30. Gumbs AA, Gagner M, Dakin G, Pomp A. Sleeve gastrectomy for morbid obesity. Obes Surg. 2007;17(7):962–9. [PubMed: 17894158]
31. Buchwald H The evolution of metabolic/bariatric surgery. Obes Surg. 2014;24(8):1126–35. [PubMed: 25008469]
32. Peck BCE, Seeley RJ. How does “metabolic surgery” work its magic? New evidence for gut microbiota. Curr Opin Endocrinol Diabetes Obes. 2018;25(2):81–6. [PubMed: 29337705]
33. Herbst CA, Hughes TA, Gwynne JT, Buckwalter JA. Gastric bariatric operation in insulin-treated adults. Surgery. 1984;95(2):209–14. [PubMed: 6364435]
34. Pories WJ, Caro JF, Flickinger EG, Meelheim HD, Swanson MS. The control of diabetes mellitus (NIDDM) in the morbidly obese with the Greenville gastric bypass. Ann Surg. 1987;206(3):316–23. [PubMed: 3632094]
35. Sjöström L, Lindroos A-K, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351(26):2683–93. [PubMed: 15616203]
36. Schauer PR, Burguera B, Ikramuddin S, Cottam D, Gourash W, Hamad G, et al. Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. Ann Surg. 2003;238(4):467–84 discussion 84–85. [PubMed: 14530719]
37. Pournaras DJ, Osborne A, Hawkins SC, Vincent RP, Mahon D, Ewings P, et al. Remission of type 2 diabetes after gastric bypass and banding: mechanisms and 2 year outcomes. Ann Surg. 2010;252(6):966–71. [PubMed: 21107106]
38. Buse JB, Caprio S, Cefalu WT, Ceriello A, Del Prato S, Inzucchi SE, et al. How do we define cure of diabetes? Diabetes Care. 2009;32(11):2133–5. [PubMed: 19875608]
39. Arterburn DE, Bogart A, Sherwood NE, Sidney S, Coleman KJ, Haneuse S, et al. A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. Obes Surg. 2013;23(1):93–102. [PubMed: 23161525]

40. Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Leccesi L, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med. 2012;366(17):1577–85. [PubMed: 22449317]

41. Courcoulas AP, Goodpaster BH, Eagleton JK, Belle SH, Kalarchian MA, Lang W, et al. Surgical vs medical treatments for type 2 diabetes mellitus: a randomized clinical trial. JAMA Surg. 2014;149(7):707–15. [PubMed: 24899268]

42•. Salminen P, Helmiö M, Ovaska J, Juuti A, Leivonen M, Peromaa-Haavisto P, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y Gastric bypass on weight loss at 5 years among patients with morbid obesity: the SLEEVEPASS randomized clinical trial. JAMA. 2018;319(3):241. [PubMed: 29340676] This RCT compares LSG to RYGB with follow-up for up to 5 years.

43•. Jakobsen GS, Småstuen MC, Sandbu R, Nordstrand N, Hofsø D, Lindberg M, et al. Association of bariatric surgery vs medical obesity treatment with long-term medical complications and obesity-related comorbidities. JAMA. 2018;319(3):291. [PubMed: 29340680] This large study evaluates resolution of complications in patients undergoing bariatric surgery.

44•. Madsen LR, Baggesen LM, Richelsen B, Thomsen RW. Effect of Roux-en-Y gastric bypass surgery on diabetes remission and complications in individuals with type 2 diabetes: a Danish population-based matched cohort study. Diabetologia. 2019;62(4):611–20. [PubMed: 30734055] One of the largest studies to date evaluating diabetes outcomes following bariatric surgery.

45. Courcoulas AP, Belle SH, Neiberg RH, Pierson SK, Eagleton JK, Kalarchian MA, et al. Three-year outcomes of bariatric surgery vs lifestyle Intervention for type 2 diabetes mellitus treatment: a randomized clinical trial. JAMA Surg. 2015;150(10):931–40. [PubMed: 26132586]

46. Ding S-A, Simonson DC, Wewalka M, Halperin F, Foster K, Goebel-Fabbri A, et al. Adjustable gastric band surgery or medical management in patients with type 2 diabetes: a randomized clinical trial. J Clin Endocrinol Metab. 2015;100(7):2546–56. [PubMed: 25909333]

47. Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Nanni G, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5-year follow-up of an open-label, single-centre, randomised controlled trial. Lancet. 2015;386(9997):964–73. [PubMed: 26369473]

48. Cummings DE, Arterburn DE, Westbrook EO, Kuzma JN, Stewart SD, Chan CP, et al. Gastric bypass surgery vs intensive lifestyle and medical intervention for type 2 diabetes: the CROSSROADS randomised controlled trial. Diabetologia. 2016;59(5):945–53. [PubMed: 26983924]

49•. Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Aminian A, Brethauer SA, et al. Bariatric surgery versus intensive medical therapy for diabetes—5-year outcomes. N Engl J Med. 2017;376(7):641–51. [PubMed: 28199805] RCT with rigorous lifestyle intervention control group focused on diabetes outcomes following bariatric surgery.

50. Courcoulas AP, King WC, Belle SH, Berk P, Flum DR, Garcia L, et al. Seven-year weight trajectories and health outcomes in the longitudinal assessment of bariatric surgery (LABS) study. JAMA Surg. 2018;153(5):427. [PubMed: 29214306]

51•. Ikramuddin S, Korner J, Lee W-J, Thomas AJ, Connett JE, Bantle JP, et al. Lifestyle Intervention and Medical management with vs without Roux-en-Y gastric bypass and control of hemoglobin A $_{1c}$, LDL cholesterol, and systolic blood pressure at 5 years in the diabetes surgery study. JAMA. 2018;319(3):266. [PubMed: 29340678] Five-year follow-up of RCT comparing medical management with RYGB.

52•. Lager CJ, Esfandiari NH, Luo Y, Subauste AR, Kraftson AT, Brown MB, et al. Metabolic Parameters, Weight Loss, and Comorbidities 4 years after Roux-en-Y gastric bypass and sleeve gastrectomy. Obes Surg. 2018;28(11):3415–23. [PubMed: 29909517] Retrospective analysis comparing metabolic outcomes in RYGB versus LSG.

53•. Simonson DC, Halperin F, Foster K, Vernon A, Goldfine AB. Clinical and patient-centered outcomes in obese patients with type 2 diabetes 3 years after randomization to Roux-en-Y gastric bypass surgery versus intensive lifestyle management: the SLIMM-T2D study. Diabetes Care. 2018;41(4):670–9. [PubMed: 29432125] RCT evaluating RYGB versus lifestyle management in patients with type 2 diabetes.

54. Isaman DJM, Rothberg AE, Herman WH. Reconciliation of type 2 diabetes remission rates in studies of Roux-en-Y gastric bypass. Diabetes Care. 2016;39(12):2247–53. [PubMed: 27737910]
55. Gloy VL, Briel M, Bhatt DL, Kashyap SR, Schauer PR, Mingrone G, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. BMJ. 2013;347:f5934. [PubMed: 24149519]
56. Halperin F, Ding S-A, Simonson DC, Panosian J, Goebel-Fabbri A, Wewalka M, et al. Roux-en-Y gastric bypass surgery or lifestyle with intensive medical management in patients with type 2 diabetes: feasibility and 1-year results of a randomized clinical trial. JAMA Surg. 2014;149(7):716–26. [PubMed: 24899464]
57. Isbell JM, Tamboli RA, Hansen EN, Saliba J, Dunn JP, Phillips SE, et al. The importance of caloric restriction in the early improvements in insulin sensitivity after Roux-en-Y gastric bypass surgery. Diabetes Care. 2010;33(7):1438–42. [PubMed: 20368410]
58. Liang Z, Wu Q, Chen B, Yu P, Zhao H, Ouyang X. Effect of laparoscopic Roux-en-Y gastric bypass surgery on type 2 diabetes mellitus with hypertension: a randomized controlled trial. Diabetes Res Clin Pract. 2013 7;101(1):50–6. [PubMed: 23706413]
59. Jackness C, Karmally W, Febres G, Conwell IM, Ahmed L, Bessler M, et al. Very low-calorie diet mimics the early beneficial effect of Roux-en-Y gastric bypass on insulin sensitivity and β-cell function in type 2 diabetic patients. Diabetes. 2013;62(9):3027–32. [PubMed: 23610060]
60. Sjöström L, Peltonen M, Jacobson P, Ahlin S, Andersson-Assarsson J, Anveden Å, et al. Association of bariatric surgery with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. JAMA. 2014;311(22):2297–304. [PubMed: 24915261]
61. Bradley D, Conte C, Mittendorfer B, Eagon JC, Varela JE, Fabbrini E, et al. Gastric bypass and banding equally improve insulin sensitivity and β cell function. J Clin Invest. 2012;122(12):4667–74. [PubMed: 23187122]
62. Peterli R, Wölnerhanssen BK, Peters T, Vetter D, Kröll D, Borbély Y, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss in patients with morbid obesity: the SM-BOSS randomized clinical trial. JAMA. 2018;319(3):255. [PubMed: 29340679]
63. Zhang H, DiBaise JK, Zuccolo A, Kudrna D, Braidotti M, Yu Y, et al. Human gut microbiota in obesity and after gastric bypass. Proc Natl Acad Sci U S A. 2009;106(7):2365–70. [PubMed: 19164560]
64. Furet J-P, Kong L-C, Tap J, Poitou C, Basdevant A, Bouillot J-L, et al. Differential adaptation of human gut microbiota to bariatric surgery-induced weight loss: links with metabolic and low-grade inflammation markers. Diabetes. 2010;59(12):3049–57. [PubMed: 20876719]
65. Kong L-C, Tap J, Aron-Wisnewsky J, Pelloux V, Basdevant A, Bouillot J-L, et al. Gut microbiota after gastric bypass in human obesity: increased richness and associations of bacterial genera with adipose tissue genes. Am J Clin Nutr. 2013;98(1):16–24. [PubMed: 23719559]
66. Palleja A, Kashani A, Allin KH, Nielsen T, Zhang C, Li Y, et al. Roux-en-Y gastric bypass surgery of morbidly obese patients induces swift and persistent changes of the individual gut microbiota. Genome Med. 2016;8(1):67. [PubMed: 27306058]
67. Liou AP, Paziuk M, Luevano J-M, Machineni S, Turnbaugh PJ, Kaplan LM. Conserved shifts in the gut microbiota due to gastric bypass reduce host weight and adiposity. Sci Transl Med. 2013;5(178):178ra41.
68. Arora T, Seyfried F, Docherty NG, Tremaroli V, le Roux CW, Perkins R, et al. Diabetes-associated microbiota in fa/fa rats is modified by Roux-en-Y gastric bypass. ISME J. 2017;11(9):2035–46. [PubMed: 28524868]
69. Jørgensen NB, Dirksen C, Bojsen-Møller KN, Jacobsen SH, Worm D, Hansen DL, et al. Exaggerated glucagon-like peptide 1 response is important for improved β-cell function and glucose tolerance after Roux-en-Y gastric bypass in patients with type 2 diabetes. Diabetes. 2013;62(9):3044–52. [PubMed: 23649520]
70. Falkén Y, Hellström PM, Holst JJ, Näslund E. Changes in glucose homeostasis after Roux-en-Y gastric bypass surgery for obesity at day three, two months, and one year after surgery: role of gut peptides. J Clin Endocrinol Metab. 2011;96(7):2227–35. [PubMed: 21543426]

71. Bose M, Teixeira J, Olivan B, Bawa B, Arias S, Machineni S, et al. Weight loss and incretin responsiveness improve glucose control independently after gastric bypass surgery. J Diabetes. 2010;2(1): 47–55. [PubMed: 20676394]

72. Laferrère B, Heshka S, Wang K, Khan Y, McGinty J, Teixeira J, et al. Incretin levels and effect are markedly enhanced 1 month after Roux-en-Y gastric bypass surgery in obese patients with type 2 diabetes. Diabetes Care. 2007;30(7):1709–16. [PubMed: 17416796]

73. Ye J, Hao Z, Mumphrey MB, Townsend RL, Patterson LM, Stylopoulos N, et al. GLP-1 receptor signaling is not required for reduced body weight after RYGB in rodents. Am J Phys Regul Integr Comp Phys. 2014;306(5):R352–62.

74. Wilson-Pérez HE, Chambers AP, Ryan KK, Li B, Sandoval DA, Stoffers D, et al. Vertical sleeve gastrectomy is effective in two genetic mouse models of glucagon-like peptide 1 receptor deficiency. Diabetes. 2013;62(7):2380–5. [PubMed: 23434938]

75. Mokadem M, Zechner JF, Margolskee RF, Drucker DJ, Aguirre V. Effects of Roux-en-Y gastric bypass on energy and glucose homeostasis are preserved in two mouse models of functional glucagon-like peptide-1 deficiency. Mol Metab. 2014;3(2):191–201. [PubMed: 24634822]

76. Jiménez A, Mari A, Casamitjana R, Lacy A, Ferrannini E, Vidal J. GLP-1 and glucose tolerance after sleeve gastrectomy in morbidly obese subjects with type 2 diabetes. Diabetes. 2014;63(10):3372–7. [PubMed: 24848069]

77. Behary P, Tharakan G, Alexiadou K, Johnson N, Wewer Albrechtsen NJ, Kenkre J, et al. Combined GLP-1, oxyntomodulin, and peptide YY improves body weight and glycemia in obesity and Prediabetes/type 2 diabetes: a randomized single-blinded placebo controlled study. Diabetes Care. 2019;8.

78•. Hayoz C, Hermann T, Raptis DA, Brönnimann A, Peterli R, Zuber M. Comparison of metabolic outcomes in patients undergoing laparoscopic roux-en-Y gastric bypass versus sleeve gastrectomy - a systematic review and meta-analysis of randomised controlled trials. Swiss Med Wkly. 2018;148:w14633. [PubMed: 30035801] Meta-analysis of RCTs comparing RYGB and LSG.

79. Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Brethauer SA, Navaneethan SD, et al. Bariatric surgery versus intensive medical therapy for diabetes–3-year outcomes. N Engl J Med. 2014;370(21):2002–13. [PubMed: 24679060]

80. Thaler JP, Cummings DE. Hormonal and metabolic mechanisms of diabetes remission after gastrointestinal surgery. Endocrinology. 2009;150(6):2518–25. [PubMed: 19372197]

81. Arble DM, Sandoval DA, Seeley RJ. Mechanisms underlying weight loss and metabolic improvements in rodent models of bariatric surgery. Diabetologia. 2015;58(2):211–20. [PubMed: 25374275]

82. Patel RT, Shukla AP, Ahn SM, Moreira M, Rubino F. Surgical control of obesity and diabetes: the role of intestinal vs. gastric mechanisms in the regulation of body weight and glucose homeostasis: surgical control of obesity and diabetes. Obesity. 2014;22(1): 159–69. [PubMed: 23512969]

83. Rajagopalan H, Cherrington AD, Thompson CC, Kaplan LM, Rubino F, Mingrone G, et al. Endoscopic duodenal mucosal resurfacing for the treatment of type 2 diabetes: 6-month interim analysis from the first-in-human proof-of-concept study. Diabetes Care. 2016;39(12):2254–61. [PubMed: 27519448]

84. Nakatani H, Kasama K, Oshiro T, Watanabe M, Hirose H, Itoh H. Serum bile acid along with plasma incretins and serum high-molecular weight adiponectin levels are increased after bariatric surgery. Metab Clin Exp. 2009;58(10):1400–7. [PubMed: 19570554]

85. Pournaras DJ, Glicksman C, Vincent RP, Kuganolipava S, Alaghband-Zadeh J, Mahon D, et al. The role of bile after Rouxen-Y gastric bypass in promoting weight loss and improving glycaemic control. Endocrinology. 2012;153(8):3613–9. [PubMed: 22673227]

86. Patti M-E, Houten SM, Bianco AC, Bernier R, Larsen PR, Holst JJ, et al. Serum bile acids are higher in humans with prior gastric bypass: potential contribution to improved glucose and lipid metabolism. Obesity (Silver Spring). 2009;17(9):1671–7. [PubMed: 19360006]

87. Kohli R, Bradley D, Setchell KD, Eagon JC, Abumrad N, Klein S. Weight loss induced by Roux-en-Y gastric bypass but not laparoscopic adjustable gastric banding increases circulating bile acids. J Clin Endocrinol Metab. 2013;98(4):E708–12. [PubMed: 23457410]

88. McGavigan AK, Garibay D, Henseler ZM, Chen J, Bettaieb A, Haj FG, et al. TGR5 contributes to glucoregulatory improvements after vertical sleeve gastrectomy in mice. Gut. 2017;66(2):226–34. [PubMed: 26511794]

89. Ryan KK, Tremaroli V, Clemmensen C, Kovatcheva-Datchary P, Myronovych A, Karns R, et al. FXR is a molecular target for the effects of vertical sleeve gastrectomy. Nature. 2014;509(7499): 183–8. [PubMed: 24670636]

90. Dixon JB, Chuang L-M, Chong K, Chen S-C, Lambert GW, Straznicky NE, et al. Predicting the glycemic response to gastric bypass surgery in patients with type 2 diabetes. Diabetes Care. 2013;36(1):20–6. [PubMed: 23033249]

91. Chikunguwo SM, Wolfe LG, Dodson P, Meador JG, Baugh N, Clore JN, et al. Analysis of factors associated with durable remission of diabetes after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2010;6(3):254–9. [PubMed: 20303324]

92. Coleman KJ, Haneuse S, Johnson E, Bogart A, Fisher D, O'Connor PJ, et al. Long-term microvascular disease outcomes in patients with type 2 diabetes after bariatric surgery: evidence for the legacy effect of surgery. Diabetes Care. 2016;39(8):1400–7. [PubMed: 27271192]

93. Panunzi S, Carlsson L, De Gaetano A, Peltonen M, Rice T, Sjöström L, et al. Determinants of diabetes remission and glycemic control after bariatric surgery. Diabetes Care. 2016;39(1):166–74. [PubMed: 26628418]

94. Arterburn DE, Olsen MK, Smith VA, Livingston EH, Van Scoyoc L, Yancy WS, et al. Association between bariatric surgery and long-term survival. JAMA. 2015;313(1):62–70. [PubMed: 25562267]

95. Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, Rosamond WD, et al. Long-term mortality after gastric bypass surgery. N Engl J Med. 2007;357(8):753–61. [PubMed: 17715409]

96. Busetto L Timing of bariatric surgery in people with obesity and diabetes. Ann Transl Med. 2015;3(7):94. [PubMed: 26015936]

97. le Roux CW, Schauer PR. Prevention is better than cure: the next frontier for bariatric surgery? Ann Intern Med. 2018;169(5):343. [PubMed: 30083758]

98. Cummings DE, Cohen RV. Beyond BMI: the need for new guidelines governing the use of bariatric and metabolic surgery. The Lancet Diabetes & Endocrinology. 2014;2(2):175–81.

99. Rubino F, Nathan DM, Eckel RH, Schauer PR, Alberti KGMM, Zimmet PZ, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. Diabetes Care. 2016;39(6):861–77. [PubMed: 27222544]

Table 1

Types of bariatric surgery procedures

Surgery type	Description	Time introduced	Estimated % of total bariatric cases performed from 2011 to 2017
Jejunoileal bypass (JIB)	Bypass of most of the intestines with gastric preservation	1950s	0 (no longer performed)
Roux-en-Y gastric bypass (RYGB)	Gastric pouch creation with bypass of the remaining stomach and first segment of small intestine	Open: 1960s Laparoscopic: 1994	17.8
Mini-gastric bypass (MGB)	Similar to RYGB but with a longer gastric pouch and a longer biliary limb	1997	*a*
Biliopancreatic diversion (BPD) and duodenal switch (DS); (BPD/DS)	BPD: Distal gastrectomy (later: vertical sleeve gastrectomy) with creation of a gastrointestinal anastomosis involving a biliopancreatic bypass DS: BPD modification involving vertical gastrectomy, some duodenal preservation, and duodenal-intestinal anastomosis involving biliopancreatic bypass	BPD: 1979 DS: 1986	0.7
Vertical banded gastroplasty (VBG)	Partition of the stomach using staples and placement of a polypropylene mesh band or ring around the outlet of the pouch	1982	*a*
Gastric banding (GB) and laparoscopic adjustable gastric banding (LAGB)	Gastric partitioning with a ring to create a small upper pouch and the rest of the stomach. Later modified to an inflatable balloon ring	GB: 1978 LAGB: 1986	2.77
Sleeve gastrectomy (SG)	Resection of 80% of the stomach leaving a tube-shaped gastric pouch.	Open: 1988 Laparoscopic: 1999	59.39

[a] All other procedures comprise under 2.5% of total cases

Table 2

Summary of studies assessing the impact of bariatric surgery on control of diabetes

Date	Reference: first author	Study design	Surgical patients	Control patients	Remission rate: surgical group	Remission rate: control group	Average follow-up (years)	Remission definition
2010	Poumaras [41]	Cohort study	109 RYGB 107 LAGB	–	72% RYGB 17% LAGB	–	2–3	FBG< 126 mg/dl, 2 h. OGTT < 200 mg/dL, Ale < 6.0% w/o meds
2012	Mingrone [44•]	RCT	20 RYGB 20 BPD	20	75% RYGB 95% BPD	0%	2	ADA definition[a]
2013	Arterbum [43•]	Retrospective cohort study	4434 RYGB	–	37.1% 1 year 63.3% 3 years 68.2% 5 years	–	3.1	ADA Definition
2013	Ikramuddin [45]	RCT	60	RYGB 60	44%	9%	1	Ale < 6.0% (secondary outcome)
2013	Liang [46]	RCT	31 RYGB	36 + 34[b]	90% [c]	0%	1	Off diabetes medications
2014	Halperin [47]	RCT	19	RYGB 19	58%	16%	1	Ale < 6.5% off meds
2014	Sjostrom [48]	Cohort study	55 RYGB 61 LAGB 227 SG	260	30.4% (composite)	6.5%	15	FBG <110 mg/dL and no meds
2015	Courcoulas [49•]	RCT	18 RYGB 20 LAGB	14	40% RYGB 29% LAGB	0%	3	ADA Definition
2015	Ding [50]	RCT	23 LAGB	22	33%	23%	1	Ale < 6.5% on or off meds
2015	Mingrone [51•]	RCT	20 RYGB 20 BPD	20	37% RYGB 63% BPD	0%	5	ADA Definition
2016	Cummings [52•]	RCT	15 RYGB	17	60%	5.9%	1	Ale < 6.0%, off all meds
2017	Schauer [53•]	RCT	49 RYGB 47 SG	38	29% RYGB 23% SG	5%	5	Ale < 6.0%
2018	Courcoulas [54]	Observational Cohort	1738 RYGB 610 LAGB	–	60.2% RYGB 20% LAGB	–	7	ADA Definition
2018	Ikramuddin [55]	RCT	57 RYGB	56	7%	0%	5	Ale < 6.0% off meds (secondary outcome)
2018	Jacobsen [56]	Registry based cohort study	855 RYGB 69 SG	956	57.5% (composite)	14.8%	7.8	No diabetes drugs dispensed
2018	Lager [57]	Retrospective cohort study	380 RYGB 334 SG	–	32.1% RYGB 22.0% SG	–	4	Ale < 6.5% off meds
2018	Salminen [58]	RCT	52 SG 49 RYGB	–	12% SG 25% RYGB	–	5	ADA Definition (secondary endpoint)
2018	Simonson [59]	RCT	19 RYGB	19	42%	0%	3	Ale <6.5% and FBG <126 mg/dL on or off meds

Date	Reference: first author	Study design	Surgical patients		Control patients	Remission rate: surgical group		Remission rate: control group	Average follow-up (years)	Remission definition
2019	Madsen [60]	population based cohort	1111	RYGB	1074	74% 54%	1 year 5 years	–	5	Ale < 6.5% off meds or Ale < 6.0% on metformin monotherapy

[a] ADA definition: normal fasting blood glucose levels and/or HgbA1c without the use of anti-diabetes medications for at least 1 year

[b] Usual medical care plus exenatide

[b] Diabetes duration of > 10 years was an exclusion criterion

RCT randomized control trial, *RYGB* Roux-en-Y gastric bypass, *LAGB* laparoscopic adjustable gastric banding, *BPD* biliopancreatic diversion, *SG* sleeve gastrectomy, *ADA* American Diabetes Association, *FBG* Fasting blood glucose, *OGTT* oral glucose tolerance test