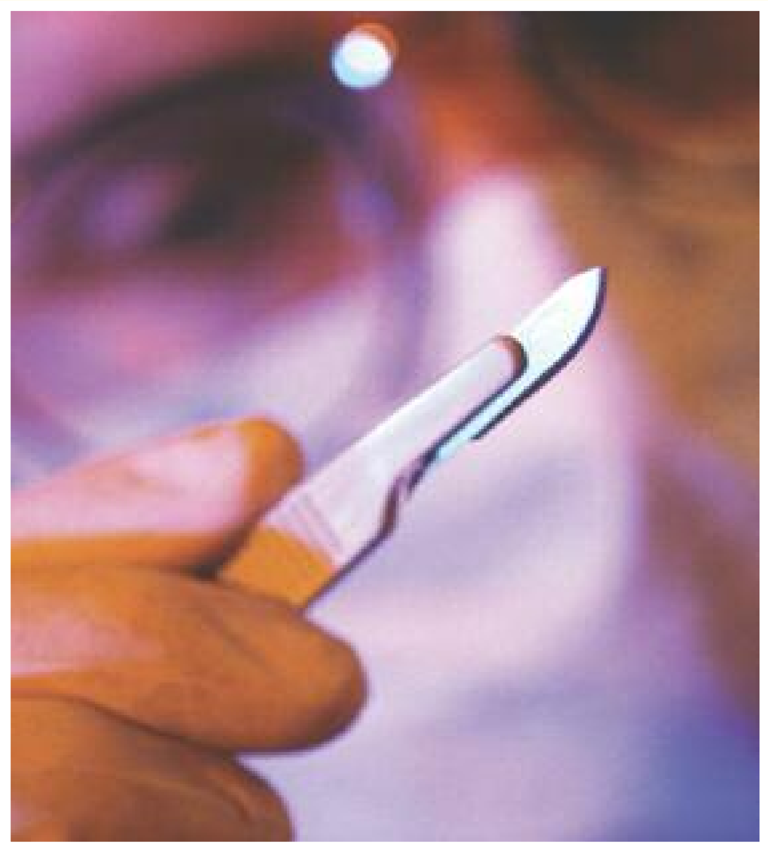
Bariatric surgery and diabetes



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Diabetes and obesity have a long and cozy relationship.[1] Generally speaking, the more body weight that an individual possesses in the form of adipose tissue, the higher the risk of developing type 2 diabetes. Unfortunately, the prevalence of obesity in the Western world, especially in the United States, had been on the increase for some time, though it thankfully hit a plateau between 2003 and 2007.[2]

From 1980 through the end of 2004, the body-mass-index (BMI, or body weight in kilograms divided by the square of the height in meters) of 30 or greater doubled, capturing almost one-third of the population.[3] In addition, the prevalence of overweight children has increased between 1999 and 2004,[2] posing an even greater threat to an already economically stressed healthcare system. Table 1 defines the World Health Organization classifications for the obese/overweight condition in adults.

The global prevalence of diabetes is on the rise and is estimated to reach over 366 million in the year 2030.[4]

Table 1.

World Health Organization Classifications for Overweight/Obesity (2000)

If your BMI is:	*Then you are considered:*
18.5-24.9 kg/m2	A healthy weight
25.0-29.9 kg/m2	Overweight
30.0-34.9 kg/m2	Class I Obesity
35.0-39.9 kg/m2	Class II Obesity
> 40 kg/m2	Class III Obesity

Source: Adapted from World Health Organization 1995, 2002, and 2004.

Obesity: A complex confluence

The development of obesity in individuals may be viewed by most as a basic construct of calories consumed exceeding the number of calories expended. However, this notion may be more simplistic than not because it seems some individuals have a metabolism programmed to gain weight more easily than others.

The "thrifty gene" hypothesis proposed by Neel[5] over 40 years ago seemed to offer at least a partial explanation for this paradox, though a "drifty gene" hypothesis has been offered in its stead more recently.[6]

The likelihood of a single gene as the cause of obesity, while an attractive notion for research, seems far-fetched. In truth, obesity is more likely a polygenic disorder that must have a strong environmental component to allow its fullest expression.

Because of this, the pathophysiology of obesity must be viewed as a very complex situation, with myriad interactions of biopsychosocial factors involved. The confluence of such factors that exist in the modern world, conspiring to increase body weight, is an ever-present threat to the health of Americans. As such, the prevalence of type 2 diabetes mellitus (T2DM) has grown right along with the collective American waistline. Unfortunately, the combination of obesity and T2DM is fast becoming a world-wide epidemic as well, as more and more cultures and societies adopt an urbanized lifestyle.[4]

Obesity has many comorbid conditions that lead to increased morbidity and mortality, among them T2DM, the metabolic syndrome (MetS), vascular diseases (coronary artery disease, peripheral artery disease), orthopedic problems leading to accelerated osteoarthritis and low back conditions, hypertension, dyslipidemia, obstructive sleep apnea, depression and others.[7-11]

MetS is a constellation of risk factors—including central obesity, dyslipidemia, hypertension and elevated plasma glucose—that often leads to diabetes itself. However, MetS has been a controversial condition due primarily to the lack of consensus of diagnostic criteria until recently.[12]

Dealing with obesity, whether accompanied by MetS or T2DM or not, requires a strong sense of the possible treatments available, including bariatric surgery. It has been known for some time that weight loss alone in obese people with T2DM can restore blood sugars and near-normal insulin sensitivities.[13]

The wave of people who are obese now, with or without MetS—or who will be in the near future—will be enormous not only in numbers of patients but also in monetary cost. The crush on the healthcare system as a whole and the stresses involved with its providers caring for these patients will prove daunting. This demands the attention of the medical community now in order to better ascertain viable treatment options that are both cost-effective and efficacious.

Despite the available medical therapies—including diet and exercise—successful treatment of obesity, particularly among those morbidly obese, is hard to achieve and viewed by many as even harder to maintain. This sense of futility on the part of patients and providers alike has placed the treatment of obesity lower on the priority list than it should be. At the same time, more and more numbers of patients are being diagnosed with diabetes secondary to obesity ("diabesity" as it has been labeled) seemingly at an increasingly earlier age.

Because weight loss through nonsurgical means has a positive impact on not only improving T2DM but all other comorbid conditions, a strong argument must be made that weight loss in such individuals must be part of the treatment plan whenever possible. To this end, when medical intervention is either ineffective or impractical, bariatric surgery should be considered and seriously discussed with the "diabese" patient as a possible treatment option, especially those with a BMI greater than 35 kg/m^2.

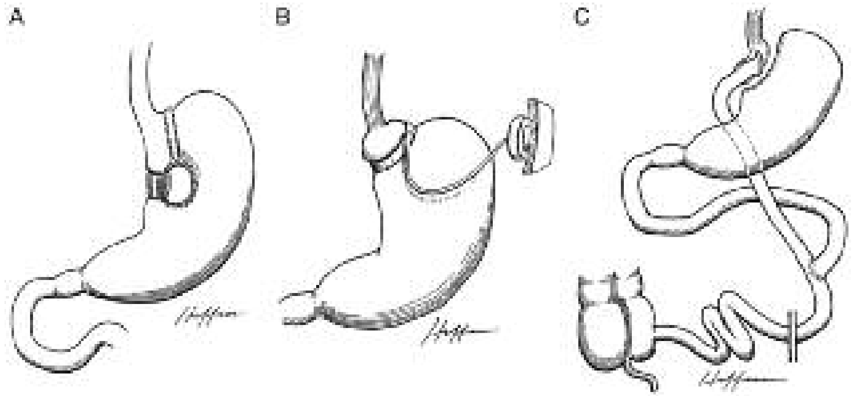
Bariatric surgery

Bariatric Surgery—Types of Procedures and Patients

Improvement of T2DM, including its remission, due to bariatric surgery

Figure 1.

Common Restrictive Techniques



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has been recognized now for over a decade.[14] Not all bariatric procedures are created equal, however. Restrictive or malabsorptive (or both) have their own categorical risks and benefits (Table 2) and have been reviewed.[15]

Deciding which procedure to choose involves many factors notwithstanding insurance coverage. Some of the critical factors that often play a role in the procedure chosen include the patient's preference, procedures with which the surgeon is comfortable, what makes sense clinically such as how much weight loss is required, comorbid conditions, age, and how long a patient has been diabetic.

For example, the endosurgical sleeve is being used more frequently as it takes about 30 minutes to insert and is placed endoscopically, creating a barrier over the duodenum and first part of the jejunum. The device likely alters the incretin and gut hormones (enteroinsular milieu) of the body leading to weight loss.[16] The role of incretins and T2DM has been reviewed elsewhere.[17]

Three main categories of bariatric surgery exist that may be used to help with weight loss: restrictive procedures, malabsorptive procedures, or a combination of the two.

Figures 1 and 2 depict the common procedures of each category. Other procedures are currently under investigation and include endoscopic duodenal-jejunal bypass sleeve, which is a nonsurgical method for weight loss in the morbidly obese.[16] Two types of procedures exist that are really a combination of both restrictive and malabsorptive mechanisms: the biliopancreatic diversion (BPD) and the gold-standard Roux-en-Y gastric bypass (RYGB).

Which procedure for which patient?

Generally speaking, malabsorptive procedures appear to be more efficacious than those that are purely restrictive. Although mechanisms have not been worked out as yet, it is obvious that success of glycemic control is not solely predicated on weight loss, as blood sugars correct within hours postsurgically and continue to improve for days to several weeks thereafter—long before any appreciable weight loss occurs—with over three-quarters of patients experiencing full resolution of their diabetes (Table 3).[18]

As such, BPD has the greatest impact with respect to changes in the enter-oinsular axis, glycemic control and weight loss, followed by RYGB then the laparoscopic gastric bypass (LAGB). As far as how restrictive procedures fare, they are overall less effective versus malabsorptive surgeries (open or laproscopic) but still have excellent efficacy with respect to weight loss and glycemic control, with most procedures being reversible. Table 2 shows the effect of different bariatric procedures on various clinical parameters of interest.

Because there are no head-to-head randomized controlled trials in the severely obese comparing any of these surgeries to one another, it would be hasty to recommend a certain surgery over another for a particular population-at-risk. Patient selection is ascertained by many more factors besides the procedure itself.

Pre-bariatric surgical patient selection is based on the same criteria for other general surgeries, and co-morbid conditions that place a patient at potential risk (heart and lung disease, for example) must be assessed. However, mood disorders, including abnormal body image, also become a critical factor in selecting which patients can tolerate this procedure. The use of BMI as the predominant criterion for bariatric surgery has been strongly criticized[19] for many reasons and current guidelines do not allow surgical candidates with BMIs less than 35 kg/m^2.

Populations-at-risk and bariatric surgery

Several different "at-risk" populations exist in which bariatric surgery of some type has been used as an intervention, beyond those who are obese. Such populations include patients with T2DM, with MetS and those who have impaired glucose tolerance (IGT), and they will be discussed briefly below.

One of the first studies to examine the effectiveness of bariatric surgery was a case-series (the Greenville series) that occurred using a population of 109 patients who were diagnosed with impaired glucose tolerance.[20] These patients were compared with a control group of 27 patients who also had IGT but did not undergo bariatric surgery. Since these individuals were not yet diabetic and the study was non-randomized, a main outcome measure was the incidence density or rate of conversion from IGT to T2DM.

After about five years of follow-up after surgery, the control group had a conversion rate of 4.72 cases per 100 person-years and the surgical group had only 0.15 cases per 100 person years. These data showed that weight loss in clinically severely obese patients with IGT due to bariatric surgery could reverse the risk of developing T2DM over time. Particularly striking was that almost 83% of the 165 patients with T2DM in this study remained in remission from their diabetes after a mean of 14 years post-Roux-en-Y gastric bypass.[14]

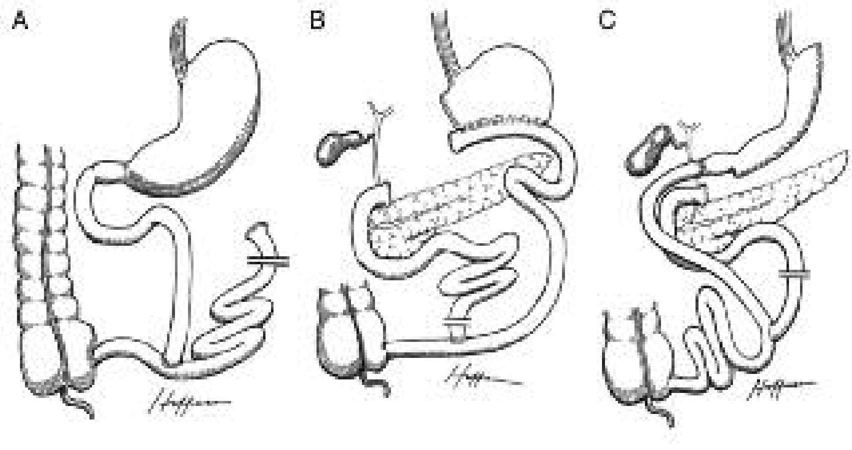
A second and larger trial, the landmark Swedish Obesity Study (SOS), directly addressed the long-term effectiveness of bariatric surgery.[21] This prospective, controlled trial examined in more than 4,000 participants the effects of bariatric surgery compared with medical therapy. About half of the patients were allocated either to the medical group or the surgical group. Many types of bariatric procedures were included, some of which are not often used now because of high complication rates.

Of the total number recruited, 156 patients in the SOS had T2DM and obesity, and after two years of follow-up, those in the surgical arm were twice as likely to not use antidiabetic agents to control their blood sugars versus those in the medical arm. Although this trial has weaknesses, such as not being randomized and the control group (medical therapy group) not receiving any structured alternative weight loss strategy, the SOS is still a key trial as other smaller and uncontrolled studies reviewed elsewhere[22] have supported the results of the Greenville series and the SOS.

In another retrospective cohort, mortality rates of 9,949 patients were examined who had gastric bypass surgery versus a control group identified using driver's license data.[23] All-cause mortality in the surgical group was 40% lower than the control group after a little over seven years follow-up and, similar to the SOS, a 92% reduction in death due to diabetes was observed.

Figure 2.

Common Malabsorptive Techniques



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Dixon et al[24] studied the effect of the LAGB procedure on glucose control in T2DM patients with BMIs of 30 to 40 kg/m^2. These patients were randomized but treated in an unblinded fashion.

Half the patients were given medical therapy (weight loss using lifestyle changes) and the other half given LAGB concomitant with their usual medical care. Remission of T2DM occurred in 73% of the surgical group but only 13% of the control group. Remission—defined as a fasting blood sugar less than 106 mg/dl and a glycosylated hemoglobin less than 6.2% while taking no antidiabetic medications—was proportional to degree of weight lost.

Another trial examined the effects of bariatric surgery in patients with MetS compared with a nonsurgical weight-reduction intervention. This was a population-based, retrospective study of patients from 1990 to 2003 (14 years inclusive) that assessed the effect of weight loss due to bariatric surgery on the prevalence of MetS and sought predictors of MetS resolution.[25]

Results showed that use of Roux-en-Y gastric bypass induces considerable and lasting improvement in MetS prevalence with decreased medication usage. After surgery, MetS patients decreased by 58% while in the nonsurgical control group they decreased only 10% after a mean follow-up of 3.4 years. The most prominent predictor for MetS resolution using logistic regression analysis was a 5% loss in excess weight (odds ratio 1.26; 95% CI: 1.19-1.34; $p>0.001$ and diabetes mellitus (odds ratio 0.32; 95% CI: 0.15-0.68; $p=0.003$).

There are many other trials looking at the use of bariatric surgeries for the treatment of obesity, however, few are or were designed to examine prospectively the use of such surgery in obese T2DM as a means of definitive treatment. Many such studies, particularly earlier on, were case-series studies and therefore not randomized and/or inadequately powered. Others were retrospective or meta-analyses of bariatric surgical procedures of patients that happened to include T2DM as a comorbidity. However, there is no disputing the fact that to date, a more substantial body of evidence of reproducible data has accumulated.

Results due to bariatric surgery, whether open or laparoscopic and regardless of technique (malabsorptive, restrictive, or a combination of the two), in individuals with a BMI more than

Table 2.

Common Bariatric Procedures: Risks and Benefits[1]

Restrictive Laparoscopic adjustable gastric banding (LAGB) Vertical banded gastroplasty (VBG) Silastic ring gastroplasty (SRBP) Roux-en-Y gastric bypass (RYGB)[2]	**Benefits:** Weight loss with improved glycemic responses Improved insulin resistance Improvement in weight related comorbid conditions Most procedures reversible (no permanent anatomical change) Most procedures can be done laparoscopically	**Risks:** Typical risks for a surgical procedure (infection, anesthesia, etc) Bowel obstruction or leakage from anastomosis Nutritional deficiencies (macro- and micronutrients) Possible need to use some nutritional supplements Nausea/vomiting/constipation/gallbladder problems Low risk of revision of procedure
Malabsorptive Roux-en-Y gastric bypass (RYGB)[2] Biliopancreatic diversion (BPD- w or w/o DS) Duodenal switch (DS) Endoluminal sleeve (ELS)[3]	**Benefits:** (results here are more pronounced than RPs) Weight loss >RP with improved glycemic responses Improvement in insulin resistance >RP Improvement in weight related comorbid conditions Some procedures may be done laparoscopically	**Risks:** Typical for a surgical procedure (infection, anesthesia, etc) Bowel obstruction/leakage more likely vs RP Nutritional deficiencies (macro- and micronutrients >RP) Lifelong need to use nutritional supplements Nausea/vomiting/diarrhea Higher risk of revision of procedure (vs RP)

1. See reference 15. Collective risks and benefits as a group (restrictive or malabsorptive) not listed for individual procedure
2. Considered both malabsorptive and restrictive
3. Considered investigational, becoming more common in its use as it does not require surgical incisions

RP=restrictive procedures

Source: Standards of Medical Care in Diabetes, 2009, American Diabetes Association.

35 kg/m^2 have a dramatic impact on weight loss, glycemic effects and blood glucose control both acutely and longer term.[14,18, 26-29]

As a result of such dramatic positive impact of bariatric procedures on T2DM in obese patients, some physicians are calling for caution when patient selection for these surgeries is involved[30] so as to avoid the overzealous application to possibly poorly selected patients. For example, use of invasive procedures such as ileal transposition in T2DM patients with lower BMIs to stimulate insulin secretion independent of weight loss have been performed[28, 31] as have procedures that quickly empty the stomach contents into the distal bowel.[32]

Because of the many types of studies of various levels of quality concerning bariatric surgery as a treatment for T2DM in differing populations, a recent consensus conference was held by leading experts from a variety of medical disciplines, including surgeons, to develop guidelines for the use of gastrointestinal surgery to treat T2DM.[33]

As a result, a Diabetes Surgery Summit Position Statement was crafted to address data gaps but to also define and delineate the foundations of the new discipline of "diabetes surgery." It was hoped these recommendations would reduce the inappropriate use of such surgeries while also legitimizing the use of these procedures in carefully selected obese T2DM patients.

The delegates of the conference unanimously agreed that those T2DM patients who had poorly controlled disease and a BMI greater than 35 kg/m^2 should be considered for bariatric surgery. This recommendation concurs with the 2009 American Diabetes Association Standards of Care.[34]

Table 3
Clinical Impact of Select Bariatric Surgeries

Results of different types of bariatric surgery

Result	Malabsorptive (BPD)	Restrictive (LAGB, VBG)	Comines RYGB
Excess weight loss, %	72	48-68	62
Resolution of comorbid conditions, %			
Type 2 diabetes	98	48-72	84
Hypertension	81	28-73	75
Dyslipidemia improved	100	71-81	94
Operative mortality rate, %	1.10	0.1	0.5

BPD=biliopancreatic diversion; **LAGB=**laparoscopic adjustable gastric banding; RYGB=Roux-en-Y gastric bypass; VBG=vertical banded gastroplasty.
Mean values from a meta-analysis of 22,094 patients.

Source: Data from Buchwald H, et al. JAMA 2004; 292-1724-37.

Mechanisms of metabolic change

Whether malabsorptive or restrictive, the end result of a bariatric surgical procedure is less macronutrients absorbed, leading to a caloric deficit and resulting loss of weight. However, there is more to bariatric surgery than just creating a caloric deficit and many other metabolic mechanisms are involved, including changes in gut hormones, the incretin system and adipokines as well.[35]

The rapid improvement seen in blood glucose control temporally occurs not from weight loss but rather from caloric restriction and the consequent changes in the enteroinsular axis.

Depending upon the choice of procedure, the prevalence period of diabetes, and the aggressiveness and types of treatments appear to determine the magnitude and duration of change in gut hormones such as glucagon-like peptide (GLP-1), glucose-dependent insulinotropic peptide, ghrelin, and peptide YY (PYY) and their subsequent effect on insulin secretion and sensitivity.[36-38]

Clearly, modulating a complex system such as the enteroinsular axis to benefit weight loss (or maintain body weight) by promoting early satiety and by stabilizing blood glucose excursions would be a huge clinical advantage. For example, Table 4 shows a few representative changes in certain incretins or hormones for different surgical procedures.

Intestinal bypass procedures increase GLP-1 and PYY levels and restrictive procedures, in contrast, do not increase incretin levels much at all.[39] While it remains unclear to what extent which gastrointestinal "enterocrine" changes contribute to improved glycemic control and beta cell function, it is apparent that caloric restriction and weight loss are the primary factors that bariatric procedures contribute in order to modulate glucose metabolism and stabilize blood sugars of patients with diabetes who undergo such surgeries.

Generally, surgical weight loss lowers the set point secretory capacity of the beta cells but heightens the dynamic responsivity of the beta cell as well.[39]

Safety and cost effectiveness

Safety of bariatric procedures has improved for many reasons. Complication rates are lower than ever and mortality is generally less than 1% for all procedures.[40, 41] This is due, in part, to less invasive techniques and efforts put forth by the American Society for Metabolic and Bariatric Surgery and the American College of Surgeons' Centers of Excellence Programs.[42]

The ongoing Longitudinal Assessment of Bariatric Surgery[40] will continue to keep safety and efficacy data for years to come as more and more randomized clinical trials are completed. All modeled economic evaluations assessed in a recent report[43] found that bariatric surgery was cost-effective in moderately to severely obese patients compared to non-surgical methods. Until uncertainties are eliminated, modeling economic evaluations will be subject to assumptions that may be inaccurate.

Final notes

Due to increased safety and efficacy, bariatric surgery, particularly LAGB,

Table 4

Changes in Hormones/Incretins Induced by Bariatric Surgeries

Hormone	Cell Type	Effect on Insulin Secretion	Changes Induced, by Surgery		
			PBD	RYGP	LAGB
Ghrelin	X/A cells	↓	↑	↑ / ↓	↑/NC
GIP	K cells	↑	↓	↓	NC
GLP-1	L cells	↑	↑	↑	NC
Peptide YY	L cells	↓	↑	↑	NC

BPD=Biliopancreatic diversion; **LABG=**laparoscopic adjustable banding; **RYGB=**Rouxen-Y gastric bypass

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has gained acceptance as a potential therapeutic tool in those type 2 diabetics who have a BMI greater than 35 kg/m^2.

Roux-en-Y appears to remain the procedure that has shown the most dramatic effective weight loss when compared to laparoscopic adjustable gastric banding but LAGB had, in one systematic review, less short-term morbidity but with higher reoperation rates.[44]

Questions will continue to be raised as to the possible use of bariatric surgery for other populations-at-risk, such as those individuals with a BMI less than 35 kg/m^2, obese pediatric groups, the obese elderly, those with MetS, those who have IGT with or without other metabolic disease (polycystic ovarian syndrome), and even the obese pregnant patient. The best type of surgery for a population in question will only be borne out of continued larger randomized, clinical trials.

Bariatric surgery not only produces weight loss but improves metabolic disease comorbid in most “diabese” patients by changing the incretin and enterocrine systems of the body, particularly in the gut. These results also enhance the patient’s quality of life.

Many other data gaps still exist regarding this new area of medicine (diabetes surgery) and these gaps must be filled as best as possible using data from well designed, well employed randomized-controlled clinical trials. It is likely that a combination of procedures (sleeve before LAGB) and specialized weight loss diet programs will be in the future of treating the type 2 diabetic.

References

1. Ferchak CV, Meneghini LF. Obesity, bariatric surgery and type 2 diabetes—a systematic review. *Diabetes Metab Res Rev*. 2004;20(6):438-445.

2. Ogden CL, Carroll MD, Curtain LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA*. 2006;295: 1549-1555.

3. Flegal KM. Epidemiologic aspects of overweight and obesity in the United States. *Physiol Behav.* 2005;86:599-602.

4. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27:1047-1053.

5. Neel JV. Diabetes mellitus: a “thrifty” genotype rendered detrimental by “progress”? *Am J Hum Genet*. 1962;14:353-362.

6. Speakman JR. Thrifty genes for obesity, an attractive but flawed idea, and an alternative perspective: the ‘drifty gene’ hypothesis. *Int J Obes* 2008;32:1611-1617.

7. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005;112(17):2735-2752. Epub 2005 Sep 12. [published corrections appear in *Circulation* 2005; 112(17):e298].

8. Pinkey JH, Daousi C. The impact of obesity on the prevalence of cardiovascular disease and diabetic complications in a hospital diabetic population. *Diabet Med.* 2003;20(suppl 2): 66 [Abstract].

9. World Health Organization. The World Health Report 2002 page. Available at: www.who.int/whr/2002/en/.Accessed December 20, 2009.

10. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *JAMA*. 1999;282:1523-1529.

11. National Institute of Diabetes and Digestive and Kidney Diseases. Overweight, obesity, and health risk. National Task Force on the Prevention and Treatment of Obesity. *Arch Intern Med*. 2000;160:898-904.

12. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome. a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009;120: 1640-1645.

13. Henry RR, Wallace P, Olefsky JM. Effects of weight loss on mechanisms of hyperglycemia in obese non-insulin dependent diabetes mellitus. *Diabetes*. 1986;35:990-998.

14. Pories WJ, Swanson MS, MacDonald KG, et al. Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. *Ann Surg*. 1995;222:339-352.

15. Shah M, Simha V, Garg A. Review: long-term impact of bariatric surgery on body weight, comorbidities, and nutritional status. *J Clin Endocrinol Metab*. 2006;91:4223-4231.

16. Gersin KS, Keller JE, Stefanidis D, et al. Duodenal-jejunal bypass sleeve: a totally endoscopic device for the treatment of morbid obesity. *Surg Innov*. 2007;14:275-278.

17. Giard J. The incretins: from the concept to their use in the treatment of type 2 diabetes. Part A: incretins: concept and physiological functions. *Diabetes Metab*. 2008;34:550-559.

18. Buchwald H, Braunwald E, Pories FW, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA*. 2004;292:1724-1737.

19. Dixon JB. Referral for a bariatric surgical consultation: it is time to set a standard of care. *Obes Surg*. 2009; 19:641-644.

20. Long SD, O'Brien K, MacDonald KG, et al. Weight loss in severely obese subjects prevents the progression of impaired glucose tolerance to type II diabetes. A longitudinal interventional study. *Diabetes Care*. 1994;17(5):372-375.

21. Sjöström L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Eng J Med*. 2004;351:2683-2693.

22. Pinkey JH, Kerrigan D. Current status of bariatric surgery in the treatment of type 2 diabetes. *Obes Rev*. 2004;5:69-78.

23. Adams TD, Gress RE, Smith SC, et al. Long term mortality after gastric bypass surgery. *N Eng J Med*. 2007;357:753-761.

24. Dixon JB, O'Brien PE, Playfair J, et al. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *JAMA* 2008;299:316-323.

25. Batsis JA, Romero-Corral A, Collazo-Clavell ML, Sarr MG, Somers VK, Lopez-Jimenez F. Effect of bariatric surgery on the metabolic syndrome: a population-based, long-term controlled study. *Mayo Clin Proc*. 2008;83(8):897-907.

26. Cummings DE, Overduin J, Foster-Schubert KE. Gastric bypass for obesity: mechanisms of weight loss and diabetes resolution. *J Clin Endocrinol Metab* 2004;89(6):2608-2615.

27. de Paula AL, Macedo AL, Prudenta AS, Queiroz L, Schraibman V, Pinus J. Laparoscopic sleeve gastrectomy with ileal interposition ("neuroendocrine brake")—pilot study of a new operation. *Surg Obes Relat Dis*. 2006;2:464-467.

28. Ramos AC, Galvao Neto MP, de Souza YM, et al. Laparoscopic duodenal-jejunal exclusion in the treatment of type 2 diabetes mellitus in patients with BMI=NOTECHANGE30 kg/m^2 (LBMI). *Obes Surg*. 2009;19:307-312.

29. Schauer PR, Burguera B, Ikramuddin S, et al. Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. *Ann Surg*. 2003;238:467-485.

30. Deitel M. From bariatric to metabolic surgery in non-obese subjects: time for some caution. *Arq Bras Endocrinol Metab*. 2009;53(2):246-251.

31. Mason EE. Ileal transposition and enteroglucagon/GLP-1 in obesity (and diabetic?) surgery. *Obes Surg*. 1999;9(3):223-228.

32. Cohen RV, Schiavon GA, Pinheiro JS, Correa JL, Rubino F. Duodenal-jejunal bypass for the treatment of type 2 diabetes with BMI 22-34 kg/m^2: a report of two cases. *Surg Obes Relat Dis*. 2007;3(2):195-197.

33. Rubino F, Kaplan LM, Schauer PR, Cummings DE; for the Diabetes Surgery Summit Delegates. The Diabetes Surgery Summit Consensus Conference. Recommendations for the evaluation and use of gastrointestinal surgery to treat type 2 diabetes mellitus. *Ann Surg*. Nov. 19, 2009 [Epub ahead of print].

34. American Diabetes Association. Standards of medical care in diabetes—2009. *Diabetes Care*. 2009;32(suppl 1):S13-S61.

35. Folli F, Pontiroli AE, Schwesinger WH. Metabolic aspects of bariatric surgery. *Med Clin North Am*. 2007;91:393-414.

36. Rubino F, Gagner M, Gentileschi P, et al. The early effect of the Roux-en-Y gastric bypass on hormones involved in body weight regulation and glucose metabolism. *Ann Surg*. 2004;240: 236-242.

37. Rubino F, Forgione A, Cummings DE, et al. The mechanism of diabetes control after gastrointestinal bypass surgery reveals a role of the proximal small intestine in the pathophysiology of type 2 diabetes. *Ann Surg*. 2006; 244:741-749.

38. Thaler JP, Cummings DE. Minireview: Hormonal and metabolic mechanisms of diabetes remission after gastrointestinal surgery. *Endocrinology*. 2009;150:2518-2525.

39. Ferrannini E, Mingrone G. Impact of different bariatric surgical procedures on insulin action and beta-cell function in type 2 diabetes. *Diabetes Care*. 2009;32:515-520.

40. The Longitudinal Assessment of Bariatric Surgery Consortium. Perioperative safety in the longitudinal assessment of bariatric surgery. *N Engl J Med*. 2009;361:445-54.

41. Pories WJ. Bariatric surgery: risks and rewards. *J Clin Endocrinol Metab*. 2008;93(11 Suppl 1):S89-S96.

42. Pratt GM, Lueck-Sneve J. Research and data collection efforts are making bariatric surgery safer and more widely available. 2006. Available at: http://www.wlslifestyles.com/cached/_downloads/2041/Research%20and%20Data%20Collection%20Efforts%20are%20Making%20Bariatric%20Surgery%20Safer%20and%20More%20Widely%20Available_ma. Accessed on December 20, 2009.

43. Picot J, Jones J, Colquitt JL, et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. *Health Technol Assess* 2009;13(41):1-190, 215-357, iii-iv.

44. Tice JA, Karliner L, Walsh J, Petersen AJ, Feldman MD. Gastric banding or bypass? A systematic review comparing the two most popular bariatric procedures. *Am J Med*. 2008;121:885-893. HW

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