Update on Treatment Strategies for Obesity

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Obesity is a disease that is defined as the accumulation of excessive amounts of body fat and is associated with increased risk of serious illness, disability, and death. In clinical practice, obesity is best assessed by calculating body mass index and measuring waist circumference. Treatment options are determined based on the body mass index, waist circumference, and adverse health consequences the patient is experiencing or is at an increased risk for facing in the future. Today, overweight and obesity impacts the majority of patients we treat in our clinical practices. Although endocrinologists are uniquely positioned to treat one of the major consequences of our current obesity epidemic, type 2 diabetes, we also need to be positioned and prepared to effectively treat one of its major causes—obesity. Type 2 diabetes and obesity are very much intertwined. Treatment of each disease affects the other. For these reasons, endocrinologists need to be experts in the treatment of obesity as well as diabetes. They should keep up with advances in obesity treatment including lifestyle, pharmaceutical, and surgical strategies. These strategies offer opportunities for improving the overall treatment for our obese patients today and will continue to improve and expand over the next decade. **(*J Clin Endocrinol Metab* 98: 1299–1306, 2013)**

Obesity is one of the most challenging chronic disease threats facing our country today. It has profound health and economic consequences for our patients and our country. The most recent data indicate that 35.5% of adult men and 35.8% of adult women are obese (1). Furthermore, 63.7% or almost two-thirds of adult women and 73.9% or almost three-fourths of adult men are classified as overweight or obese, meaning that healthy weight people have become the minority (1). These alarming statistics are highly relevant for endocrinologists for at least 2 reasons: 1) as a result of the existing high prevalence of overweight and obesity, we will be seeing more and more type 2 diabetic patients in our practices for the years to come; and 2) most our patients already need our help in managing their excessive weight to improve their health and prevent other adiposity-related diseases. Currently, it is reported that only about one-third of obese patients receive an obesity diagnosis or weight-related treatment advice from their physicians (2). This is an unfortunate statistic that I believe presents an opportunity for endocrinologists. In this update, I will discuss the current evidenced-based treatment strategies for obesity and highlight clinically relevant advances in treatment involving diet, physical activity (PA), and drug and surgical therapy. Pivotal articles published over the last 24 months will be emphasized.

The Current Approach to Obesity Treatment

In clinical practice, overweight and obesity are diagnosed by body mass index (BMI), which represents a measure of a patient's weight for their height. It is a surrogate marker, not a direct measure for body fatness. BMI is highly correlated with the percentage of body fat on a population basis (3). As BMI increases, the health risks (diabetes, coronary heart disease, degenerative joint disease, and certain cancers) associated with high adiposity also increase. More accurate methods to measure body fatness such as air displacement, bioelectrical impedance, dual-energy x-

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Abbreviations: BID, twice a day; BMI, body mass index; BMOD, behavioral modification; NAL/BUP, naltrexone and bupropion; PA, physical activity; PHEN/TPM, phentermine and topiramate; QD, once a day; RYGB, roux-en-Y gastric bypass; SR, sustained release.

ray absorptiometry, and skin fold calipers all have limitations or are currently not practical to provide in a typical clinical practice. BMI alone, however, does not always accurately reflect a patient's complete risk profile. BMI can be misleadingly elevated because of increases in muscle or edema or misleadingly low in the elderly. Even when the BMI is high because of body fatness, it does not alert the physician to the location of the excess fat. Waist circumference can be added to a BMI measurement to provide a more precise risk assessment given that increased intra-abdominal fat is associated with greater morbidity than peripheral or subcutaneous fat accumulation.

BMI has become a routine vital sign in most clinical practices and, coupled with a waist circumference measurement, is becoming a standard part of clinical care. Obesity is defined as a BMI $\geq$ 30 kg/m^2, and overweight is defined as a BMI between 25.0 and 29.9 kg/m^2 (4). A waist circumference of >40 inches (>102 cm) for a white man and >35 inches (>88 cm) for a white woman has been identified as representing an increased disease risk for cardiovascular disease. In some populations, waist circumference is a better indicator of relative disease risk than is BMI; examples include Asian Americans or persons of Asian descent living elsewhere. In an effort to more accurately stratify patients, ethnic-specific cut points for waist circumference have also been suggested. For example, in Asian Americans the high-risk "threshold" values for waist circumference have been decreased to >85cm for a man and >80 cm in women.

It is important to realize, however, that these current cut points for risk stratification have limitations. There is a curvilinear relationship between BMI or waist circumference and health risk as opposed to a true "threshold effect." Health risk rises incrementally as BMI and waist circumference increase and can vary over a large range of BMI values for any individual. For this reason, other obesity classification systems such as the Edmonton Obesity Staging System have been proposed as a more comprehensive measure of obesity-related disease burden and predictors of mortality (5). More research is needed to better stratify risk of our patients in the future.

All obesity treatments involve some degree of risk, with the goal being to balance the potential risk and benefits of the treatment for a specific individual. Obesity is no different than other diseases; the most aggressive and high-risk treatments are reserved for patients at the highest medical risk because of their excess weight. They also represent the patients that potentially will experience the most benefit from a weight reduction. It makes sense that we are willing to prescribe a more aggressive obesity treatment with a greater risk profile (such as drugs or surgery) in these higher risk individuals. Table 1 shows the current options for treatment based on the BMI and associated comorbidities. The treatment table is created from the Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: Evidence Report, developed by the NHLBI Expert Panel and released in 1998 (4). The NHLBI has announced that new guidelines for obesity, hypertension, and lipids will be released jointly in 2013.

Diet and PA Treatment for Obesity

The foundation of any obesity treatment involves decreasing energy intake (food intake/diet) and/or increasing energy expenditure (PA/exercise) in order to create a negative energy balance. The method or treatment strategy by which the caloric intake reduction is achieved varies from diet to diet and results in many choices for the actual structure or type of diet. For example, some diets emphasize counting calories, limiting portions, or using formulated meal replacements, whereas others reduce or limit certain types of foods or reduce or eliminate specific macronutrients in the diet. All of these strategies ultimately result in a reduction in calories consumed.

Researchers have been constantly looking for the optimal diet composition for weight loss. Doctors and patients alike want to know: what is the absolute best diet for weight loss? With this question in mind, low fat, moderate fat, low carbohydrate, low glycemic, high protein, and Mediterranean diets have been studied extensively in both

Table 1. Obesity Treatment Options Based on the Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: Evidence Report Released in 1998

Treatment Options	Potential Treatment Risk	Current Patient Risk (BMI Range, kg/m^2)				
		Low		→		High
		25–26.9	27–29.9	30–34.9	35–39.9	≥40
Diet, exercise, and behavioral therapy	Low	+	+	+	+	+
Pharmacotherapy	↓		With a comorbidity	+	+	+
Surgery	High				With a comorbidity	+

short- and long-term time periods and in clinically controlled settings as well as real-world settings. In general, all of these diets have had comparable weight loss results. Recently, Wadden et al (7) presented a comprehensive review highlighting the randomized, controlled trials that have compared diets with varying macronutrient composition. In this review, no single diet emerged as a clear winner, despite a very robust number of clinical studies in this area. These equivalent dietary results have led clinical investigators to assert that the impact of the caloric restriction a diet produces outweighs the impact of the macronutrient composition of the calories consumed in that diet. This concept is perhaps best illustrated and supported by the 2008 *New England Journal of Medicine* (*NEJM*) article by Sacks et al (8). This large, well-designed study compared diets that provided either a low or high proportion of calories from fat (20 vs 40%), crossed with a low or high proportion of calories from protein (15 vs 25%). This cross resulted in 4 different diet macronutrient combinations for diet group assignment and 4 levels of carbohydrate content (65, 55, 45, and 35%). All 811 participants in the trial received the same daily caloric deficit instructions, regardless of their macronutrient assignment (750 kcal/deficit/day), and the same intensive lifestyle intervention. As similarly demonstrated in multiple other smaller studies, no significant differences in weight were appreciated among the 4 diet groups over 2 years, supporting the concept that the macronutrient composition of a weight reduction diet does not influence weight loss when caloric deficit is held constant.

Over the last decade, adherence to a diet has been shown to be a much better predictor of weight loss success than the actual type of diet a patient eats (9). It appears that it is not what you eat but instead how long you can eat it. Any diet can work in any given individual if they can successfully adhere to the reduction in calories most diets create. The window of adherence for any diet, however, is relatively short-lived. After 3–6 months, adherence to most diets has been shown to wane (9). In the future, the ability to correctly match a patient to the diet type or strategy he or she can best adhere to for a 3- to 6-month period would significantly improve our initial weight loss outcomes. Although a few authors have recently reported an association between higher insulin levels and better weight loss on a low glycemic load diet, very few larger studies have been successful at finding predictors of weight loss success, and currently no one has been successful in providing a reproducible strategy for accomplishing this task (10, 11).

A study by Sumithran et al (12), published in the *NEJM* in 2011, may have exposed at least part of the reason why adherence to diets is constantly problematic for patients. In this study, 50 patients were enrolled into a 10-week weight loss program utilizing a very low calorie diet. Circulating levels of several peripheral hormones involved in the homeostatic regulation of body weight were measured at baseline (before weight loss), at the end of the 10-week diet, and at 62 weeks. The investigators found that many of the compensatory hormonal changes we typically see with a weight loss (such as decreased leptin, increased ghrelin, reduced peptide YY and cholecystokinin) were sustained and remained sustained even at the 62-week mark. These compensatory changes are in the directions that would favor weight regain. This would explain perhaps why dietary changes are very hard to sustain over the long term and why adherence to any diet fades over time. These findings support the possibility that compensatory physiological changes eventually overpower the patient's behavioral ability to adhere to a reduced number of calories required to maintain the reduced body weight state. It also supports the hypothesis that weight regain has a strong physiological basis and is not simply the result of the voluntary resumption of poor eating habits. This is an important concept for endocrinologists to understand when treating obese patients because it validates why medications that change one's physiology or hormone levels may be indicated and helpful in long-term weight loss treatment.

PA is a key part in the treatment of obesity. Although PA has been repeatedly shown not to be as effective as diet for causing an acute weight loss, it has proven to be one of the most important factors for preventing weight regain (13–18). PA may also improve the amount of weight that is lost as fat during weight loss; however, not all studies have confirmed this. Although diet is critical initially for weight loss, because adherence fades over a typical 3- to 6-month period, PA becomes more important over time.

Researchers over the past decade have spent a good deal of time determining exactly how much activity we need to prescribe to our patients, not for weight loss but to prevent regain of lost weight. It takes a large amount of PA for patients to maintain a weight reduction. I say "most" patients because there are some that can be successful using a diet-only approach to maintain or with lesser amounts of PA. However, the data consistently show that for most patients, 60 minutes of moderate-intensity activity (such as brisk walking) most days of the week is an amount required to prevent or mitigate weight regain. A recent review of randomized trials and observational data by Donnelly et al (19) in 2009 highlighted and confirmed this PA recommendation. This high level of PA is also supported by self-reports and objective measures of individuals in the National Weight Control Registry, a group of individuals successful at maintaining at least a 13.6-kg

weight loss for a minimum of 1 year, as well as a recent prospective analysis in the Nurses' Health Study published in 2010 (20–22). At first glance, a patient may think this goal is insurmountable, but if increased slowly over time and accumulated in smaller bouts throughout the day, it is achievable. Although the mechanisms determining why high levels of PA repeatedly facilitate weight loss maintenance are not fully understood, in 2012 clinical research continues to strongly show that this treatment strategy is one of the best predictors of weight loss maintenance in our patients. The challenge of meeting the requirement for a high level of PA to prevent weight regain also means that physicians should encourage their patients to tackle the weight problem urgently, because the longer action is postponed and the heavier the patient gets, the harder it is to both lose it and maintain that loss.

Drug Treatment for Obesity

Perhaps the most exciting advances in obesity treatment are in drug therapy. Drug therapy for obesity is indicated as an adjunct to diet and exercise in adults with a BMI of at least 30 kg/m^2 or of at least 27 kg/m^2 if accompanied by an obesity-related comorbidity (4). The US Food and Drug Administration (FDA) has recently approved 2 new drugs for use in obesity treatment (Table 2). These will soon join orlistat, a gastric and pancreatic lipase inhibitor, as drugs indicated for the long-term treatment of obesity. Detrimental side effects have caused obesity drugs initially approved to be either removed (fenfluramine, dexfenfluramine, phenylpropylamine) by the FDA or voluntarily withdrawn (sibutramine). Several new drugs (rimonabant, taranabant, high-dose topiramate) have been halted in the US clinical research pathway because of what was felt to be unacceptable risk (side effects).

Lorcaserin is a selective serotonin 2C receptor agonist that works by decreasing food intake. It is similar in mechanism of action to fenfluramine and dexfenfluramine, except that it is specific for the 2C serotonin receptor that is not found on the heart or heart valves. The result is thought to be a compound with a desirable increased satiety and inhibitory hunger effect and no heart valve damage. Echocardiogram studies were performed in clinical studies with no increased incidence of FDA-defined cardiac valvulopathy. There is some concern that the studies were not powered adequately for complete confidence because of a lower than expected event rate. The FDA advisory panel voted 18 to 4 in favor of approval in May 2012, and lorcaserin was officially approved by the FDA in June 2012. It should be available in 2013.

Three pivotal phase 3 US trials have been recently published for lorcaserin (23–25). In the BLOSSOM Trial (24) published in 2011, 4008 obese or overweight patients with obesity-related comorbid conditions were studied. A total of 2224 (55.5%) completed the 1-year trial. Patients were randomly assigned in a 2:1:2 ratio to receive lorcaserin, 10 mg twice a day (BID), lorcaserin 10 mg once a day (QD), or placebo. All received diet and exercise counseling. Significantly more subjects receiving the lorcaserin BID (47.2%) and lorcaserin QD (40.2%) lost at least 5% body weight at 1 year than placebo (25%). Weight loss of at least 10% was achieved in 22.6% of the lorcaserin BID group vs 9.7% in the placebo group. The BLOOM study (25) published earlier in *NEJM* in 2010 evaluated 3182 patients for up to 2 years with similar results. The BLOOM-DM study (23) evaluated the safety and efficacy of lorcaserin in 604 patients with type 2 diabetes with

Table 2. Weight Loss Medications Recently Evaluated or Approved by the FDA

Obesity Drug	Trade Name	Mechanism	Proposed Dosage	Phase 3 Clinical Trials	Average Expected Weight Loss	Most Common Adverse Events	Safety Concern Raised by the FDA
Lorcaserin	Belviq	Selective serotonergic 2C receptor agonist	10 mg po BID	BLOSSOM, BLOOM, BLOOM- DM	Drug, 5–6%; placebo, 2–3%	Headache, nausea, dizziness, fatigue	Carcinogenicity, valvulopathy, cardiovascular risk
PHEN/TPM	Qsymia	Sympathomimetic amine and anticonvulsant agent	Low, 3.75/23 mg; mid, 7.5/46 mg; high,15/92 mg po QD	EQUATE, EQUIP, CONQUER, SEQUEL	Drug, 5–11%; placebo, 1–2%	Headache, paresthesia, dry mouth, altered taste, dizziness	Depression, cognitive issues, cardiovascular risk from increased heart rate, birth defects
Bupropion SR/ naltrexone SR	Contrave	Dopamine and norepinephrine reuptake inhibitor and opioid receptor antagonist	Sustained release 360/32 mg po QD	COR I, COR-II, COR-BMOD, COR-Diabetes	Drug, 5–6%; placebo, 1–2%	Nausea, headache, insomnia, constipation, tremor	Cardiovascular risk from increased blood pressure and heart rate

Abbreviation: po, by mouth.

glycated hemoglobin of 7–10% and treated with metformin, a sulfonylurea, or both. The study found that 37.5% of patients on lorcaserin BID, 44.7% on lorcaserin QD, and 16.1% on placebo lost at least 5%. Approximately half of the patients in the lorcaserin treatment arms achieved a glycated hemoglobin (HbA1c) level <7%, almost twice the rate in the placebo group. It is not clear at this time whether lorcaserin has effects on glycemic control that are independent of weight loss.

Although lorcaserin meets FDA weight loss criteria, I believe the efficacy is modest, but the risk profile is also low. For this drug, it is important for clinicians to realize that certain individuals may respond more (have a significantly greater weight loss) than other individuals. This drug may be one that eventually will be helpful in a smaller subset of obese "responders" and need to be discontinued because of a lack of significant weight loss in other patients. Lorcaserin's reduction in HbA1c levels appears more substantial than the weight loss reduction in the BLOOM-DM study, and therefore persons with diabetes may also prove to be a subset that may have greater benefit from this new obesity drug. Lorcaserin has not been studied in combination with other drugs such as phentermine. Although combining the 2 drugs (phentermine and lorcaserin) may increase weight loss, the safety of the combination has not been evaluated, making it an uncertain and potentially risky recommendation to prescribe at this time.

The drug combination of phentermine and topiramate (PHEN/TPM) was also recently approved by the FDA. Phentermine (15–30 mg/d) induces central norepinephrine release and promotes weight loss by decreasing food intake. It is currently approved as a monotherapy only for short-term use in obesity treatment. Topiramate monotherapy (200–400 mg/d) was approved in 1996 for the treatment of seizures and in 2004 for migraine prophylaxis (100 mg/d in 2 divided dosages) and is currently not approved as a monotherapy for weight management. Topiramate exhibits a combination of properties such as effects on sodium channels, enhancements of γ-aminobutyric acid (GABA)-activated chloride channels, and inhibition of carbonic anhydrase isoenzymes, but the specific mechanism promoting weight loss is unclear. In combination, the drugs have shown greater weight reduction than either agent alone. Potential safety issues of concern have been depression, anxiety, cognitive-related complaints, cardiovascular risk with a small increase of heart rate, and reduced bicarbonate, which could exacerbate metabolic acidosis as well as the potential for teratogenicity. Initial obesity trials with higher dose topiramate as a monotherapy were halted because of the cognitive and depressive side effects. The combination of PHEN/TPM allows a lower dose of controlled release topiramate to be used, and therefore a more acceptable adverse events profile. The combination of phentermine and topiramate received a vote of 20 to 2 in favor from the February 2012 FDA advisory panel and was FDA approved in July of 2012. It became available for use in late 2012.

Four pivotal phase 3 trials have been published within in the last 2 years. The EQUATE trial (n = 756) compared high-dose PHEN/TPM (15 mg of phentermine/92 mg of topiramate controlled release) and mid-dose PHEN/TPM (7.5/46 mg) with placebo and the respective single agent phentermine and topiramate components for 28 weeks in adults with BMI > 27 kg/m^2. The EQUIP trial (n = 1267) compared high-dose and low-dose (3.75/23 mg) PHEN/TPM with placebo for 56 weeks in obese individuals (BMI > 35 kg/m^2) (26). The CONQUER trial (n = 2487) compared full-dose and mid-dose PHEN/TPM with placebo for 56 weeks, including obese and overweight adults (BMI, 27–45 kg/m^2) who had to have 2 or more weight-related comorbidities (27). The most recent and perhaps timely study was SEQUEL, which was an extension study of the CONQUER study. SEQUEL was designed to evaluate the long-term efficacy and safety of the PHEN/TPM combination in obese subjects with cardiometabolic disease for an additional 52 weeks (total, 2 y) (28). A total of 676 (78.1%) of 866 eligible subjects continued in the extension study. Eighty-four percent completed the study, and 79.3% in the high-dose PHEN/TPM (15/92 mg) group and 75.2% in the mid-dose PHEN/TPM (7.5/46 mg) group lost > 5%, compared to 30% in the placebo group. Mean weight loss results were −10.7% and −9.3% for the treatment groups, respectively, and −1.8% for the placebo group. More than 50% of the PHEN/TPM-treated subjects achieved a 10% or greater weight loss. This weight loss produced equal reductions in diastolic and systolic blood pressure in the placebo and PHEN/TPM groups, but this was accompanied by a net decrease in concomitant antihypertensive medications in the PHEN/TPM groups, whereas antihypertensive medications were increased in the placebo group. Perhaps most importantly, heart medications were decreased in the treatment groups. Improvements in glycemic control and dyslipidemia were also noted.

Weight loss with the combination of PHEN/TPM is better than any of the obesity drugs in the pipeline at this time. Along with this increase in efficacy, however, comes a more troublesome risk profile that clinicians need to understand and actively address with their patients. Depression and cognitive issues have not been major issues in the more recent controlled-release trials. Cardiovascular events and birth defects appear to be the issues that will need to be monitored closely.

Another drug combination, naltrexone and bupropion (NAL/BUP), is awaiting FDA approval. The combination medication has been evaluated in several 56-week phase 3 trials (29–32). The naltrexone sustained release (SR)/bupropion SR combination functions as an opioid receptor antagonist combined with a norepinephrine and dopamine receptor reuptake inhibitor. Bupropion has neuronal effects that lead to reduced energy intake and increased energy expenditure. Naltrexone was chosen as a complement to bupropion in order to block compensating mechanisms that attempt to prevent long-term, sustained weight loss. The FDA advisory panel voted 13 to 7 in favor of approval of this combination in December of 2010; however, the FDA declined to approve the drug in early 2011, going against the advisory panel recommendation in a somewhat surprising decision. The FDA is requiring a large-scale safety study evaluating cardiovascular events to be conducted before approval will be reexamined. This was an interesting and unexpected decision by the FDA, given that bupropion, which is the drug potentially associated with the increase in cardiovascular risks, is currently available and used by millions of Americans for the treatment of mild depression or to stop smoking. In the initial obesity trials, blood pressure and pulse were slightly increased, indicating the potential for an increased risk for heart attacks or cardiovascular events. Increased risk of seizures as well as syncope in the treatment group compared to the placebo group was also a safety concern that was noted. A study of this size and scope will take tremendous resources and time to complete. The earliest this drug could be approved is late 2014 or early 2015.

Four pivotal trials comprising the Contrave Obesity Research (COR) program have been performed, and 2 have been published (33). The COR-I assesses the safety and efficacy of NAL/BUP in 1742 healthy, nondiabetic, obese patients and was published in 2010 (32). COR-II is a 56-week study designed to assess the safety and efficacy of the combination in 1496 healthy, nondiabetic, obese patients. COR-Diabetes is a 56-week study designed to assess the safety and efficacy of NAL/BUP in 505 obese subjects with type 2 diabetes. COR-BMOD, published in 2011, is a study designed to evaluate the safety and efficacy of NAL/BUP alone or when combined with intense diet, exercise, and behavior modification in 793 patients over 56 weeks (29). The COR-BMOD trial had a unique study design that showed the potential effect the drug could achieve if combined with a more intensive behavioral change program. In the COR-BMOD trial, participants were randomly assigned in a 1:3 ratio to receive placebo and intensive weight loss behavioral modification (BMOD) or NAL/BUP (32/320 mg) and intensive weight loss behavioral modification. The placebo plus BMOD group lost 5.1% of initial body weight vs 9.3% weight loss in the NAL/BUP with BMOD group. Depression and suicidal ideation were more frequent in the placebo group compared to the combination group.

Surgical Treatment for Obesity

The use of bariatric surgery as a treatment for obesity has grown dramatically over the last several years. Because outcomes in obese persons with type 2 diabetes have been so impressive, the International Diabetes Federation has recently recommended consideration of bariatric surgery as an accepted treatment option in patients with a BMI of 30–35 kg/m^2 when diabetes cannot be adequately controlled by traditional medical management (34). In 2011, the FDA expanded approval of the LAP-BAND adjustable gastric banding system to be used in patients who have not been successful losing weight with a nonsurgical method and have a BMI of 30–34 kg/m^2 with an existing condition related to their obesity. Prior approval had been limited to a BMI $\geq$ 35 kg/m^2 with a comorbidity or 40 kg/m^2 without. This controversial concept of lowering the BMI cutoff for surgery has been evaluated by several pivotal papers published over the last 24 months in high-profile journals.

In 2012, Mingrone et al (35) compared weight loss surgery to conventional medical treatment for type 2 diabetes mellitus. In this prospective randomized clinical trial published in the *NEJM*, 2 surgical procedures, roux-en-Y gastric bypass (RYGB) and biliopancreatic diversion, were compared with conventional medical treatment of type 2 diabetes in a severely obese population. At 2 years, diabetes remission, defined as a fasting glucose level of $<$ 100 mg/dL and a HbA1c level of $<$ 6.5%, had occurred in no patients in the medical therapy group vs 75% in the gastric bypass group and 95% of the biliopancreatic-diversion group ($P < .001$). HbA1c levels showed greater improvement in both surgical groups than the medical therapy group, leading the authors to conclude that weight loss surgery may be more effective than conventional medical therapy in controlling hyperglycemia in severely obese patients with type 2 diabetes.

In a second similar study by Schauer et al (36), the efficacy of intensive medical therapy alone vs medical therapy plus RYGB or sleeve gastrectomy was evaluated in obese uncontrolled persons with diabetes. The study also showed that medical therapy plus surgery resulted in better glycemic control in significantly more severely obese patients than medical therapy alone. In this study and others, preoperative BMI did not predict control of diabetes after the surgical procedure. Metabolic surgery for type 2 diabetes even at lower BMI ranges, although not standard

of care for the disease at this time, may be coming closer to the mainstream.

The previous large "treatment gap" resulting from the lack of approved obesity drugs as well as complications and risks associated with surgical procedures such as RYGB have fueled the investigation of endoscopic devices and procedures as a possible middle ground treatment option located somewhere between bariatric surgery and lifestyle treatments. Supporters of this developing field believe endoscopic obesity treatments may offer many of the benefits of weight loss surgery including treating metabolic comorbidities such as diabetes while being reversible, and with a lower risk profile than traditional surgical approaches. Endoscopic procedures also may be treatment options for patients who are poor surgical candidates, and they could be used to address weight regain after bariatric surgery. The development of these newer endoscopic procedures and devices has led to clinical trials being published in this new developing therapeutic area (6, 37).

Conclusion and Perspectives

Obesity and overweight affect most patients who walk into our clinics today. Although obesity treatment is still in its infancy (very similar to type 2 diabetes treatment 20 y ago), we do have evidence-based treatment strategies to use today. These strategies encompass modifying diet, increasing PA, utilizing weight loss medications, as well as recommending surgical procedures in appropriate patients. Assessing obesity and treating it with all the strategies available is now becoming a clinical standard of care. Although still challenging, effective obesity treatment is not a hopeless or futile endeavor in 2013. Obesity treatments will only continue to improve as our understanding of the physiology of the disease improves and as researchers refine existing treatment strategies and new options are developed. It is my hope that endocrinologists actively engage in the diagnosis, embrace early treatment of obesity with their own patients, and become experts for this challenging and important disease.

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