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Obesity and Nutrition (O Pickett-Blakely, Section Editor)

An Approach to Obesity Management for Gastroenterologists and Hepatologists

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Abstract

Purpose of Review Obesity is associated with multiple gastrointestinal and liver diseases such as gastroesophageal reflux disease, Barrett's esophagus, esophageal adenocarcinoma, cholelithiasis, colon polyps, and fatty liver disease. To effectively manage obesity, it is imperative to understand current and emerging therapies and procedures.
Findings Obesity is becoming increasingly prevalent and is associated with a growing monetary health care burden. Cardiac disease, cerebrovascular disease, and diabetes are among the leading causes of preventable and premature death of Americans related to obesity. In addition to behavioral modification (diet and exercise) and bariatric surgery, multiple pharmacotherapies and endoscopic procedures are newly approved and available for the management of obesity.
Summary This paper reviews the current literature on the treatments available for the management of obesity including behavior modification, pharmacotherapy, endoscopic weight loss procedures (endobariatrics), and bariatric surgery.

Introduction

Obesity is a widely recognized, progressive public health problem. In the USA, the proportion of adults with obesity (body mass index of greater than or equal to 30 kg/m^2) has risen to ~ 30% [1], and worldwide, severe obesity (BMI ≥ 40 kg/m^2) affects 7.7% of the population [2]. Because cardiac disease, cerebrovascular disease, and diabetes are the leading cause of preventable death, the medical, financial, and societal impact of the obesity epidemic is vast [3]. The American Heart Association (AHA) guidelines on obesity management recommend modest weight loss of 5–10% of initial body weight to achieve meaningful cardiovascular risk modification [4]. Therefore, all physicians and health care providers should strive to equip our patients with the tools necessary to encourage weight loss.

Given the profound impact of obesity in gastrointestinal and liver diseases, leading societies have all published articles on the important role of gastroenterologists and hepatologists in obesity management, including the AASLD Diagnosis and Management of NAFLD, the ASGE Position Statement on Endobariatric Therapies in Clinical Practice, and the AGA Practice Guide on Obesity and Weight Management, Education, and Resources (POWER) in 2017 [5,6,7•].

In hepatitis C therapy, obesity is associated with lower response to antiviral therapy [8] and weight loss via behavioral modifications (diet and exercise) is the foundation of management for non-alcoholic fatty liver disease (NAFLD). Additionally, weight loss in obese individuals is linked to decreased colorectal cancer risk [9]. Because of the complex pathophysiology of obesity, it is imperative to learn a multidisciplinary approach for management, including counseling for behavior modification, pharmacotherapy, and endoscopic and surgical weight loss procedures.

Behavioral Modification

Behavior modification is the core of obesity therapy and focuses on modifiable factors that impact energy balance, specifically, excess energy intake and inadequate energy expenditure. To achieve weight loss, a relative energy deficit must be achieved by reducing energy intake (via diet modification) and increasing energy expenditure (via exercise). A reduction of ≥ 500 kcal/day typically leads to 1 lb of weight loss per week which is medically safe [10].

Diet

Overall calorie or energy restriction is the most common method of using diet to reduce energy intake. A 1200–1500-kcal/day diet for women and 1500–1800-kcal/day diet for men is often recommended [4]. Altering specific dietary macronutrient (carbohydrate, protein, and fat) content is the basis of many popular diets such as low-carbohydrate, high-protein, low-fat, and others commercial diets. However, patients and physicians alike have fallen victim to ever changing, and at times conflicting data, on the best dietary approach for weight loss.

The culture of dieting has been popularized and dominated by consumerism leading to multiple so-called fad diets, though the data regarding the effectiveness, safety, and sustainability of these diets is minimal. The low-fat, low-fat/high-protein, high-fat, or high-fat/high-protein/low-carb diets were compared in a large randomized trial by Sacks et al. Although the macronutrient content varied between diets, each diet was 750 kcal deficient and accompanied by moderate physical activity (90 min per week). The trial showed no significant difference in reduction in weight or waist circumference between diets [11].

Another randomized trial compared energy-deficient low-carbohydrate and low-fat diets accompanied by a behavioral intervention and showed similar weight loss in both groups, with a mean weight loss of 11% and 7% of initial body weight (IBW) at 1 year and 2 years, respectively [9].

Popular diets and diet plans based on altered macronutrient composition and reduced energy intake include, but are not limited to, the Atkins, Ornish, Zone, Ketogenic, Paleolithic, Weight Watchers, Jenny Craig, and Nutrisystem diets. The Atkins diet predominantly restricts carbohydrates, without restricting fats, while the Ornish diet limits fat intake. The Weight Watchers, Jenny Craig, and Nutrisystem diet plans restricts overall caloric intake using a point system and meal replacements respectively [12]. The Zone diet limits overall caloric intake, with protein and healthy fats comprising most of the caloric intake, while limiting carbohydrates to those with low glycemic-index [13]. There are few studies comparing the effectiveness of the many available diet plans, but Dansinger and colleagues compared the Atkins, Ornish, Weight Watchers, and Zone diets in a randomized trial [12]. After 1 year, there was no observed significant difference in weight loss or cardiovascular risk factor modification between the diet groups [12]. A more recent review by Gudzone and colleagues indicated that commercial diets like Weight Watchers, Jenny Craig, and Nutrisystem are effective for weight loss when compared with behavioral modifications [14]. Additional studies are needed to investigate the sustainability and efficacy of commercial programs and fad diets.

Similar to Atkins in terms of macronutrient distribution, the Ketogenic and Paleolithic diets focus on limiting carbohydrate and liberalizing fat intake. The very low carbohydrate content results in fat metabolism for energy and with significant carbohydrate restriction, a state of ketosis which decreases body weight and BMI and improves other metabolic parameters [15–17]. The Ketogenic diet has been utilized for many years for symptomatic treatment of epilepsy by increasing neuroprotective serum ketones [18]. Obese patients randomized to low-calorie versus very-low-calorie ketogenic (VLCK) diet experienced 7 kg vs. 19.9 kg at 1 year, with greater than 88% of the VLCK diet group achieving 10% reduction of initial body weight [19]. However, small studies suggest potential adverse effects of the Ketogenic diet on cognitive performance, bowel function, liver-associated enzymes, and micronutrient status; thus, patients should be closely followed by a physician [20–22]. The low-carbohydrate, Paleolithic diet (Paleo) composition resembles that of primitive man in the "hunter-gatherer" era and includes lean meats, wild game, nuts, and vegetables [23]. Small trials suggest that the Paleo diet can induce weight loss, although potentially poor long-term compliance may compromise its impact [23–25].

Intermittent fasting (IF) has quickly become a popular method for weight loss. The goal is to alternate feeding and length of fasting, consuming calories when your metabolic system is most active. There are multiple methods including alternate-day fasting and time-restricted feeding [26,27]. Initial studies suggest that IF can improve insulin sensitivity, lower blood pressure, decrease appetite, and lower LDL and triglyceride levels [28,29]. However, a randomized control trial comparing daily calorie restriction to alternate-day fasting, following participants for 1 year, determined no significant difference in actual weight loss [30]. One small randomized study suggests that some of the metabolic benefits may be independent of weight loss and due to alignment of circadian rhythms in metabolism by early time-restricted feeding [28]. Larger

randomized studies are needed to better understand the safety and efficacy of IF in humans.

Based on the current available literature, there is no specific diet that is more efficacious for weight loss. Nonetheless, the available data suggests that diet modification with an overall caloric deficit, as opposed to specific micronutrient alteration, is fundamental for weight loss, particularly when combined with exercise.

Exercise

Exercise is an essential component of obesity management. At least 150 min of moderate intensity activity or 75 min of vigorous activity per week is recommended by the AHA to maintain a healthy lifestyle [31]. Greater weight loss can be achieved with increased intensity of aerobic exercise (200 min/week) [32,33]. Though levels of activity vary for each person, when medically appropriate, patients should aim for a goal heart rate (HR) of 40–59% of the age-based maximum HR (MHR) for moderate intensity and 60–84% MHR for vigorous activity [34]. Aerobic training (AT) or "cardio" is a common method of exercise, consisting of varied intensity physical activity. AT alone can induce weight loss and improve cardiovascular parameters [35]. However, AT combined with a diet modification induces significantly more weight loss that can be sustained beyond 1 year [32,36].

Strength training or resistance training (RT) utilizes external resistance to build muscle strength and density. This form of exercise also improves metabolic parameters and improves hepatic steatosis [37–40]. RT can be a particularly advantageous exercise method for patients with cardiorespiratory compromise, as it requires less energy consumption [37]. A randomized trial comparing AT and RT demonstrated that AT is superior for reduction of body fat and body mass [41]. Another study randomized diabetic patients to standard diet vs. high-protein (HP) diet with RT; the HP/RT group had superior weight loss, reduction in waist circumference, and CV risk modification [42]. Although AT is superior for weight loss, strength training should be incorporated into patient's exercise program to improve/maintain muscle mass and strength as fat mass is lost.

Other Behavioral Therapy

Adjunctive strategies such as mindfulness and cognitive behavioral therapy can be considered in the management of obesity. The addition of these therapies can bolster adherence to healthy habits, which can be sustained in the long term and prevent weight regain [43–45].

Pharmacotherapy

Behavioral modification, although effective, is limited by non-compliance and eventual weight regain, but the addition of pharmacotherapy can augment weight loss [36,37]. Some physicians can be fearful of prescribing anti-obesity agents due to historical associations with serious adverse events and lack of training to use these drugs [46]. However, current options have improved safety profiles and greater efficacy for weight loss. At the time of this review, there are

seven FDA-approved anti-obesity medications; however, only six are readily available for obesity management (Table 1).

Phentermine, a norepinephrine-releasing agent, is the most well-known anti-obesity medication that has been in use for over 50 years. Its original release on the market was in combination with Fenfluramine, a serotonin 5-HT_{2B} receptor agonist, popularly known as "Fen-Phen." This combination was withdrawn from the market because of associated severe valvular heart disease. But phentermine alone has proved to be safe for both short- and long-term use, producing up to an additional 3.6-kg weight loss above diet and exercise alone [47,48]. The brands on the market are Adipex®, 15- and 37.5-mg capsules, and Suprenza®, 15-, 30-, and 37.5-mg tablets. Side effects include anxiety, insomnia, restlessness, elevation in heart rate, dizziness, tremors, and GI distress [49]. This medication is contraindicated in pregnant or breastfeeding women, as well as patients with a history of cardiovascular disease, hyperthyroidism, or concurrent use with monoamine oxidase inhibitors (MAOI) [50].

The combination drug phentermine/topiramate is marketed under the brand name Qsymia®. Topiramate is a GABA receptor modulator and its alteration of GABA activity induces appetite suppression and satiety; it is not marketed for weight loss as monotherapy because of side effects such as slowed cognition and poor cognition. The fixed dose combination was approved in 2012; the starting dose is 3.75 mg of phentermine/23 mg of topiramate daily for 2 weeks with incremental increase up to the standard 7.5 mg of phentermine/46 mg of topiramate daily dose. The high-dose regimen of 15 mg of phentermine and 96 mg of topiramate can be used if weight loss is not achieved at lower doses. Average weight loss over a year with standard dose phentermine/topiramate is 8.1 kg and 10.2 kg at the high dose [51]. Adverse effects include dry mouth, paresthesias, constipation, insomnia, depression, and anxiety. Additionally, this medication can cause birth defects and should be avoided in pregnant women. Contraindications include concurrent use with MAOIs, adrenergic agonists, and in breastfeeding [47,50].

Orlistat, a pancreatic and gastric lipase inhibitor, induces maldigestion and subsequent malabsorption of dietary fat. Known by the brand names, Alli® or Xenical®, this medication can induce 2.5–3.4 kg of weight loss when added to behavioral modifications compared with placebo at doses of 60–120 mg with meals. Due to its mechanism of action, adverse effects include steatorrhea, fecal urgency, and incontinence, which are directly related to higher amounts of dietary fat intake [49]. Additionally, Orlistat can cause malabsorption of essential fat-soluble micronutrients and it is recommended that patients take a multivitamin during treatment with Orlistat. In 2010, the FDA issued revised safety label information to include the rare risk of serious liver injury due to post-marketing reports of hepatocellular necrosis or acute liver failure. There were 13 cases (12 Xenical®, 1 Alli®) reported. After the case review by the FDA, it was recognized that other medications or comorbid conditions could have contributed as liver injury was not demonstrated in the FDA clinical trial data [52]. There is also a risk of oxalate nephrolithiasis and nephropathy with renal failure in some patients due to increased

Table 1. Overview of antiobesity medications approved by the food and Drug Administration

Medication	Phentermine	Orlistat (Xenical)	Phentermine/Topirimate ER (Qsymia)	Lorcaserin (Belviq)	Naltrexone SR/Bupropion SR (Contrave)	Liraglutide 3.0 mg (Saxenda)
Mechanism	Adrenergic agonist	Lipase inhibitor	Adrenergic agonist/neurostabilizer	5-HT_{2C} receptor agonist	Opioid receptor antagonist/dopamine and NE reuptake inhibitor	GLP-1 analog
Estimated % weight loss (medication compared with placebo, ITT data)	5.1% at 28 wk 15 mg daily	3.1% at 1 y 120 mg TID	6.6% at 1 y 7.5/46 mg daily	3.6% at 1 y 10 mg BID	4.8% at 56 wk 16/180 mg BID	5.4% at 56 wk 3 mg daily
Dosage/Administration	15 mg or 37.5 mg daily (can also use 1/4 0r 1/2 pill)	120 mg TID with meals	3.75/23 mg daily with gradual dose escalation (7.5/46 mg daily, then 11.25/69 mg daily, then 15/92 mg daily)	10 mg BID	890 mg daily (in the morning) with dose escalation (8/90 mg BID then 16/80 mg in the morning, 8/90 mg in the evening then 16/180 mg BID)	0.6 mg daily with gradual dose escalation (1.2 mg daily then 1.8 mg daily then 2.4 mg daily then 3.0 mg daily)
Available formulations	Capsule, tablet, powder	Capsule	Capsule	Tablet	Tablet	Prefilled pen for SC injection
Approved for long-term use	No	Yes	Yes	Yes	Yes	Yes
Schedule IV controlled substance	Yes	No	Yes	Yes	No	No
Side effects	Dizziness, dry mouth, difficulty sleeping, constipation, irritability	Bloating, diarrhea	Paresthesia dizziness, dysgeusia, insomnia, constipation, dry mouth	Headache, dizziness, fatigue, nausea, dry mouth, constipation, hypoglycemia, back pain, cough, fatigue	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea	Nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase
Contraindications	Pregnacy, nursing, CVD, during or within 14 d of MAOIs, hyperthyroidism, glaucoma, agitated states, history of drug abuse	Pregnancy, chronic malabsorption syndrome, cholestasis	Pregnancy, glaucoma, hyperthyroidism, during or within 14 d of MAOIs	Pregnancy	Pregnancy uncontrolled HTN, history of seizures or at risk of seizure, bulimia or anorexia, use of opioid agonists or partial agonists, during or within 14 d of MAOIs	Pregnancy, personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2

Abbreviations: 5-HT_{2C}, serotonin; BID, twice daily; CVD, cardiovascular disease; ER, extended release; GLP-1, glucan-like peptide-1; HTN, hypertension; IT intention-to-treat; MAOI, monoamine oxidase inhibitor; NE, norepinephrine; SC, subcutaneous; SR, sustained release; TID, 3 times daily.

Adapted from Apovian CM, Aronne L, Powell AG. Clinical management of obesity. West Islip (NY); Professional Communications, Inc; 2015. p. 186-92; with permission.

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urinary oxalate excretion that occurs as a result of fat maldigestion [47]. Orlistat is contraindicated in malabsorption, cholestasis, pregnancy/breastfeeding, and patients taking cyclosporine. This medication should be avoided in patients taking antiepileptics, warfarin, vitamin D, levothyroxine, and amiodarone due to interference with absorption [47].

Locaserin, marketed under the brand name of Belviq®, is a selective 5-HT_{2C} serotonin-receptor agonist that causes appetite suppression. When added to diet and exercise, patients can experience an average of 3.2 kg of weight loss using 20 mg daily, in one or two divided doses. Side effects include constipation, nausea, headache, dizziness, fatigue, and cough, and in patients with type 2 diabetes, it can cause hypoglycemia [49]. There is a low risk of valvular heart disease, because the drug selectively targets the 5-HT_{2C} receptors in the brain as opposed to heart value tissue. For monitoring, it is recommended that this medication be discontinued in patients who do not lose at least 5% of starting body weight after treatment for 12 weeks [47]. Locaserin is contraindicated in pregnancy and should be avoided in patients taking MAOIs, buproprion, triptans, or St. John's wort due to risk of serotonin syndrome [47,50].

The combination therapy Naltrexone/Buproprion (Contrave®) modulates CNS reward pathways to produce weight loss [53]. The drug is increased over 3–4 weeks to reach a max treatment dose of 31 mg of naltrexone and 390 mg of buproprion. A weight loss of 6.8 kg is observed after 1 year of treatment with significant improvement of quality of life [53]. Side effects include nausea, constipation, dry mouth, vomiting, and dizziness. There can be minimal increases in blood pressure (1–2 mmHg) or heart rate during the induction of therapy. If patients have not demonstrated 5% loss of initial body weight by 12 weeks, then this medication should be discontinued. Naltrexone/Buproprion is contraindicated in patients with uncontrolled hypertension, eating disorders, seizure disorders, and chronic opioid abuse, or in patients who are pregnant, breastfeeding, or using MAOIs [47,50,53].

Liraglutide (Saxenda®) is a GLP-1 (glucagon-like peptide) agonist initially approved for the treatment of type 2 diabetes and subsequently approved for obesity treatment in 2014. Weight loss is thought to be achieved through appetite suppression and delayed gastric emptying [54]. Administered as a once-daily injection, at a treatment dose of 3 mg, an average weight loss of 8.4 kg can be observed in conjunction with diet and exercise [55]. Side effects include nausea, vomiting, diarrhea, pancreatitis, gallbladder disease, and hypoglycemia. Additionally, resting heart rate can increase on this medication and it should be discontinued if tachycardia is sustained. Liraglutide causes thyroid cancer in mouse models; however, this has not been observed in humans. Nonetheless, the FDA issued a black box warning stating the use of this medications is contraindicated in patients with history or family history of medullary thyroid cancer or multiple endocrine neoplasia (MEN) [54,55].

The FDA recently approved Plenity® for obesity. The drug is a hydrogel capsule system that works by inducing fullness, thereby reducing energy intake. However, this medication is not yet widely available [56].

Endobariatrics

Endoscopic bariatric therapy (EBT) has emerged as a class of innovative minimally invasive endoscopic weight loss procedures. Although bariatric surgery can produce greater than 25% total weight loss (TWL) in obese individuals and reverse/improve obesity-related comorbid illnesses, less than 1% of eligible patients undergo surgery [57]. EBT is an option for patients who are unable to achieve meaningful weight loss with behavioral modification and pharmacotherapy but are unwilling or not eligible to have surgery. Currently, there are devices that are FDA approved for weight loss therapy including intragastric balloons and aspiration therapy. There are also devices that are not FDA approved for weight loss but are being studied for use in obesity treatment and only available in select medical centers. Endobariatrics is a rapidly evolving field, and for the purpose of this paper, we will review the approved and currently available modalities for the management of obesity.

Intragastric Balloons

The Orbera® intragastric balloon (IGB) and Reshape Duo® are silicon-based saline filled balloons approved by the FDA in 2015 for obesity management, though currently, only the Orbera® is commercially available. The balloon is placed endoscopically and inflated with 450 to 700 cc of saline [58]. The balloon is endoscopically removed after 6 months with a continued diet and exercise program for at least an additional 6 months. A meta-analysis of 17 studies revealed the Obera® IGB achieved ~ 25% excess weight loss over controls at 1 year [59•]. An ASGE review of the safety of Orbera reported that the most frequent side effects were pain and nausea, which occurred in approximately 1/3 of patients. Serious side effects reported as rare include migration and perforation with an incidence of 1.4% and 0.1%, respectively. Half of the patients with perforations (4/8) had previous gastric surgery. Four deaths were reported, related to aspiration or perforation [59•]. The FDA issued a warning in 2017 regarding the fluid-filled balloons following reports of spontaneous hyperinflation of balloons and risk of pancreatitis due to compression [60,61]. No etiology for hyperinflation has been identified, but physicians should be aware of these potential risks.

The Obalon® gastric balloon system (OGB, Obalon Therapeutics, Carlsbad, CA) was FDA approved in 2016. The delivery system consists of a gelatin capsule connected to a catheter which is orally ingested with confirmed entry into the stomach by fluoroscopy. The gelatin dissolves and frees the balloon; it is inflated with 250 cc of gas via the connecting catheter. Up to three balloons can be placed in a patient in the same session or successive sessions, to remain in place for up to 12–24 weeks, after which they are endoscopically removed [58]. No anesthesia or endoscopy is required for placement. Average total body weight loss was 6.81%. One serious adverse event was reported, a gastric ulcer in the setting of prohibited NSAID use; otherwise, 89% of patients reported

nausea and cramping [62].

The ReShape Duo® (ReShape Medical, San Clemente, CA) is a dual balloon system that is also endoscopically inserted and retrieved. Although this balloon system demonstrated efficacy for weight loss, it is no longer commercially available.

Aspiration Therapy

The Aspire Assist® device (Aspire Bariatrics, King of Prussia, PA) was FDA approved in 2016. This device is a specialized gastrostomy tube known as the "A-Tube," which is inserted in a similar fashion as a PEG tube. Two weeks after insertion, the skin portion is exchanged for a connector valve, and following a meal, patients aspirate (e.g., empty the gastric contents) and discard about one-third of each meal. A multicenter randomized trial of 111 patients who underwent Aspire Assist placement experienced a total body weight loss of 14.2% at 1 year [63]. Long-term data reveals that at 4 years, patients experienced a mean total weight loss (TWL) of 18.7%, and 69% of patients achieved at least 10% TWL [64]. Adverse events included gastric ulcer, stoma infection, stoma granulation tissue, and peritonitis [59•,65].

Gastric Remodeling

Endoscopic sleeve gastroplasty (ESG) is a volume reduction procedure using an endoscopic suturing device (Overstitch®; Apollo Endosurgery). Full-thickness sutures are placed along the greater curvature of the stomach to create a sleeve configuration. A multicenter study of 242 patients who underwent ESG achieved a total weight loss (TWL) of 19.8% at 18 months [66]. More recently, unpublished 5-year data presented up to 15–20% TWL with ESG [67]. Adverse events included perigastric fluid collection, pulmonary embolism, pneumothorax, and pneumoperitoneum, though no patients required surgery [63,68]. Recent studies indicate that ESG outperforms laparoscopic banding and intragastric balloon in terms of weight loss with fewer adverse events [66,69].

Bariatric Surgery

Bariatric surgery is the most effective and sustainable method of weight loss. Surgical treatment of obesity results in higher remission of metabolic syndrome and type 2 diabetes than nonsurgical management [70]. In 1953, Dr. Varco of the University of Minnesota performed the first weight loss procedure, a jejunoileal bypass (JIB), on a human subject in the USA. This malabsorptive surgery achieved significant weight loss but caused multiple complications including severe electrolyte abnormalities, vitamin deficiencies, gallbladder disease, malnutrition, liver dysfunction, and rarely liver failure [71]. In 1967, Dr. Mason of the University of Iowa performed the first gastric bypass, a restrictive and malabsorptive procedure. Following a similar mechanism, the biliopancreatic diversion was created in 1979, which involved a partial gastrectomy and creation of a gastrojejunal anastomosis. Although this technique resulted in significant weight loss, it was wrought with post-operative complications including protein malabsorption, dumping syndrome, and neuropathy.

In 1977, the Roux-en-Y gastric bypass (RYGB) was created. With introduction of the laparoscopic technique in 1994, patients had shorter lengths of stay and earlier return to activity; thus the RYGB's significant weight loss and fewer complications lead to its wide spread adoption [72]. Sleeve gastrectomy (SG) was created in the late 1980s as a restrictive procedure, and years after the laparoscopic technique was developed in 1999, it became the most commonly performed bariatric procedure [71–73]. Figure 1 shows schematic representations of the aforementioned bariatric surgery procedures [74].

In 2018, two large randomized control trials were published comparing outcomes of SG and RYGB at 5 years. The SM-Boss trial found no significant difference in EWL at 5 years between patients who received LSG versus RYGB [75]. However, the SLEEVEPASS trial, an open-label

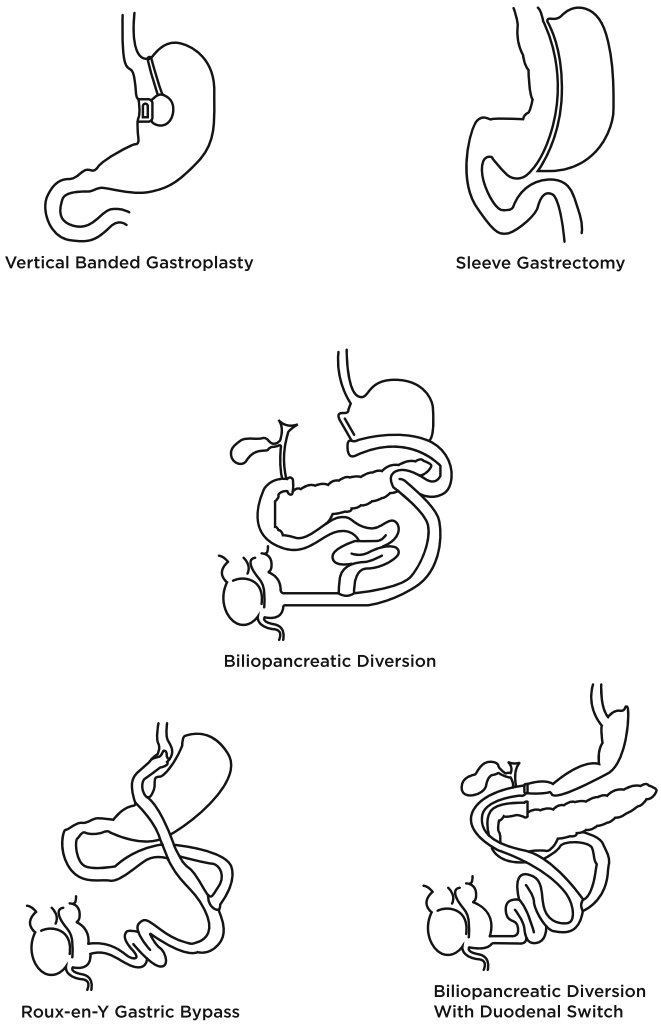

Fig. 1. Bariatric surgeries. Adapted from Karra et al. Trends Endocrinol Metab. 2010

randomized equivalence trial, reported that laparoscopic SG did not meet equivalence criteria for excess weight loss at 5 years compared with RYGB, EWL of 49% and 57% respectively [76]. Patients who undergo bariatric surgery are at risk for severe micronutrient deficiencies due to the mechanisms of weight loss; thus, they require pre/post-operative evaluation and monitoring by a registered dietician. The American Society for Metabolic and Bariatric Surgery Integrated nutritional guidelines recommends pre-surgical screening levels of thiamin, B12, folate, iron, vitamins A, D, E, and K, calcium, zinc, and copper. Post-surgical monitoring of micronutrient levels is recommended every 3–6 months in the first year depending on which surgery was performed. Preventative supplementation is also standard of care post-operatively [77]. Gastroenterologists and hepatologists will increasingly encounter pre and post-operative bariatric patients in their practice; it is important to understand the anatomy and physiology of current and past bariatric procedures to provide high-quality care.

Conclusion

Obesity has become a major public health issue that directly affects the care of our patients as gastroenterologists. Beyond lifestyle changes, as practitioners, we should recognize ineffective weight loss in our patients and consider incorporating alternative or complimentary therapies such as pharmacotherapy and endobariatric procedures, as the literature supports the safety and efficacy of these therapies. Bariatric surgery is the most effective therapy for weight loss and risk factor modification if patients are eligible and willing to undergo surgery. A comprehensive understanding of all available therapies for management is necessary to provide high-quality care and actively combat the sequela of obesity.

Keypoints

- The current data does not suggest any one specific diet is superior for weight loss, but rather, adherence to a well-balance diet with a relative energy deficit is essential to induce and maintain weight loss.
- The American Heart Association recommends at least 150 min of moderate intensity activity or 75 min of vigorous activity per week to maintain a healthy lifestyle.
- Aerobic exercise combined with a behavioral weight loss program induces sustained weight loss.
- Strength training is effective for risk factor modification and increase in fat-free mass, but it may not produce significant weight loss alone.
- There are six anti-obesity medications approved and available by the FDA that are safe and effective for weight loss when used under the direction of a physician.

- Endobariatric therapies (EBT) are novel, minimally invasive options for patients who are unable to achieve meaningful weight loss with behavioral modification and pharmacotherapy and are unwilling or not eligible to have surgery.
- There are multiple devices that are FDA approved for clinical use for EBT that can induce significant and sustainable weight loss.
- Bariatric surgery has evolved considerably and is the most effective method of weight loss and treatment for the metabolic complications of obesity.

Compliance with Ethical Standards

Conflict of Interest

Jessica Briscoe declares that she has no conflict of interest. Monica Saumoy declares that she has no conflict of interest. Octavia Pickett-Blakely declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

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

1. DNPAO Data, Trends and maps: explore by location | CDC. https://nccd.cdc.gov/dnpao_dtm/rdPage.aspx?rdReport=DNPAO_DTM.ExploreByLocation&rdRequestForwarding=Form. .
2. Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007-2008 to 2015-2016. JAMA. 2018;319(16):1723–5. https://doi.org/10.1001/jama.2018.3060.
3. Adult Obesity Facts | Overweight & obesity | CDC. https://www.cdc.gov/obesity/data/adult.html. Published January 31, 2019. Accessed February 25, 2019.
4. 2013 AHA/ACC/TOS Guideline for the management of overweight and obesity in adults. :37.
5. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 2012;55(6):2005–23. https://doi.org/10.1002/hep.25762.
6. Sullivan S, Kumar N, Edmundowicz SA, et al. ASGE position statement on endoscopic bariatric therapies in clinical practice. Gastrointest Endosc. 2015;82(5):767–72. https://doi.org/10.1016/j.gie.2015.06.038.
7.• Acosta A, Streett S, Kroh MD, et al. White Paper AGA: POWER — Practice guide on obesity and weight management, education, and resources. Clin Gastroenterol Hepatol. 2017;15(5):631–649.e10. https://doi.org/10.1016/j.cgh.2016.10.023.
This study provides a comprehensive weight management guide for physicians.
8. Negro F, Clément S. Impact of obesity, steatosis and insulin resistance on progression and response to therapy of hepatitis C. J Viral Hepat. 2009;16(10):681–8. https://doi.org/10.1111/j.1365-2893.2009.01186.x.
9. Frezza EE, Wachtel MS, Chiriva-Internati M. Influence of obesity on the risk of developing colon cancer. Gut. 2006;55(2):285–91. https://doi.org/10.1136/gut.2005.073163.
10. Low AK, Bouldin MJ, Sumrall CD, Loustalot FV, Land KK. A Clinician's Approach to medical management of obesity. Am J Med Sci. 2006;331(4):175–82. https://doi.org/10.1097/00000441-200604000-00003.
11. Sacks FM, Bray GA, Carey VJ, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. N Engl J Med. 2009;360(9):859–73. https://doi.org/10.1056/NEJMoa0804748.
12. Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone Diets for weight loss and heart disease risk reduction: a randomized trial. JAMA.

2005;293(1):43–53. https://doi.org/10.1001/jama.293.1.43.
13. Zone diet: what to know | US News Best Diets. https://health.usnews.com/best-diet/zone-diet. Accessed March 17, 2019.
14. Gudzune KA, Doshi RS, Mehta AK, et al. Efficacy of commercial weight loss programs: an updated systematic review. Ann Intern Med. 2015;162(7):501–12. https://doi.org/10.7326/M14-2238.
15. Dashti HM, Al-Zaid NS, Mathew TC, et al. Long term effects of Ketogenic diet in obese subjects with high cholesterol level. Mol Cell Biochem. 2006;286(1-2):1–9. https://doi.org/10.1007/s11010-005-9001-x.
16. Bueno NB, Melo ISV. de, Oliveira SL de, Ataide T da R. Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. Br J Nutr. 2013;110(7):1178–87. https://doi.org/10.1017/S0007114513000548.
17. Westman EC, Yancy WS, Mavropoulos JC, Marquart M, McDuffie JR. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. Nutr Metab. 2008;5(1):36. https://doi.org/10.1186/1743-7075-5-36.
18. Gasior M, Rogawski MA, Hartman AL. Neuroprotective and disease-modifying effects of the ketogenic diet. Behav Pharmacol. 2006;17(5-6):431–9.
19. Moreno B, Bellido D, Sajoux I, et al. Comparison of a very low-calorie-ketogenic diet with a standard low-calorie diet in the treatment of obesity. Endocrine. 2014;47(3):793–805. https://doi.org/10.1007/s12020-014-0192-3.
20. Wheless JW. The Ketogenic diet: an effective medical therapy with side effects. J Child Neurol. 2001;16(9):633–5. https://doi.org/10.1177/088307380101600901.
21. Wing RR, Vazquez JA, Ryan CM. Cognitive effects of ketogenic weight-reducing diets. Int J Obes Relat Metab Disord J Int Assoc Study Obes. 1995;19(11):811–6.
22. Ballaban-Gil K, Callahan C, O'Dell C, Pappo M, Moshé S, Shinnar S. Complications of the Ketogenic diet. Epilepsia. 1998;39(7):744–8. https://doi.org/10.1111/j.1528-1157.1998.tb01160.x.
23. Frassetto LA, Schloetter M, Mietus-Synder M, Morris RC Jr, Sebastian A. Metabolic and physiologic improvements from consuming a Paleolithic, hunter-gatherer type diet. Eur J Clin Nutr. 2009;63(8):947–55. https://doi.org/10.1038/ejcn.2009.4.
24. Mellberg C, Sandberg S, Ryberg M, et al. Long-term effects of a Palaeolithic-type diet in obese postmenopausal women: a 2-year randomized trial. Eur J Clin Nutr. 2014;68(3):350–7. https://doi.org/10.1038/ejcn.2013.290.
25. Genoni A, Lo J, Lyons-Wall P, Devine A. Compliance, palatability and feasibility of Paleolithic and Australian guide to healthy eating diets in healthy women: a 4-week dietary intervention. Nutrients. 2016;8(8):481. https://doi.org/10.3390/nu8080481.
26. Longo VD, Panda S. Fasting, circadian rhythms, and time-restricted feeding in healthy lifespan. Cell Metab. 2016;23(6):1048–59. https://doi.org/10.1016/j.cmet.2016.06.001.
27. Patterson RE, Sears DD. Metabolic effects of intermittent fasting. Annu Rev Nutr. 2017;37(1):371–93. https://doi.org/10.1146/annurev-nutr-071816-064634.
28. Sutton EF, Beyl R, Early KS, Cefalu WT, Ravussin E, Peterson CM. Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes. Cell Metab. 2018;27(6):1212–1221.e3. https://doi.org/10.1016/j.cmet.2018.04.010.
29. Klempel MC, Kroeger CM, Varady KA. Alternate day fasting (ADF) with a high-fat diet produces similar weight loss and cardio-protection as ADF with a low-fat diet. Metabolism. 2013;62(1):137–43. https://doi.org/10.1016/j.metabol.2012.07.002.
30. Trepanowski JF, Kroeger CM, Barnosky A, et al. Effect of alternate-day fasting on weight loss, weight maintenance, and cardioprotection among metabolically healthy obese adults: a randomized clinical trial. JAMA Intern Med. 2017;177(7):930–8. https://doi.org/10.1001/jamainternmed.2017.0936.
31. American Heart Association recommendations for physical activity in adults and kids. www.heart.org. https://www.heart.org/en/healthy-living/fitness/fitness-basics/aha-recs-for-physical-activity-in-adults. Accessed March 22, 2019.
32. Jakicic JM, Marcus BH, Gallagher KI, Napolitano M, Lang W. Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. JAMA. 2003;290(10):1323–30. https://doi.org/10.1001/jama.290.10.1323.
33. Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? Am J Clin Nutr. 2003;78(4):684–9. https://doi.org/10.1093/ajcn/78.4.684.
34. Current Guidelines - health.gov. https://health.gov/paguidelines/second-edition/. Accessed July 17, 2019.
35. Blumenthal JA, Sherwood A, Gullette ECD, et al. Exercise and weight loss reduce blood pressure in men and women with mild hypertension: effects on cardiovascular, metabolic, and hemodynamic functioning. Arch Intern Med. 2000;160(13):1947–58. https://doi.org/10.1001/archinte.160.13.1947.
36. Goodpaster BH, DeLany JP, Otto AD, et al. Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: a randomized trial. JAMA. 2010;304(16):1795–802. https://doi.org/10.1001/jama.2010.1505.
37. Hashida R, Kawaguchi T, Bekki M, et al. Aerobic vs. resistance exercise in non-alcoholic fatty liver disease: a systematic review. J Hepatol. 2017;66(1):142–52. https://doi.org/10.1016/j.jhep.2016.08.023.
38. Lemes ÍR, Ferreira PH, Linares SN, Machado AF, Pastre CM, Netto J. Resistance training reduces systolic blood

pressure in metabolic syndrome: a systematic review and meta-analysis of randomised controlled trials. Br J Sports Med. 2016;50(23):1438–42. https://doi.org/10.1136/bjsports-2015-094715.

39. Cauza E, Hanusch-Enserer U, Strasser B, et al. The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. Arch Phys Med Rehabil. 2005;86(8):1527–33. https://doi.org/10.1016/j.apmr.2005.01.007.
40. Hallsworth K, Fattakhova G, Hollingsworth KG, et al. Resistance exercise reduces liver fat and its mediators in non-alcoholic fatty liver disease independent of weight loss. Gut. 2011;60(9):1278–83. https://doi.org/10.1136/gut.2011.242073.
41. Willis LH, Slentz CA, Bateman LA, et al. Effects of aerobic and/or resistance training on body mass and fat mass in overweight or obese adults. J Appl Physiol. 2012;113(12):1831–7. https://doi.org/10.1152/japplphysiol.01370.2011.
42. Wycherley TP, Noakes M, Clifton PM, Cleanthous X, Keogh JB, Brinkworth GD. A high-protein diet with resistance exercise training improves weight loss and body composition in overweight and obese patients with type 2 diabetes. Diabetes Care. 2010;33(5):969–76. https://doi.org/10.2337/dc09-1974.
43. Castelnuovo G, Pietrabissa G, Manzoni GM, et al. Cognitive behavioral therapy to aid weight loss in obese patients: current perspectives. Psychol Res Behav Manag. 2017;10:165–73. https://doi.org/10.2147/PRBM.S113278.
44. Daubenmier J, Moran PJ, Kristeller J, et al. Effects of a mindfulness-based weight loss intervention in adults with obesity: a randomized clinical trial. Obesity. 2016;24(4):794–804. https://doi.org/10.1002/oby.21396.
45. Katterman SN, Kleinman BM, Hood MM, Nackers LM, Corsica JA. Mindfulness meditation as an intervention for binge eating, emotional eating, and weight loss: a systematic review. Eat Behav. 2014;15(2):197–204. https://doi.org/10.1016/j.eatbeh.2014.01.005.
46. Kang JG, Park C-Y. Anti-obesity drugs: a review about their effects and safety. Diabetes Metab J. 2012;36(1):13–25. https://doi.org/10.4093/dmj.2012.36.1.13.
47. Keith JN. Pharmacotherapy in treatment of obesity. Gastroenterol Clin North Am. 2016;45(4):663–72. https://doi.org/10.1016/j.gtc.2016.07.011.
48. McMahon FG, Fujioka K, Singh BN, et al. Efficacy and safety of sibutramine in obese White and African American Patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. Arch Intern Med. 2000;160(14):2185–91. https://doi.org/10.1001/archinte.160.14.2185.
49. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. JAMA. 2014;311(1):74–86. https://doi.org/10.1001/jama.2013.281361.
50. Srivastava G, Apovian C. Future pharmacotherapy for obesity: new anti-obesity drugs on the horizon. Curr Obes Rep. 2018;7(2):147–61. https://doi.org/10.1007/s13679-018-0300-4.
51. Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. The Lancet. 2011;377(9774):1341–52. https://doi.org/10.1016/S0140-6736(11)60205-5.
52. Research C for DE and. FDA Drug Safety Communication: completed safety review of Xenical/Alli (orlistat) and severe liver injury. *FDA*. 2018. http://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fda-drug-safety-communication-completed-safety-review-xenicalalli-orlistat-and-severe-liver-injury. Accessed June 17, 2019.
53. Apovian CM, Aronne L, Rubino D, et al. A randomized, phase 3 trial of naltrexone SR/bupropion SR on weight and obesity-related risk factors (COR-II). Obesity. 2013;21(5):935–43. https://doi.org/10.1002/oby.20309.
54. Mehta A, Marso SP, Neeland IJ. Liraglutide for weight management: a critical review of the evidence. Obes Sci Pract. 2016;3(1):3–14. https://doi.org/10.1002/osp4.84.
55. Pi-Sunyer X, Astrup A, Fujioka K, et al. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. N Engl J Med. 2015;373(1):11–22. https://doi.org/10.1056/NEJMoa1411892.
56. https://www.gelesis.com/2019/04/14/gelesis-granted-fda-clearance-to-market-plenitytm-a-new-prescription-aid-to-weight-management/. https://www.gelesis.com/2019/04/14/gelesis-granted-fda-clearance-to-market-plenitytm-a-new-prescription-aid-to-weight-management/. Accessed July 25, 2019.
57. Jirapinyo P, Thompson CC. Training in bariatric and metabolic endoscopic therapies. Clin Endosc. 2018;51(5):430–8. https://doi.org/10.5946/ce.2018.148.
58. Abu Dayyeh BK, Kumar N, Edmundowicz SA, et al. ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. Gastrointest Endosc. 2015;82(3):425–438.e5. https://doi.org/10.1016/j.gie.2015.03.1964.
59.• Abu Dayyeh BK, Edmundowicz S, Thompson CC. Clinical practice update: expert review on endoscopic bariatric therapies. Gastroenterology. 2017;152(4):716–29. https://doi.org/10.1053/j.gastro.2017.01.035.

This study provides an expert review of available and emerging endoscopic weight loss therapies. Additionally, the authors provide best practice indications, contraindications, and ways to incorporate these procedures into clinical practice.

60. Health C for D and R. Health Care Providers (Medical Devices) - The FDA alerts health care providers about potential risks with liquid-filled intragastric balloons.

https://www.fda.gov/medicaldevices/resourcesforyou/healthcareproviders/ucm540655.htm. Accessed March 24, 2019.
61. Health C for D and R. UPDATE: potential risks with liquid-filled intragastric balloons - letter to health care providers. FDA. 2018. http://www.fda.gov/medical-devices/letters-health-care-providers/update-potential-risks-liquid-filled-intragastric-balloons-letter-health-care-providers-0. Accessed June 20, 2019.
62. Sullivan S, Swain JM, Woodman G, et al. 812d The Obalon swallowable 6-month balloon system is more effective than moderate intensity lifestyle therapy alone: results from a 6- month randomized sham controlled trial. Gastroenterology. 2016;150(4):S1267. https://doi.org/10.1016/S0016-5085(16)34281-0.
63. Sullivan S. Aspiration therapy for obesity. Gastrointest Endosc Clin N Am. 2017;27(2):277–88. https://doi.org/10.1016/j.giec.2016.12.001.
64. Thompson CC, Dayyeh BKA, Kushnir V, et al. Aspiration therapy for the treatment of obesity: 4-year results of a multicenter randomized controlled trial. Surg Obes Relat Dis. 2019;0(0). https://doi.org/10.1016/j.soard.2019.04.026.
65. Thompson CC, Abu Dayyeh BK, Kushner R, et al. Percutaneous gastrostomy device for the treatment of class II and class III obesity: results of a randomized controlled trial. Am J Gastroenterol. 2017;112(3):447–57. https://doi.org/10.1038/ajg.2016.500.
66. Lopez-Nava G, Sharaiha RZ, Neto MG, et al. 101 endoscopic sleeve gastroplasty for obesity: a multicenter study of 242 patients with 18 months follow-up. Gastroenterology. 2016;150(4):S26. https://doi.org/10.1016/S0016-5085(16)30212-8.
67. Hajifathalian K, Ang B, Dawod QM, et al. 175 LONG-TERM FOLLOW UP AND OUTCOMES AFTER ENDOSCOPIC SLEEVE GASTROPLASTY FOR TREATMENT OF OBESITY (5 YEAR DATA). Gastrointest Endosc. 2019;89(6):AB58. https://doi.org/10.1016/j.gie.2019.04.019.
68. Novikov AA, Afaneh C, Saumoy M, et al. Endoscopic sleeve gastroplasty, laparoscopic sleeve gastrectomy, and laparoscopic band for weight loss: how do they compare? J Gastrointest Surg Off J Soc Surg Aliment Tract. 2018;22(2):267–73. https://doi.org/10.1007/s11605-017-3615-7.
69. Fayad L, Cheskin LJ, Adam A, et al. Endoscopic sleeve gastroplasty versus intragastric balloon insertion: efficacy, durability, and safety. Endoscopy. 2019;51(6):532–9. https://doi.org/10.1055/a-0852-3441.
70. Gloy VL, Briel M, Bhatt DL, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. BMJ. 2013;347:f5934. https://doi.org/10.1136/bmj.f5934.
71. Celio AC, Pories WJ. A history of bariatric surgery: the maturation of a medical discipline. Surg Clin North Am. 2016;96(4):655–67. https://doi.org/10.1016/j.suc.2016.03.001.
72. Baker MT. The history and evolution of bariatric surgical procedures. Surg Clin North Am. 2011;91(6):1181–201. https://doi.org/10.1016/j.suc.2011.08.002.
73. English WJ, DeMaria EJ, Brethauer SA, Mattar SG, Rosenthal RJ, Morton JM. American Society for Metabolic and Bariatric Surgery estimation of metabolic and bariatric procedures performed in the United States in 2016. Surg Obes Relat Dis. 2018;14(3):259–63. https://doi.org/10.1016/j.soard.2017.12.013.
74. Karra E, Yousseif A, Batterham RL. Mechanisms facilitating weight loss and resolution of type 2 diabetes following bariatric surgery.Trends Endocrinol Metab. 2010;21(6):337-344. https://doi.org/10.1016/j.tem.2010.01.006.
75. Peterli R, Wölnerhanssen BK, Peters T, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss in patients with morbid obesity. JAMA. 2018;319(3):255–65. https://doi.org/10.1001/jama.2017.20897.
76. Salminen P, Helmiö M, Ovaska J, 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. JAMA. 2018;319(3):241–54. https://doi.org/10.1001/jama.2017.20313.
77. Parrott J, Frank L, Rabena R, Craggs-Dino L, Isom KA, Greiman L. American Society for Metabolic and Bariatric Surgery Integrated Health Nutritional Guidelines for the Surgical Weight Loss Patient 2016 Update: micronutrients. Surg Obes Relat Dis. 2017;13(5):727–41. https://doi.org/10.1016/j.soard.2016.12.018.

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