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## An Overview of Modern Strategies for Treating Obesity

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## ABSTRACT

**Introduction:** In the last few years, obesity has become a central issue with more than 2.6 billion people worldwide being overweight or obese. While the risks associated with this condition and its rising significance are widely known, the effect of this attention on screening

and treatment remains unsatisfying. This paper explores multiple treatment strategies and evaluates their effectiveness in preventing obesity-related complications.

**Review methods:** We conducted our study as a literature review, with data being gathered via PubMed and Embase.

**The state of knowledge:** Physical activity, behavioral therapy, and proper nutrition remain the foundation for obesity therapy. However, in many cases these approaches are insufficient. Recently, there has been a dynamic development of bariatric surgery and new drugs, which in comparison to lifestyle modification, result in better long-term results and improved quality of life. New surgery procedures, such as sleeve gastrectomy and adjustable gastric banding, have shown to be one of the most effective but still carry a risk of complications. As an alternative pharmacotherapy could be considered with currently used medications including liraglutide, semaglutide, tirzepatide, phentermine-topiramate, orlistat, and bupropion-naltrexone.

**Conclusions:** Growing treatment options allow physicians to choose more targeted approaches, based on the patient's risk factors, overall health status, and compliance.

**KEYWORDS:** obesity; overweight; bariatric surgery; pharmacotherapy in obesity

## INTRODUCTION

Obesity is defined by The World Health Organization as abnormal or excessive fat accumulation that may impair health.[1] Several factors are known to be affecting this disease, among them genetic predisposition and environment are the most crucial.[2] According to studies genetic component may be responsible for about 40-50% of cases of morbid obesity. [3] With over 2.6 billion people worldwide overweight or obese, and projections indicating a continued rise, the urgency of addressing obesity is evident.[4] That results in the development of more targeted approaches, such as pharmacotherapy and metabolic surgery. Several methods are used to evaluate obesity. Currently recommended are body mass index (BMI, defined as the weight in kilograms divided by height in meters squared), waist circumference, waist-to-hip ratio, and skinfold thickness. [5][6] All of the above-mentioned methods should be used together with clinical assessment.

Obesity is associated with an increased risk of diseases and an elevated risk of mortality.[7][8] Among the diseases, that are proven to be related to obesity are cardiovascular diseases, type 2 diabetes mellitus, and hormonal disorders. [6][7]

Despite growing awareness, effective screening and treatment efforts are still lacking. The paper aims to address this gap by exploring various treatment strategies and assessing their efficacy in preventing obesity-related complications, ultimately aiming to improve quality of life.

## **REVIEW METHODS**

This study was conducted in the form of a literature review, with data being gathered via PubMed and Embase, and it set out to explore the effectiveness and safety of lifestyle interventions and current pharmacological treatments for obesity.

## **THE STATE OF KNOWLEDGE**

### **Lifestyle intervention**

In most cases of overweight patients lifestyle intervention remains the first course of treatment, with the main components being a reduced-calorie diet, increased physical activity, and behavioral therapy.[9] These 3 elements are recommended in all obesity management approaches for a BMI of 25 kg/m<sup>2</sup> or higher.[10] Actual guidelines recognize difficulties, that the patients might be facing and recommend participation in counseling programs, that ideally consist of at least 14 sessions in the first 6 months.[9]

There are lots of different dietary approaches aiming for a reduction in energy intake. Low-energy diets (LEDs) are usually recommended and typically prescribe about 1200–1500 kcal/d for women and 1500–1800 kcal/d for men. In some cases very low energy diets (VLEDs) of less than 800 kcal/d are required for a short period, providing essential nutrients.[11] It is important to remember that weight management consists not only of a reduced-calorie diet and amount of food eaten, but also of different factors like type and ingredients of food consumed, and timing of the meals.[12] Research shows that most successful diets focus on macronutrient composition and healthy food patterns. Dietary strategies of increasing the proportion of lower-energy-dense foods and choosing appropriately sized portions are also recommended.[13]

Present guidelines for exercise training in obese patients recommend aerobic physical activity for at least 150 min of moderate intensity and 75 min of vigorous intensity per week.

Currently, new research is being conducted to find out if more time-efficient exercises, like HIIT training, could be a good alternative to the present recommendations.[14] Behavioral therapy (BT-OB) provides a set of strategies and techniques to facilitate compliance with diet and physical activity recommendations.[9] Some of the components include self-monitoring of physical activity, food intake, and weight, stimulus control, problem-solving as well as goal setting.[15] Personalized cognitive-behavioral therapy for obesity, known as CBT-OB, is an innovative type of treatment, which includes a more individual approach to a patient's needs and concerns. Its purpose is to mainly focus on cognitive change and the development of a stable "weight-control mindset" for long-term weight-loss maintenance.[16] Digital resources improve the accessibility of different lifestyle modification methods, which helps with maintaining weight loss. [17]

### **Pharmacotherapy**

When lifestyle modifications have not been successful or in case of obesity-related complications pharmacotherapy should be considered.[10] The decision to initiate pharmacotherapy should be based on the patient's risk factors, overall health status, and compliance. In every case, lifestyle modifications should accompany the drug treatment.[10] The pharmacological treatments for obesity have recently gained popularity. The growing range of medications attracts the interest of many patients, which has various consequences. Below we described the main drugs currently used in obesity treatment, the indications to use them, and their effects.

#### *Glucagon-like peptide 1 (GLP-1) agonist*

Glucagon-like peptide (GLP-1) agonists are successfully used in type 2 diabetes pharmacotherapy. Due to their metabolic effects, such as the inhibition of food intake and the decrease of gastric emptying [18], they are promising for obesity treatment.[19]

There are several possible explanations for the decrease in GLP-1 secretion and how it results in the bodyweight loss.[19][20] In the central nervous system, GLP-1 and GLP-2 were found in the nucleus tractus solitarius, which plays a role in energy homeostasis. GLP-1 targets parts of the brain related to non-hunger (hedonic) feeding, such as reward, motivation, and addiction. Studies on mice indicate that administration of GLP-1 and GLP-2 reduces food intake.[21][22] Other tests conducted on rodents revealed that the decrease of GLP-1 reduces a variety of reward behaviors, including hedonic feeding.[23][24] Furthermore, GLP-1 improves postprandial glucose handling by inhibiting gastric emptying and elongating glucose

absorption into circulation.[18] Several GLP-1 agonists are used in type 2 diabetes therapy, however, only liraglutide (Saxenda) and semaglutide (Wegovy) are currently approved by the Food and Drug Administration (FDA) for obesity treatment.[25]

Liraglutide is administered daily via subcutaneous injections in higher doses than recommended in type 2 diabetes treatment. Studies have shown that after 52 weeks, weight loss typically ranges from 5-10%.[26] For example, a trial conducted by Kelly et al. revealed, that 43% of obese adolescents treated with liraglutide had lost 5% of their BMI after 56 weeks. [27] In comparison, in the placebo group, it was observed only in 18.7% of cases.[27] Liraglutide is generally well-tolerated, the most common side effects being nausea, vomiting, and diarrhea. They are mostly observed at the beginning of therapy and may discourage patients from continuing the treatment.[28][29][30][31]

Semaglutide is also administered via subcutaneous injection, but only once a week. The largest placebo-controlled trial, which enrolled adults without diabetes, showed an average weight loss of 12.4% after 68 weeks of treatment. Another trial, this time in patients with type 2 diabetes, resulted on average in 6.2% bodyweight loss.[25] [31]

Many studies have compared liraglutide with semaglutide. One of them demonstrated that participants had greater odds of losing body mass with semaglutide (70.9% participants) versus liraglutide (25.6% participants). The average weight loss with semaglutide was 15.8% compared to 6.4% with liraglutide.[32] Side effects were reported by a similar number of participants, however, more patients stopped liraglutide treatment ahead of time in comparison to the semaglutide group.[32]

#### *Phentermine and phentermine/topiramate CR (Qsymia)*

Phentermine is an anorectic and sympathomimetic amine that stimulates the release of norepinephrine in appetite centers in the brain. It is a structural analog to amphetamine, having similar effects on suppressing appetite, but with a much lower abuse potential. In the US it was approved for obesity therapy in 1959 and has since been widely used, but only as a short-time treatment of 12 weeks.[33] [34] Some recent studies show that it could potentially be used for longer treatments without increasing cardiovascular risk.[35] Topiramate is a weak carbonic anhydrase inhibitor that blocks voltage-gated sodium channels, enhances GABA - A receptor activity, and is mainly used in the treatment of epilepsy and migraines. Although its exact mechanism for treating obesity is uncertain, it augments appetite and provides a feeling of satiety.[36]

The combination of both drugs was proven to achieve greater weight loss in patients than the use of only one at a time.[37] After consumption, phentermine is immediately released with peak concentration in the morning, while the delayed release of topiramate makes its concentration higher in the evening.[33] In a 56-week clinical trial data, about 62-70% of patients on both phentermine and topiramate achieved 5% weight loss, while 37-48% of patients lost more than 10% of their body weight, depending on the dose of medicine.[38] The extension study showed about 9,3-10,5% weight loss maintenance in 2 years.[39]

The most common side effects include dry mouth, constipation, paresthesia, and elevations in resting pulse rate. Mood disorders, like depression, anxiety, sleep disorders, and suicidal ideation are also linked to the usage of the drug. The inhibition of carbonic anhydrase activity by topiramate may also lead to metabolic acidosis, hypokalemia, and angle-closure glaucoma.[36] [40][38][41]

### *Orlistat*

Orlistat, also known as tetrahydrolipstatin, inhibits pancreatic and gastric lipases in the lumen of the gastrointestinal tract, which prevents these enzymes from hydrolyzing dietary fat to their absorbable forms.[42][43] [44] Undigested triglycerides are eliminated by the fecal route.[45] This all leads to a decrease in systemic absorption of dietary fat by approximately 32% compared to 5% with placebo administration.[46]

A meta-analysis of 28 randomized clinical trials showed that 44% of participants lost at least 5% body mass compared to 23% placebo during 1 year. [47] Another study found that taking orlistat can help to reduce body weight by about 2,12kg. Additionally, it causes a lowering of total cholesterol up to -0,27mmol/L, LDL up to -0,27mmol/L, HDL up to -0.034mmol/L, and triglyceride up to -0,09 mmol/L.[48] Studies also indicate that orlistat has a beneficial effect on carbohydrate metabolism and lowering blood pressure. [49][50] [51][52]

However, research conducted by Davidson et al. revealed that patients taking orlistat experienced gastrointestinal adverse events, like flatus with discharge, oily spotting, fecal urgency, and fatty stool (79% compared to 59% placebo).[52] They are also mentioned in other studies.[52][53] Some trials indicate that this treatment may affect the levels of fat-soluble vitamins, but the changes are minimal.[54] [55] What is more, a few cases of orlistat possibly causing serious hepatic adverse effects, acute renal injury, and pancreatitis have also been reported.[56][57] [58]

### *Naltrexone/bupropion*

Naltrexone/bupropion consists of bupropion, a norepinephrine, and dopamine uptake inhibitor that can aid long-term smoking cessation, and naltrexone - an opioid-receptor antagonist used in the treatment of alcohol and opioid addiction.[59] [60] It is said that this dual treatment has a synergistic effect causing a change in brain reactivity to food cues resulting in appetite suppression. [61] [62] [36]

In a study of 1496 obese and overweight participants a greater weight loss was observed with NB admission vs. placebo at 56 weeks of trials (6,4% vs. 1,2%) The results of this study also demonstrate an improvement in levels of triglycerides and HDL.[63] These findings are consistent with other 56-week studies on 505 patients, which furthermore revealed a significant HbA1c reduction in participants receiving NB (-0,6% vs -0,1% placebo).[64] Additionally, a meta-analysis demonstrated that taking NB leads to a 2,53kg reduction in body weight compared with a placebo. [65] The most common adverse events reported in studies are nausea, even vomiting, constipation, headache, dry mouth, and dizziness. They are told to be generally mild.[63] [64] [65]

### *Tirzepatide*

Tirzepatide is a glucose-dependent insulintropic polypeptide (GIP) as well as a GLP-1 receptor agonist. Both GIP and GLP-1 are incretin hormones, which are gut peptides that stimulate insulin secretion and hyperglycemia. GLP-1 also influences the reduction of appetite and food intake. Tirzepatide was first approved by the FDA as Mounjaro for treatment of type 2 diabetes in May 2022.[66][67] In November 2023 it was approved as Zepbound for weight management in obese or overweight patients with weight-related conditions in the US.[68]

In the SURPASS-1 trial tripeptide showed promising glucose-lowering effect and bodyweight reduction.[69] SURMOUNT-1 was a 72-week trial in obese, non-diabetic adults. Patients, who were prescribed tripeptide at the dose of 5 mg, 10 mg, and 15 mg lost about 15.0%, 19.5%, and 20.9% of body weight respectively, and only around 3.1% with placebo.[70] Participants of the SURMOINT-2 trial were adults with a BMI of 27 kg/m<sup>2</sup> or higher and type 2 diabetes with glycated hemoglobin (HbA1c) of 7–10%. At week 72 there was -12.8% and -14.7% mean body weight change in patients receiving tirzepatide 10 mg and 15 mg respectively and only -3.2% with placebo.[71] SURMOUNT-4 trial showed that withdrawing tirzepatide caused a significant regain of lost weight.[72] In all studies, the most frequently

reported side effects were gastrointestinal, such as nausea, diarrhea, constipation, and vomiting.[70][71][72]

### **Bariatric surgery**

According to recent studies lifestyle interventions and pharmacotherapy in morbid obese patients often do not achieve the desired results.[73] Bariatric also called metabolic surgery is currently recognized as one of the most developing therapy options. Furthermore, extensive research has shown that it is the most effective weight loss intervention, with an average weight loss of 27% over 15 years [73][74], and is associated with improved quality of life.[75] Not all patients could be qualified for this treatment. Recommended criteria for the surgical approach, are a BMI greater than 40 or a BMI greater than 35 with obesity-related complications.[76][77] The consequences of excessive body weight were exhaustively mentioned above in this article. In the context of bariatric surgery, it is important to notice, that current studies described increased cardiopulmonary morbidity among adult, obese individuals.[76] Cardiopulmonary complications are likely a result of hypertension, hyperlipidemia, type II diabetes mellitus, and sleep apnea, all being related to obesity. The therapy of this disease alone, without treating the main course of them, may be insufficient. Bariatric surgery allows patients to lose enough weight to improve their health and quality of life in the long term. On average patients lose 50% to 60% of excess body weight and a decrease in BMI of about 10 kg/m<sup>2</sup> is observed during the first 12 to 24 postoperative months. [76]

### *Surgical Procedures*

In the 1950s the jejunio-ileal bypass (JIB) was introduced and the era of bariatric surgery began. Since then the increased development of procedures was observed with a shift from an open incisional approach to minimally invasive or laparoscopic techniques.[73] Several approaches are used to treat obesity, among them are the techniques that decrease the stomach volume and/or establish partial selective malabsorption.[76] The restrictive procedures result in food limitation and a quicker feeling of fullness after meals, whereas the malabsorptive procedures result in decreased nutritional absorption.[78] Currently, the most performed procedures are Roux-en- Y gastric bypass (RYGB), sleeve gastrectomy (SG), adjustable gastric banding (AGB), and biliopancreatic diversion/biliopancreatic diversion with duodenal switch(BPD/DS). [79]



### *Biliopancreatic diversion with duodenal switch*

BPD/DS are malabsorptive procedures that use intestinal bypass with gastric reduction. Biliopancreatic diversion is no longer used because of the high incidence of postgastrectomy syndrome and was replaced by modification with a duodenal switch.[80] Research showed that BPD/DS allows weight loss without significant changes in eating habits, which results in greater long-term weight loss and less weight regain.[81] These procedures are described as technically demanding and are mostly indicated for superobese patients with a BMI greater than 50. [82] [80]

### *Adjustable gastric banding*

Another approach is AGB, which involves placing a silicone band around the upper part of the stomach and could be performed laparoscopically. As a result of gastric binding a small superior gastric pouch with an adjustable outlet is created.[73] It is important to notice, that currently used bands allow the adjustment even after surgery. AGB restricts the amount of food, that can be ingested at once and strongly influences the effect of fullness after meals. [83] AGB is known to be the least invasive of purely restrictive bariatric surgery procedures and is technically reversible. [80]

### *Sleeve gastrectomy*

This approach facilitates weight loss by dividing the stomach vertically to create a smaller, sleeve-shaped stomach pouch, which limits the amount of food that can be consumed. In most of the cases, the fundus is removed and the pyloric valve at the bottom of the stomach remains intact. That allows normal stomach function and digestion.[80] Additionally, fundus is the main source of ghrelin, a hormone that stimulates appetite and promotes fat storage.[84] The procedure is considered minimally invasive with faster recovery times and fewer complications.[80][85][86]

### *Roux-en-Y gastric bypass*

This approach is a combination of restriction and malabsorption. During the procedure, a small stomach pouch is created by stapling the upper part of the stomach. Then the pouch is attached to the small intestine, which creates a "Roux limb." This allows food to bypass the majority of the stomach and the major part of the duodenum.[87] The next steps are jejunojejunostomy and gastrojejunostomy creation.[87] RYGBP is currently considered one of the most recommended approaches for the surgical treatment of morbid obesity.[88] It is

reported, that patients who undergo RGYB experience approximately 60% to 70% excess body weight loss.[89] It is important to notice, according to studies, that the mortality for RYGBP is approximately 0.2%, higher than SG and AGB. [86]

#### *Complications after bariatric surgery*

Currently, bariatric procedures are considered effective, and safe and are known to significantly reduce obesity-related comorbidities and improve a Quality of life more than other obesity therapies. [90][75] However surgical procedures are also associated with various complications with rates ranging from 10% to 17% and reoperation rates of approximately 7%.[91] One of the most common complications following bariatric surgery is cholelithiasis with incidents up to 30%[92]. The patients may experience cholecystitis, cholangitis, and pancreatitis. It is important to notice, that because of altered anatomy and postoperative adhesions imaging and treatment of these patients may be difficult.[93]. Debate continues about the need for prophylactic cholecystectomy during bariatric surgery, but this course of treatment remains controversial.[94] Another complication worth mentioning is Venous thromboembolism. Also, the pulmonary embolism rate after bariatric operations is low, it remains the major cause of death in early postoperative days, [95] Suggested approaches that may reduce the risk are intra-operative pneumatic calf compression, early mobilization postoperatively and pre-operative heparin. The use of low molecular weight heparin should be closely monitored, because of the increased risk of bleeding, which is the next major complication of bariatric surgery.

Especially in the context of bariatric surgery researchers observed complications such as postoperative dysphagia, which is usually described after AGB. Patients may also present reflux symptoms.[93] A special diet should be followed in the early weeks after surgery, that consists of liquids and soft foods. One of the greatest challenges after metabolic surgery is malnutrition, most significantly protein malnutrition. Another concern is vitamin D deficiency, which may affect metabolic bone diseases and increase the risk of fractures.[96] Studies also described microbiome changes and small intestinal bacterial overgrowth after bariatric surgery, which also may potentially cause malnutrition.[97]

It is important to acknowledge above mentioned complications before referring a patient to a surgical course of treatment.

## **Other treatments**

### *Intragastric balloon system*

Intragastric balloons (IGBs) are temporary devices introduced into the stomach to induce weight loss. They are considered a non-surgical, minimally invasive approach to aid in weight loss for individuals struggling with obesity.[98] [99]

They are recommended for patients who have previously not achieved weight loss with diet and exercise alone and who may not be suitable candidates for surgical weight loss procedures or who prefer a non-surgical option. BMI indications are considered: in the USA – BMI of 30 to 35 kg/m<sup>2</sup>, and in Europe - of 27 to 35 kg/m<sup>2</sup>. [100] Intragastric balloons can also be utilized for patients with an extremely high BMI (>50), not meeting the BMI criteria for bariatric surgery as a preoperative measure, a bridging intervention before undergoing a bariatric operation to reduce weight and by decreasing the complexity of the surgery and surgical risk.[101] As used as a bridging therapy to bariatric operations further research is needed to evaluate the intragastric balloon.

Since the Orbera balloon received FDA approval in 2015 ( 1997 in Europe) many different intragastric balloon systems have been developed.[98] Typically, they are made of soft, durable silicone and are inserted into the stomach endoscopically while deflated, then inflated with a sterile saline solution or air, expanding to occupy a significant portion of the stomach's volume. This leads to earlier feelings of satiety, reduced food intake, and subsequent weight loss. These balloons usually remain in the stomach for up to six months, in some cases, for example, the Spatz3 balloon, even up to 12 months, and are then removed endoscopically.[98] [102][103] Innovations aimed at reducing the necessity for endoscopic procedures have led to the development of the Obalon system, comprising three separable swallowable balloons, though endoscopy is required for their retrieval.[104]The other system, that does not require any endoscopic procedure is called the Elipse. This type of balloon is made of a resorbable degradable material and then is removed via natural excretion.[105]

The working of the intragastric balloon system depends mostly on reducing the stomach's volume, however, researchers are also considering other effects like delayed gastric emptying and influence on a neuro-humoral axis that regulates the feeling of satiety. It is important to notice, that the efficacy of IGBs is dependent on patient adherence to both diet and exercise modifications. [106][107]

The effectiveness of IGBs varies, depending on the specific device used, the patient's characteristics, and the commitment to lifestyle modifications. Studies have shown results of

weight loss typically around 10-15% of total body weight within six months of placement. [99][108] However, the IGBs are less effective for long-term weight maintenance, especially compared to bariatric surgery. [98] [100][102] The American Society for Gastrointestinal Endoscopy (ASGE) confirms these outcomes in several meta-analyses. Currently, the most comprehensively studied is the Orbera intragastric balloon, which efficiency was able to achieve 11.3% total body weight loss (TWL) and 25.4% excess weight loss (EWL) at 12 months post-balloon placement.[109][110] From other devices, the ReShape Integrated Dual Balloon (IDB) system had resulted in an EWL of 25.1% after 48 weeks [111], the Obalon's multi-center randomized sham-controlled trial resulted in twice as much weight loss in the group with inserted balloons compared to the control group [%TWL of 7.1% vs 3.6%] [112], and the implantation of Spatz balloon in 12-month pilot three studies showed a mean %EWL of 48.8%, of 45.7% and 42.9%, respectively. [113][114][115]

While IGBs are generally considered safe, they carry certain risks and potential complications. Common mild adverse effects include nausea, vomiting, abdominal discomfort, and gastroesophageal reflux, especially during the initial adjustment period after balloon placement, which typically resolves within a few weeks. Although uncommon, more serious complications may occur and may include balloon deflation or rupture, balloon migration to other parts of the digestive tract, bowel obstruction, ulceration of the stomach lining, gastric or esophageal perforation, and pancreatitis. Therefore, it's important to carefully select patients and monitor them closely during IGBs therapy. [99][102][116]

### *Hydrogels*

Superabsorbent hydrogels, which are already used in many fields of medicine, are other options for the newest forms of obesity treatment.[117][118][119][120] They are cross-linked polyelectrolyte polymers that can absorb and retain large amounts of fluid. [121]

The first in its class approved by the FDA is Gelesis1000.[120] It is an encapsulated form of hydrogel, which should be taken before the meal. Next, Gelesis1000 is mixed with the ingested food in the stomach and increases in volume and firmness, creating many small pieces of gel that have the elasticity of solid foods.[120][122] It results in stretching and exerting tension on the gastrointestinal tract and this mechanical effect causes activation of the vagus nerve and triggers signals of satiety.[123][124][125] The residual Gelesis100 particles are then naturally degraded, the released water is absorbed in the large intestine and the rest of the material is expelled in feces.[120], [122]

Scientists are constantly trying to create ingestible hydrogel devices for long-term gastric retention and optimize as much as possible how much will the OSH (oral superabsorbent hydrogel) increase its volume, achievable elasticity, time to hydrate, and time of degradation, to help obese patients at the expense of the least side effects.[120] There are a few other encapsulated gastric space fillers using superabsorbent hydrogel technologies in progress, but none have been accepted by the FDA yet. [126][127]

The multicenter Gelesis Loss Of Weight Study illustrated that OSH is efficacious and well-tolerated. Around 27% of overweight or obese participants lost at least 10% of their total body weight, furthermore, 60% of patients also attained significant weight loss, which is 5% or more. In addition to that, weight loss was upheld during the 24-week follow-up period.[122] The most commonly reported side effects were those from the gastrointestinal tract like diarrhea, abdominal distension, or infrequent bowel movements. In one study, the overall incidence of adverse events in participants taking Gelesis100 was no different than in those taking a placebo. [122]

## **CONCLUSIONS**

Lifestyle intervention remains the foundation for obesity treatment and includes mainly physical activity, behavioral therapy, and proper nutrition. In many cases, where lifestyle modification alone is insufficient or inadequate, comprehensive obesity management must also include pharmacotherapy and surgical procedures. In recent years, there has been a dynamic development of new drugs and surgery, as well as non-surgical treatments. Currently used medications for long-term treatment include liraglutide and semaglutide (GLP-1 agonists), tirzepatide (glucose-dependent insulinotropic polypeptide/GLP-1 receptor agonists), phentermine-topiramate, orlistat, and bupropion-naltrexone. Bariatric surgery has shown to be one of the most effective approaches but still carries a high risk of postoperative complications. When contraindications for surgery are present, other treatments, like intragastric balloon systems and hydrogels, may also be considered. It is important to remember that the treatment should be adjusted to patients' needs, and restrictions as well as compliance and aiming for long-term results.

## **DISCLOSURES**

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