

The Evolving Role of Weight Loss Pharmacotherapy

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Abstract: Obesity is a complex disease, afflicting millions of individuals worldwide. Multiple treatment options exist, including dietary and lifestyle modifications, pharmacotherapy, endobariatrics, and surgery. Although diet and exercise remain crucial to the long-term management of obesity, their effectiveness as monotherapy is limited. Adjunctive therapy, therefore, has become a tool associated with more durable weight loss results. This article serves to explore the expanding pharmacologic options available for the treatment of obesity. Traditional pharmacotherapy includes phentermine/topiramate and bupropion/naltrexone, both of which have been shown to aid in weight loss. More recent novel therapies include glucagon-like peptide-1 (GLP-1) and GLP-1/glucose-dependent insulinotropic polypeptide receptor agonists, which have shown even more marked weight loss and improvement in obesity-associated comorbid conditions compared with alternative medications. Despite their effectiveness, barriers to widespread use include their cost, insurance approval, and side effect profile. Further studies are underway examining the role of pharmacotherapy in conjunction with endoscopic bariatric therapies as well as bariatric surgery.

Keywords

Obesity, weight loss, type 2 diabetes mellitus,
phentermine, bupropion, glucagon-like peptide-1
receptor agonist

Obesity is a chronic disease characterized as a disorder of energy homeostasis involving complex physiologic pathways regulating appetite and energy metabolism as well as neurohormonal and metabolic responses.¹ On a global scale, there are more than 1.9 billion adults characterized as being overweight (defined as a body mass index [BMI] ≥ 25) with a prevalence of obesity (BMI ≥ 30) that has nearly tripled within the past 4 decades.^{2,3} This rise in obesity mirrors increases in several associated comorbid conditions such as type 2 diabetes mellitus (T2DM), hypertension, dyslipidemia, obstructive sleep apnea

(OSA), coronary artery disease (CAD), and cancer with severe downstream health and economic consequences.⁴⁻⁶ As the prevalence of individuals with a BMI of at least 30 has continued to grow, so too has investment in safe and effective treatment options, including the introduction of novel pharmacotherapy and the evolving role it plays in the management of obesity. The aim of this article is to summarize the current landscape of weight loss pharmacotherapy and highlight emerging treatment strategies for obesity.

Traditional Approach With Lifestyle Interventions

The conventional paradigm of weight management and obesity treatment has long been focused on diet and exercise. Indeed, lifestyle modifications remain the first-line treatment for weight management and are the crux of all other weight loss interventions such as pharmacotherapy, endoscopic therapy, and bariatric surgery. It remains critically important that all strategies employ a multidisciplinary approach involving physicians, dietitians, behavioral psychologists, and exercise physiologists. However, even with caloric restriction, moderate exercise activity, and behavioral therapy when required, traditional lifestyle interventions alone result in only 3% to 5% total body weight loss (TWL).⁷⁻⁹ Furthermore, this weight loss becomes more difficult to sustain over time, with many patients experiencing weight regain.

Role of Bariatric Surgery

On the other end of the spectrum remains bariatric surgery, providing the most robust and durable weight loss results. Patients eligible for bariatric surgery are individuals with class II obesity (defined as BMI ≥ 35) with comorbid conditions or individuals with class III obesity (BMI ≥ 40) who have not responded to traditional lifestyle interventions. Surgical treatment with laparoscopic sleeve gastrectomy has become the most common type of bariatric surgery over the past 10 years, with Roux-en-Y gastric bypass (RYGB) still remaining a common strategy, especially for patients with T2DM. In striking juxtaposition to lifestyle interventions alone, sleeve gastrectomy and RYGB provide approximately 25% to 35% TWL and may improve obesity-associated comorbid conditions such as hypertension, T2DM, dyslipidemia, and OSA, among many others. This weight loss and improvement of obesity-related comorbidities is considered significantly more robust and durable than with lifestyle interventions alone. Yet, despite the efficacy of surgeries such as sleeve gastrectomy and RYGB, less than 1% of eligible patients undergo surgery, in part owing to cost, lack of

universal insurance coverage, access to health care, and individual patient interest in surgery, as well as general stigma surrounding the treatment of obesity.^{10,11} In fact, the number of bariatric surgeries has reached a relative plateau over the past 2 decades.^{12,13} Given the increasing number of individuals with obesity, there continues to be a large gap in access to effective bariatric and metabolic treatments.¹⁴ Although generally well tolerated with a low adverse-event profile, bariatric surgery is not without risk of complications, including but not limited to gastric leak, reflux, Barrett esophagus, dumping syndrome, vitamin and mineral nutritional deficiencies, hernias, fistulas, stenoses, and ulceration.¹⁵

Endoscopic Therapies

As the global burden of obesity and associated comorbid conditions has continued to increase, more tools and available treatment options have become increasingly necessary. Endoscopic treatment options have emerged to provide safe and effective alternatives to patients wishing to avoid surgery, as well as for individuals who are not surgical candidates, including those with a BMI of 30 to 35. Ultra-minimally invasive treatment options such as intragastric balloon (IGB) and suturing procedures such as endoscopic sleeve gastropasty (ESG) or transoral outlet reduction are approved by the US Food and Drug Administration (FDA) for the treatment of obesity and aim to bridge the gap to reach more individuals by offering other treatment options.¹⁶⁻²¹ Although weight loss associated with endoscopic therapies is slightly lower compared with traditional surgical approaches, the procedures are less invasive, durable, and generally considered safer with fewer associated adverse events and no risk of malabsorption.²²⁻²⁴ For these reasons, endoscopic options have been increasingly adopted for individuals with class I obesity or those with class II or III obesity who wish to avoid surgery.

Traditional Pharmacotherapy

Another, and perhaps historically underutilized, treatment option for obesity has been pharmacotherapy. Up until the past decade with the rise of glucagon-like peptide-1 (GLP-1) receptor agonists and more novel dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists, prescription drugs for weight management have been limited to medical weight loss clinics and mostly endocrinology providers. Pharmacotherapy for weight loss is approved for adults with a BMI of at least 30 or adults with a BMI of at least 27 with at least 1 weight-related comorbidity.²⁵

Medications for weight loss, such as phentermine

Table 1. Current FDA-Approved GLP-1 and GLP-1/GIP Receptor Agonists

Medication	Brand name	Date of FDA approval	Dosage form	Typical dosage	Frequency	Dosing schedule
<i>FDA-approved GLP-1 and GLP-1/GIP receptor agonists for diabetes mellitus</i>						
Exenatide	Byetta	April 2005	Subcutaneous injection	5 mcg or 10 mcg	Twice daily	Start with 5 mcg twice daily for 1 month, and then 10 mcg twice daily if tolerated
Liraglutide	Victoza	January 2010	Subcutaneous injection	0.6 mg, 1.2 mg, or 1.8 mg	Once daily	Start with 0.6 mg daily for 1 week, then 1.2 mg daily, and increase to 1.8 mg if needed
Exenatide ER	Bydureon	January 2021	Subcutaneous injection	2 mg	Once weekly	2 mg once weekly
Dulaglutide	Trulicity	September 2014	Subcutaneous injection	0.75 mg or 1.5 mg	Once weekly	Start with 0.75 mg once weekly; can increase to 1.5 mg if needed
Semaglutide	Ozempic	December 2017	Subcutaneous injection	0.25 mg, 0.5 mg, or 1 mg	Once weekly	Start with 0.25 mg once weekly for 4 weeks, then 0.5 mg once weekly, and increase to 1 mg if needed
Semaglutide	Rybelsus	September 2019	Oral tablet	3 mg, 7 mg, or 14 mg	Once daily	Start with 3 mg once daily for 30 days, and then increase to 7 mg once daily; can increase to 14 mg if needed
Tirzepatide	Mounjaro	May 2022	Subcutaneous injection	2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, or 15 mg	Once weekly	Start with 2.5 mg once weekly, and increase to 5 mg, 7.5 mg, 10 mg, 12.5 mg, or 15 mg as tolerated
<i>FDA-approved GLP-1 and GLP-1/GIP receptor agonists for weight management</i>						
Liraglutide	Saxenda	December 2014	Subcutaneous injection	0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg, or 3 mg	Once daily	Start with 0.6 mg daily for 1 week, and increase by 0.6 mg each week until 3 mg daily is reached
Semaglutide	Wegovy	June 2021	Subcutaneous injection	0.25 mg, 0.5 mg, 1 mg, 1.7 mg, or 2.4 mg	Once weekly	Start with 0.25 mg once weekly for 4 weeks, then 0.5 mg for 4 weeks, then 1 mg for 4 weeks, then 1.7 mg for 4 weeks, and then 2.4 mg once weekly
Tirzepatide	Zepbound	June 2023	Subcutaneous injection	2.5 mg, 5 mg, 10 mg, 15 mg, or 20 mg	Once weekly	Start with 2.5 mg once weekly, and increase to 5 mg, 10 mg, 15 mg, or 20 mg as tolerated

FDA, US Food and Drug Administration; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1.

which was approved by the FDA in 1959, have been available for a long time; however, uptake has been limited by lack of provider knowledge, side effect profile, and modest weight loss when compared with bariatric surgery. Combination pharmacotherapy such as phentermine/topiramate has been shown to be more effective than either agent alone, with an average weight loss of 10.2 kg or TWL of 9.8% at the maximum dose.²⁶ Common side effects of phentermine include insomnia, anxiety, dry mouth, hypertension, and increased heart rate, although the drug should be avoided in individuals with valvular heart disease. Importantly, all weight loss pharmacotherapy is contraindicated in the setting of pregnancy, and topiramate is associated with an increased risk of birth defects, including oral clefts, other malformations, and conotruncal heart defects (FDA category D); therefore, 2 forms of contraception are often recommended.

The FDA-approved combination bupropion/naltrexone results in 5% to 15% TWL; however, data on long-term safety and efficacy are limited, with nausea, vivid dreams, and constipation as common side effects.²⁷ Owing to their relative affordability compared with GLP-1 and GLP-1/GIP receptor agonists, separate prescriptions of phentermine, topiramate, bupropion, or naltrexone may be considered for patients with restrictive insurance reimbursement or for uninsured individuals, as the combinations may be prohibitively expensive. The oral weight loss 5-HT_{2c} receptor agonist medication lorcaserin was associated with greater weight loss than phentermine/topiramate and bupropion/naltrexone, although it was removed from the market owing to an association with malignancy. Overall, both traditional pharmacotherapy as well as more novel injectable weight loss treatment have reliably demonstrated effective weight loss at 1 year

Table 2. Improvements in Obesity and Associated Comorbid Conditions With GLP-1 and GLP-1/GIP Receptor Agonists

Comorbid conditions	Improvement with GLP-1 and GLP-1/GIP receptor agonists
Obesity	Substantial weight loss (5%-20% total body weight loss)
Type 2 diabetes	Significant A1c reduction, improved glycemic control
Cardiovascular disease	Reduced risk of major adverse cardiovascular events, improved lipid profiles (cholesterol, LDL, triglycerides), lowered blood pressure
Metabolic dysfunction-associated steatotic liver disease and metabolic dysfunction-associated steatohepatitis	May reduce liver fat content and liver enzyme levels (ALT, AST) and may improve fibrosis
Obstructive sleep apnea	May reduce sleep apnea severity (improve Apnea-Hypopnea Index)
Polycystic ovarian syndrome	Weight loss, may improve insulin sensitivity, may regularize menstrual cycles
Chronic kidney disease	May slow progression of kidney function decline

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; LDL, low-density lipoprotein.

follow-up in many studies; however, weight regain after cessation remains a concern.²⁸ For many of the reasons previously discussed, pharmacotherapy has traditionally been a less emphasized treatment option for patients with obesity.

Novel Pharmacotherapy for Weight Loss

The advent of GLP-1 and GLP-1/GIP receptor agonists has revolutionized pharmacotherapy for obesity, offering significant weight loss and metabolic benefits and vastly expanding the treatment options for providers. Primary care providers, endocrinologists, gastroenterologists, and bariatric surgeons have embraced these drugs overall, with an exponential increase in utilization over the past half decade.²⁹ A complete list of FDA-approved GLP-1 and dual GLP-1/GIP receptor agonist medications is included in Table 1. These drugs mimic the action of natural incretin hormones to enhance glucose-dependent insulin secretion by pancreatic beta cells. Dual agonists such as tirzepatide enhance insulin secretion more effectively than GLP-1 monotherapy.³⁰ These GLP-1 and GLP-1/GIP receptor agonist medications also suppress glucagon secretion, which reduces hepatic glucose production and contributes to improved blood glucose levels as well as slows gastric emptying, which enhances satiety and reduces postprandial hunger. Tirzepatide has additionally been shown to increase energy expenditure.³¹

Weight Loss and Comorbidity Improvement With GLP-1 and GLP-1/GIP Receptor Agonists

The most widely used and increasingly prescribed types of injectable weight loss medications include semaglutide and tirzepatide. These drugs have outperformed previous weight loss results associated with oral medications

alone, with individuals achieving TWL of 15% to 22% at approximately 1 year in the pivotal STEP-1 and SURMOUNT-1 trials.^{32,33} In addition to dramatic weight loss, these pharmacotherapies have shown substantial reductions in obesity-associated comorbid conditions (Table 2).

Recent literature has also shown significant improvement in insulin resistance and hemoglobin A1c as well as a reduction in the risk of major adverse cardiovascular events (decreasing low-density lipoprotein cholesterol and triglycerides) and a reduction in blood pressure.³⁴⁻³⁶ This has led to the FDA approval of semaglutide for reduction in the risk of cardiovascular death, heart attack, and stroke in adults with concomitant obesity and cardiovascular disease. Tirzepatide is the only pharmacotherapy approved by the FDA for individuals with obesity and moderate-to-severe OSA. Recent literature has also demonstrated improvements for obesity-associated comorbid conditions such as metabolic dysfunction-associated steatotic liver disease and metabolic dysfunction-associated steatohepatitis, OSA, polycystic ovarian syndrome, chronic kidney disease, CAD, and heart failure.³⁷⁻⁴²

Side Effects With GLP-1 and GLP-1/GIP Receptor Agonists

Weight loss results and improvements in comorbid conditions appear to be dose-dependent and so too are side effects. Common side effects associated with GLP-1 and GLP-1/GIP receptor agonists include a variety of gastrointestinal symptoms such as nausea, vomiting, diarrhea, and constipation. Nausea may be present in approximately 30% of patients, which is typically mild to moderate and resolves with continued use, although it may flare with dose escalation. Vomiting, although less common, is a significant concern owing to the potential

Table 3. Side Effects Associated With GLP-1 and GLP-1/GIP Receptor Agonists

Adverse event	GLP-1 receptor agonists	GLP-1/GIP receptor agonists	Incidence rate	Clinical implications	Management strategies
Nausea	Common	Common	~30%	Initial treatment phase, often mild to moderate. Can impact patient adherence	Gradual dose escalation, antiemetics, dietary adjustments
Vomiting	Less common	Less common	~5%-10%	Severe cases of nausea may lead to vomiting. Can cause dehydration and electrolyte imbalances	Hydration, dose adjustments, antiemetics
Diarrhea	Common	Common	~15%-20%	Typically occurs in early treatment stages. Can lead to discomfort and inconvenience	Dietary modifications, antidiarrheal agents
Constipation	Common	Common	~10%-15%	Owing to slowed gastrointestinal motility. Can cause discomfort and affect adherence	Dietary changes, increased fiber intake, laxatives
Abdominal pain	Common	Common	~10%-15%	Associated with changes in gastrointestinal function. Can be mild to moderate in intensity	Dietary adjustments, over-the-counter pain relief, supportive care
Indigestion (dyspepsia)	Common	Common	~10%	Symptoms such as bloating and heartburn. Can affect quality of life and adherence	Antacids, dietary modifications
Headache	Common	Common	~5%-10%	Mild to moderate in intensity. Can affect daily activities	Over-the-counter pain relief, adequate hydration
Dizziness	Less common	Less common	~5%	Can be related to blood pressure changes. Typically mild	Adequate hydration, monitoring of blood pressure
Fatigue	Less common	Less common	~5%-10%	Can impact daily functioning and adherence	Ensuring adequate rest, gradual dose escalation
Injection site reactions	Common	Common	~10%-15%	Localized reactions such as redness or swelling. Typically mild	Rotating injection sites, proper injection technique
Hypoglycemia	Rare ^a	Rare ^a	<5%	Low blood sugar levels, primarily in patients on concomitant insulin or sulfonylurea therapy	Monitoring blood glucose levels, adjusting concomitant medications

^aRare unless when combined with insulin or sulfonylureas.

GIP, glucose-dependent insulintropic polypeptide; GLP-1, glucagon-like peptide-1.

to cause dehydration and electrolyte imbalances. Patients should be counseled on these side effects, with dietary adjustments recommended and antiemetic medications occasionally used. Alterations in bowel habits are also frequently reported, especially in early stages of treatment, although they typically resolve with time. Many of these common side effects are shown in Table 3.^{32,33,43} Prior to initiation of therapy, the patient's medical history should be reviewed for contraindications, including multiple endocrine neoplasia type 2 and medullary thyroid cancer.⁴⁴ Additionally, there is evidence to suggest that GLP-1 receptor agonists pose an increased risk of cholelithiasis and cholecystitis with a relative risk of 1.27 and 1.36, respectively, although these risks are likely related to all interventions that reduce weight rapidly.⁴⁵ There may also be a risk for development of acute pancreatitis, with

reports of an odds ratio greater than 2, although results have been conflicting in some studies.^{46,47} More recently, there have been concerns regarding a potential association with optic neuritis from a retrospective observational study; however, this has not yet been substantiated as the disease itself is associated with more severe T2DM and these patients are more likely to be on pharmacotherapy such as GLP-1 and GLP-1/GIP receptor agonists.⁴⁸

Furthermore, and viewing obesity through the lens of a chronic disease model, it is not surprising to realize that weight regain and return of weight-associated comorbid conditions may occur with cessation of pharmacotherapy. In fact, 1 year after withdrawal of once-weekly subcutaneous semaglutide, participants regained two-thirds of their prior weight loss, with similar changes in cardiometabolic variables.⁴⁹ For this reason, providers may counsel

patients that these medications are intended to be taken indefinitely with limited data to guide how to taper off or stop these medications for patients to reduce the risk of weight recurrence. Ultimately, it is important to acknowledge that GLP-1 and GLP-1/GIP receptor agonists are effective tools in the pharmacologic management of obesity; however, gastrointestinal side effects are common and require careful management to optimize treatment adherence and outcomes.

Cost and Reimbursement

The largest burden to further uptake of these novel pharmacotherapies has been the sporadic and slow adoption of insurance reimbursement. Although GLP-1 and dual GLP-1/GIP receptor agonist medication approvals for T2DM have become almost universal, reimbursements for weight loss indications, despite FDA approval, have been few and far between. This has led to enormous out-of-pocket costs and created a landscape of alternative, nonverified drug formulations from compound and online pharmacies as well as less scrupulous sources. In fact, drugs approved for weight loss are estimated to be covered by just 1% of marketplace prescription drug plans, require time-consuming prior authorizations despite meeting FDA-approval measures, and typically amount to upward of \$1000 per month of out-of-pocket expenses, becoming prohibitively expensive for a growing number of individuals who would potentially benefit.

A previous cost-effectiveness study compared ESG, an FDA-approved endoscopic suturing system for the treatment of obesity, to semaglutide, modeling the socioeconomic impact over a 5-year period for patients with class II obesity. This study found that ESG was cost-effective compared with semaglutide among this patient population.⁵⁰ In another cost-effectiveness study, this time comparing pharmacotherapy vs endoscopic treatment and bariatric surgery, ESG was cost-effective for individuals with class I obesity, with surgical sleeve gastrectomy being the ideal strategy for patients with class II or III obesity.⁵¹ GLP-1 and GLP-1/GIP receptor agonist medications only have the potential to become cost-effective with substantial cost reduction. Until a streamlined investment or general acceptance to cover treatment for one of the most common diseases among US adults is made, the prevalence of obesity and associated comorbid conditions will likely continue to increase.

The Changing Landscape of Obesity Treatment

Pharmacotherapy such as GLP-1 and GLP-1/GIP receptor agonists has significantly impacted the landscape of obesity treatment, altering both the approach to obesity

management and the decision to initiate endoscopic or surgical interventions. Some individuals may prefer pharmacologic interventions over endoscopic or surgical options owing to the noninvasive nature and reversible effects of medication. This preference has contributed to a shift away from surgery as the first-line treatment for adults with obesity who have not responded to traditional lifestyle interventions, particularly for individuals with class II obesity who have contraindications to surgery.

Although data have shown that endoscopic and bariatric surgery interventions are associated with a greater reduction in mortality compared with GLP-1 and GLP-1/GIP receptor agonists, each treatment, whether lifestyle interventions, pharmacotherapy, endoscopic options, or bariatric surgery, is not meant to be antagonist toward the others.⁵² Previously siloed, antiquated practice patterns must adapt to an era of personalized medicine, offering a multitude of potential treatment options independently or in combination to achieve desired weight loss goals and resolution of obesity-associated comorbid conditions.

Pharmacotherapy With Endoscopic or Bariatric Interventions

Drugs such as GLP-1 and GLP-1/GIP receptor agonists have been increasingly utilized in the preoperative period to assist patients in achieving weight loss before undergoing endoscopic interventions or bariatric surgery. This preoperative weight reduction may lower anesthetic or surgical risks, improve perioperative outcomes, and enhance postoperative recovery.

Furthermore, early initiation of these medications may reduce body weight and improve metabolic profiles, allowing previously ineligible patients to become suitable candidates for surgery.

Importantly, these drugs may also be used in combination to achieve synergistic weight loss results or greater reduction in comorbid conditions. Combination therapy, as this approach is sometimes referred to, has the ability to achieve significant results and can be utilized prior to, simultaneously, or after endoscopic or surgical interventions to achieve desired weight loss goals. It can also be used as a treatment for recurrent weight gain, in which it may be referred to as sequential therapy.

When GLP-1 receptor agonists were combined with endoscopic suturing (ie, ESG), patients achieved significantly more weight loss with a greater reduction in percent body fat than patients who underwent the ESG procedure alone.⁵³ Similar findings were achieved for patients receiving IGB and GLP-1 combination therapy vs IGB alone.⁵⁴ Notably, there was no increase in the side effect profile for patients undergoing ESG or IGB in these studies.

Owing to the nature of bariatric surgery, simultaneous pharmacotherapy is not often employed. However,

GLP-1 or GLP-1/GIP receptor agonists for patients who do not achieve initial weight loss goals or those patients who develop weight regain may be appropriate. In the BARI-OPTIMISE study, adjuvant liraglutide for patients who did not achieve adequate initial weight loss following sleeve gastrectomy and RYGB resulted in significant weight loss results.⁵⁵ Given the recurrence of weight gain in approximately 15% to 25% of individuals after bariatric surgery, use of pharmacotherapy has been increasingly studied. Among patients with and without a history of bariatric surgery, GLP-1 receptor agonist-directed therapies have shown reliable weight loss results, regardless of weight regain after surgery.^{56,57}

Current Practice Patterns and Perspective on Future Directions

In our own practice as gastroenterologists with board certification in obesity medicine, we manage patients medically, endoscopically through various therapies, as well as treat patients with a history of bariatric surgery. The management approach is highly individualized, with considerations for combination therapy among individuals with class II or III obesity as well as the presence of obesity-associated comorbid conditions. It is important to counsel patients that these medications are meant to be taken indefinitely when started; however, anecdotally when used as a bridge to endoscopic procedures or bariatric surgery where the anatomy is altered, we have been able to slowly taper off successfully with minimal weight regain.

We also tend to prescribe tirzepatide in favor of semaglutide given the current literature regarding greater weight loss results and evidence regarding the side effect profile.³⁰ When used simultaneously with endoscopic therapies, there is no consensus regarding time of initiation, whether before or after the procedure. Our own practice is to initiate pharmacotherapy 3 to 4 months prior to endoscopic treatment or trial pharmacotherapy prior to bariatric surgery for patients with class III obesity and multiple comorbid conditions to improve suitability for surgery or achieve greater comorbid resolution. We acknowledge this is largely anecdotal and institution-based practice and hope that future tailored treatments may be designed.

Continued pharmaceutical investment and drug design is currently underway, with more novel drugs, many of which are oral medications, possessing the potential to push the boundaries of pharmacotherapy-associated weight loss even further. Attempts to identify a biomarker to predict response to these agents may also help select the most appropriate candidates for treatment, optimizing outcomes and reducing unnecessary exposure to medications. This approach could enhance efficacy and

minimize adverse effects, allowing for ideal candidates to be selected based on potential response to the variety of available obesity treatments. Ultimately, physicians and treatment teams must continue to adopt and accept emerging data and the changing landscape of available obesity treatment.

Conclusions

The evolving role of pharmacotherapy in the treatment of obesity does not mean the end for endoscopic procedures and bariatric surgery, although GLP-1 and GLP-1/GIP receptor agonists provide a much-needed tool in the treatment armamentarium for obesity. Practitioners should be encouraged to embrace a multidisciplinary approach and understand each therapy, whether lifestyle modifications, pharmacotherapy, endoscopic treatment, or bariatric surgery, as these modalities are not competing against one another. Rather, they constitute a spectrum of available options to patients, some of whom may need to consider more than 1 treatment.

Disclosures

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