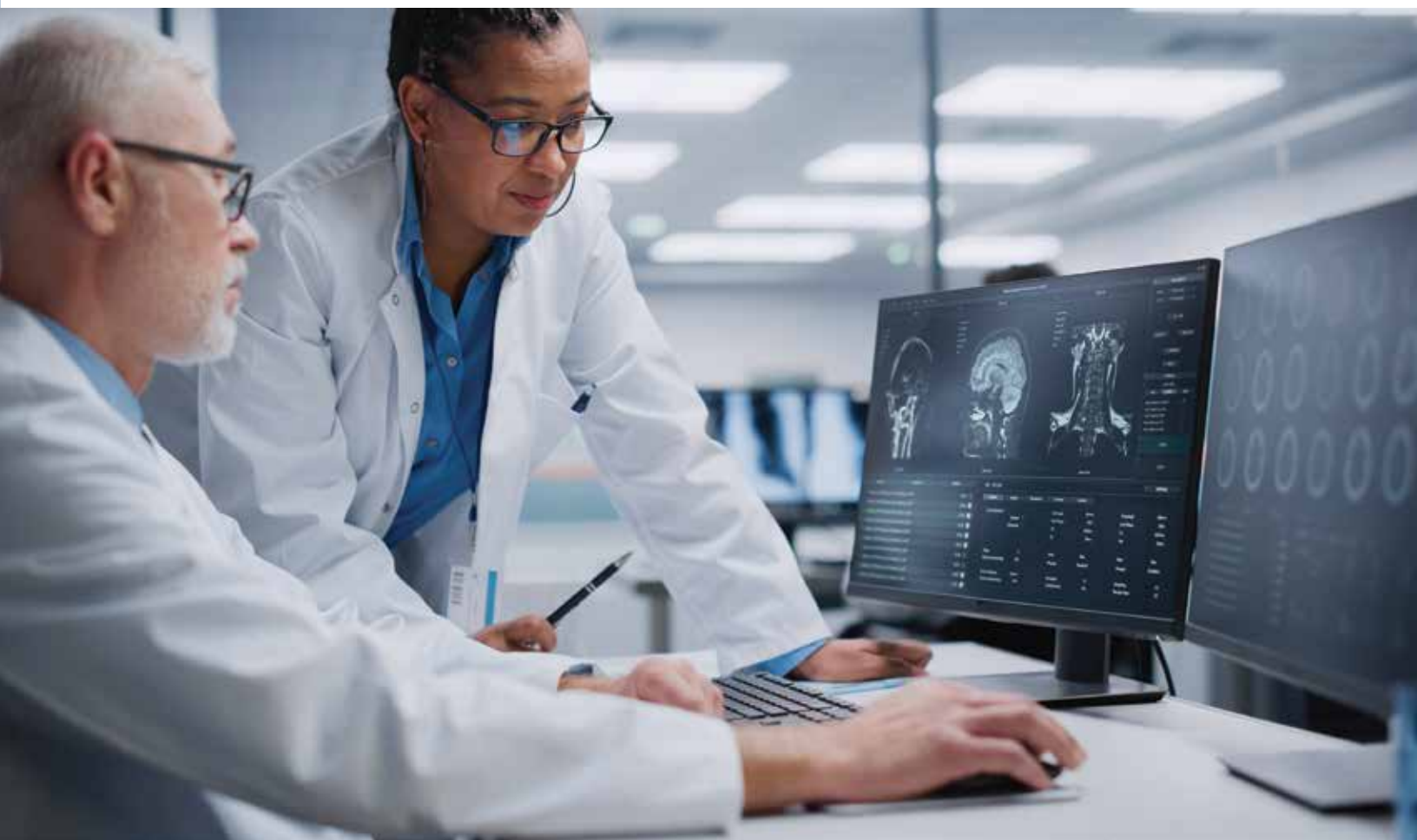


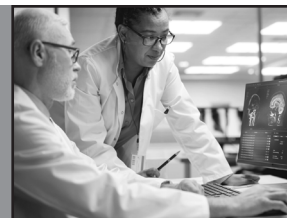


FROM THE EXPERTS IN ENDOCRINOLOGY

2025 ENDOCRINE CASE MANAGEMENT: MEET THE PROFESSOR

FROM THE EXPERTS IN ENDOCRINOLOGY

ENDO 2025
MEET THE PROFESSOR



ENDOCRINE

CASE MANAGEMENT

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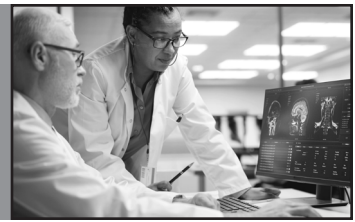
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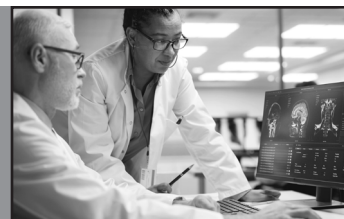
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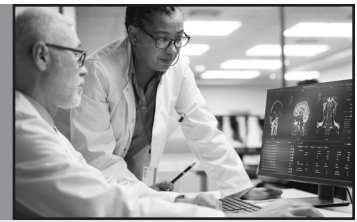
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ENDO 2025 OVERVIEW



OVERVIEW

Endocrine Case Management: Meet the Professor is designed to provide physicians with a concise and high-quality review of more than 40 common and rare endocrine disorders to help you keep your practice current. It consists of case-based clinical vignettes and rationales written by experts in all areas of endocrinology, diabetes, and metabolism.

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The Endocrine Society is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education (CME) for physicians. The Endocrine Society has received Accreditation with Commendation.



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LEARNING OBJECTIVES

Endocrine Case Management: Meet the Professor will allow learners to assess their knowledge of all aspects of endocrinology, diabetes, and metabolism.

Upon completion of this educational activity, learners will be able to:

- Recognize clinical manifestations of endocrine and metabolic disorders and select among current options for diagnosis, management, and therapy.
- Identify risk factors for endocrine and metabolic disorders and develop strategies for prevention.
- Evaluate endocrine and metabolic manifestations of systemic disorders.
- Use existing resources pertaining to clinical guidelines and treatment recommendations for endocrine and related metabolic disorders to guide diagnosis and treatment.

TARGET AUDIENCE

Endocrine Case Management: Meet the Professor provides case-based education to clinicians interested in improving patient care.

STATEMENT OF INDEPENDENCE

As a provider of CME accredited by the Accreditation Council for Continuing Medical Education, the Endocrine Society has a policy of ensuring high-quality content in this educational activity that is balanced, independent, objective, and scientifically rigorous. The scientific content of this activity was developed under the supervision of the Endocrine Society's Annual Meeting Steering Committee.

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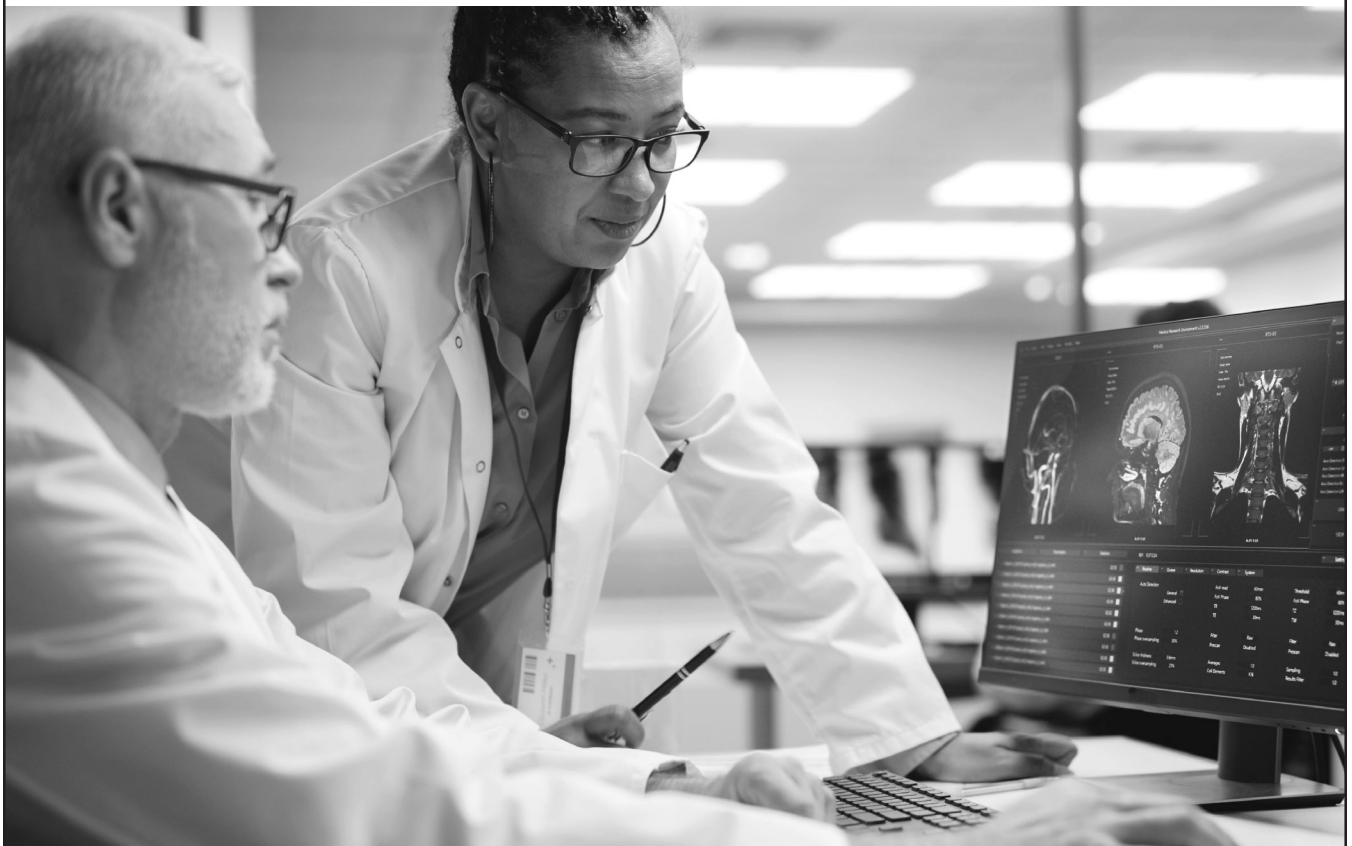
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ACTH = corticotropin	GH = growth hormone	NPH insulin = neutral protamine Hagedorn insulin
ACE inhibitor = angiotensin-converting enzyme inhibitor	GHRH = growth hormone–releasing hormone	PCSK9 inhibitor = proprotein convertase subtilisin/kexin 9 inhibitor
ALT = alanine aminotransferase	GLP-1 receptor agonist = glucagonlike peptide 1 receptor agonist	PET = positron emission tomography
AST = aspartate aminotransferase	GnRH = gonadotropin-releasing hormone	PSA = prostate-specific antigen
BMI = body mass index	hCG = human chorionic gonadotropin	PTH = parathyroid hormone
CNS = central nervous system	HDL = high-density lipoprotein	PTHrP = parathyroid hormone–related protein
CT = computed tomography	HIV = human immunodeficiency virus	SGLT-2 inhibitor = sodium-glucose cotransporter 2 inhibitor
DHEA = dehydroepiandrosterone	HMG-CoA reductase inhibitor = 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor	SHBG = sex hormone–binding globulin
DHEA-S = dehydroepiandrosterone sulfate	IGF-1 = insulinlike growth factor 1	T₃ = triiodothyronine
DNA = deoxyribonucleic acid	LDL = low-density lipoprotein	T₄ = thyroxine
DPP-4 inhibitor = dipeptidyl-peptidase 4 inhibitor	LH = luteinizing hormone	TPO antibodies = thyroperoxidase antibodies
DXA = dual-energy x-ray absorptiometry	MCV = mean corpuscular volume	TRH = thyrotropin-releasing hormone
FDA = Food and Drug Administration	MIBG = <i>meta</i> -iodobenzylguanidine	TRAb = TSH-receptor antibodies
FGF-23 = fibroblast growth factor 23	MRI = magnetic resonance imaging	TSH = thyrotropin
FNA = fine-needle aspiration		VLDL = very low-density lipoprotein
FSH = follicle-stimulating hormone		



ADIPOSE TISSUE, APPETITE, OBESITY, AND LIPIDS

Weight-Loss Pharmacotherapy in the Spectrum of Obesity Care

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Educational Objectives

After reviewing this chapter, learners should be able to:

- Recognize obesity as a chronic disease with relevant comorbidities.
 - Describe FDA-approved and in-development obesity pharmacotherapy as an adjunct to lifestyle intervention for weight loss.
 - Discuss the spectrum of obesity care, including dietary, pharmacologic, and surgical therapies.
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Significance of the Clinical Problem

The prevalence of obesity in adults in the United States increased to more than 40% in recent years.¹ Obesity contributes to metabolic complications, such as type 2 diabetes, dyslipidemia, hypertension; increased risk of mechanical complications, such as osteoarthritis and obstructive sleep apnea; and comorbid diseases, including several major cancers.² Weight loss of 5% to 10% reduces obesity-related complications and improves quality of life.³ Lifestyle interventions are currently the first-line therapy for weight loss; however, weight loss is difficult to maintain with lifestyle intervention alone.⁴ The emergence of various pharmacotherapies for weight loss has significantly changed the landscape of obesity management over the past decade. Most approved first-generation antiobesity medications result in 5% to

10% total body weight loss (TBWL).⁵ However, newer second-generation drugs, such as the GLP-1 agonist semaglutide, induce up to 17.4% weight loss from baseline in individuals without diabetes.

Similar to lifestyle interventions, of those who achieve at least 10% TBWL, many struggle to maintain this weight loss achieved with antiobesity medications.⁶ Bariatric surgery induces more durable weight loss than pharmacotherapy or lifestyle interventions alone. More recently, endoscopic bariatric surgery, such as intragastric balloons and endoscopic sleeve gastropasty, has offered a less-invasive option for weight loss.⁷ Similar to other interventions for weight loss, there remains a common issue of weight regain or weight-loss plateau after surgical interventions. Studies have examined the benefit of combination therapy with antiobesity pharmacotherapy and endoscopic interventions, which results in more effective weight loss.⁶ There are currently 6 FDA-approved medications for the long-term treatment of obesity, including orlistat, phentermine/topiramate, naltrexone/bupropion, liraglutide, semaglutide, and tirzepatide. Their effectiveness in treating postbariatric weight regain remains an active area of investigation. Herein, we present the pivotal trial evidence for each approved obesity pharmacotherapy agent, as well as the emerging data of its combination with available bariatric procedures.

Practice Gaps

- Six medications are FDA-approved for the long-term treatment of obesity, including orlistat, phentermine/topiramate, naltrexone/bupropion, liraglutide, semaglutide, and tirzepatide, yet their effectiveness in combination or sequence is not established.
- New drugs, such as retatrutide and orforglipron, are currently being evaluated for their efficacy in weight-loss management causing weight loss of similar magnitude to that of procedures.
- Surgical options, such as bariatric surgery, induce more durable weight loss than pharmacotherapy or lifestyle interventions alone. Recently, endoscopic bariatric surgery has offered a less-invasive option for weight loss. These procedures remain underused despite known longer-term effectiveness in weight loss and maintenance.
- The addition of pharmacotherapy has been shown to be a promising tool to address the common issue of weight regain or weight-loss plateau after surgical bariatric interventions. The choice of optimal pharmacotherapy to support weight-loss procedures remains unknown.
- The optimal timing of obesity pharmacotherapy with surgical and endoscopic interventions requires further investigation.

Discussion

Orlistat

Orlistat was FDA-approved for the treatment of obesity in 1999.⁸ It is widely available, both as an over-the-counter medication at a dosage of up to 60 mg 3 times daily and at prescription dosages up to 120 mg 3 times daily. Orlistat can address weight-loss plateaus after weight-loss surgeries, such as adjustable gastric banding. The drug was associated with weight loss in a nonrandomized intervention study of 38 patients experiencing a weight-loss plateau after adjustable gastric

banding, with a mean weight loss of 9 ± 3 kg in study participants compared with 3 ± 2 kg in the placebo group after 8 months of treatment with orlistat, 120 mg 3 times daily.⁹ It was thought that perhaps orlistat was effective particularly for the high-calorie liquid diet required after bariatric procedures, which is often high in fat. Due to orlistat's mechanism, it also interferes with the absorption, and therefore effectiveness, of drugs, such as warfarin, amiodarone, cyclosporine, levothyroxine, and fat-soluble vitamins, which modifies their effectiveness. The only contraindications include pregnancy, breastfeeding, and cholestasis. However, despite these adverse effects, drug interactions, and some contraindications, orlistat remains a widely used, easily accessible therapy for weight loss.

Phentermine and Phentermine/Topiramate

Phentermine and phentermine/topiramate are currently approved for weight-loss management in the United States and came to the market as combination therapy in 2012.¹⁰ Phentermine and phentermine/topiramate have been studied as adjunct therapy for weight loss for bariatric surgery and have been shown to be viable options for weight loss in patients with weight regain or weight-loss plateau after bariatric surgery. In a retrospective study of patients who had undergone Roux-en-Y gastric bypass or laparoscopic adjustable gastric banding, patients on phentermine lost 6.45 kg (12.8% excess weight loss), and those on phentermine/topiramate lost 3.81 kg (12.9% excess weight loss) at 90 days post surgery, but this study was limited by a short-term follow-up period.¹¹ An open-label trial of patients with a BMI of 50 kg/m² or higher who planned to undergo laparoscopic sleeve gastrectomy were prescribed phentermine/topiramate 7.5/46-15/92 mg or no therapy for at least 3 months preoperatively and 2 years postoperatively. Investigators found that the combination therapy group (phentermine/topiramate + laparoscopic sleeve gastrectomy) lost more than twice as

months will be a key point of clinical comparison. Tirzepatide was approved for weight loss in 2022 as a new class of antiobesity medications, and it is a valuable addition to available weight-loss pharmacotherapies and may be an effective adjunct therapy for surgical and endoscopic weight-loss interventions.

Summary

Our multidisciplinary group at the Margaret Corbin (Manhattan) Campus of the VA New York Harbor Healthcare System initiated care for veterans with obesity and excess weight complications in 2017, and since this time has integrated obesity pharmacotherapy with endoscopic bariatric therapies into combined therapy. In our initial 1-year follow-up cohort study, we observed that weight-loss outcomes were significantly greater in the combined cohort compared with outcomes in the bariatric endoscopy-only cohort. In comparison, all weight-loss parameters were significantly greater in the combined therapy cohort at 12 months compared with parameters in the obesity pharmacotherapy cohort. This difference, specifically percentage change in BMI and percentage excess weight loss, was sustained at 24 months. In a cohort of 58 patients who underwent outpatient intragastric balloons or endoscopic sleeve gastroplasty and had at least 12 months of follow-up data, 43% of patients were also trialed on obesity pharmacotherapy with phentermine/topiramate, bupropion/naltrexone, liraglutide, or semaglutide. At 1-year follow-up after endoscopic bariatric therapies, there was no difference in TBWL, change in BMI, or excess weight loss between intragastric balloons and endoscopic sleeve gastroplasty cohorts. By year 3, excess weight loss was significantly greater in patients who had undergone endoscopic sleeve gastroplasty ($40.4\% \pm 31.6\%$) compared with patients who had received intragastric balloons ($17.4\% \pm 19.8\%$) ($P = .025$). These promising longitudinal results suggest combination of obesity pharmacotherapy and bariatric endoscopy results in greater sustained

weight loss than each modality alone, and that it address the chronic nature of obesity and weight management requiring multimodal therapies.

Optimal timing for pharmacotherapy initiation with bariatric intervention (both surgical and endoscopic) remains unclear. In a prospective study of 1000 consecutive patients undergoing endoscopic sleeve gastroplasty, the greatest rate of weight loss was observed within the first 6 months following the procedure. Average percentage TBWL at 1-, 3-, 6-, 9-, 12-, and 18-month follow-up was $8.9\% \pm 2.9\%$, $10.5\% \pm 4.5\%$, $13.7\% \pm 6.8\%$, $15.2\% \pm 8.3\%$, $15.0\% \pm 7.7\%$, $14.8\% \pm 8.5\%$, respectively, with a plateau in weight loss observed at 9 months after the procedure.²² Obesity medications could be considered during this deceleration in weight loss following endoscopic sleeve gastroplasty before any weight regain. This finding is corroborated by a study by Badurdeen et al, in which patients who had undergone endoscopic sleeve gastroplasty and opted to take liraglutide 5 months after the procedure had superior weight loss compared with those who underwent endoscopic sleeve gastroplasty alone.¹⁷ GLP-1 receptor agonist initiation at the onset of endoscopic bariatric intervention may increase adverse effects, such as nausea and abdominal pain. However, in a recent study of 58 patients randomly assigned to either semaglutide or placebo just 1 month after endoscopic sleeve gastroplasty, those in the semaglutide cohort had approximately 7% higher TBWL compared with TBWL in the placebo group, and there were no serious adverse effects.¹⁷

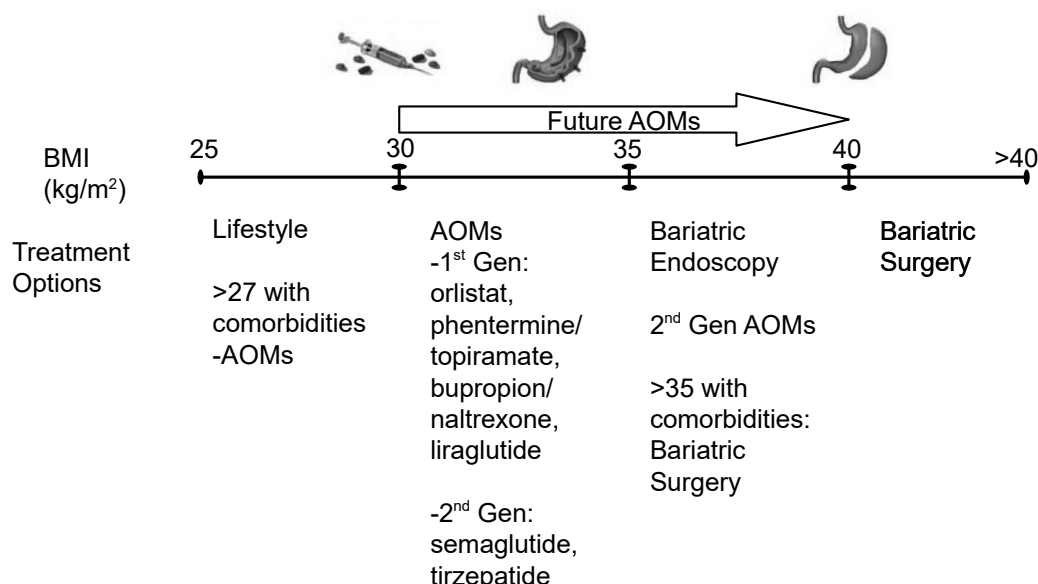
A qualitative study of 16 patients examining weight-loss patterns after gastric bypass described patterns that may help inform the optimal timing of pharmacotherapy. In the “honeymoon” period immediately after surgery and continuing for 6 to 12 months, weight loss was significant and rapid. This was followed by a weight “stabilization” period, followed by a “work begins” period when patients needed to implement cognitive and behavioral effort to maintain weight loss. Participants who regained weight reported a return to previous dietary habits, including lack

semaglutide at 28 weeks approximated 12% from baseline, and weight loss of 14.9% was reported from baseline at the formal 68-week study end point. The effectiveness of other antiobesity medications is commonly reported 1 year after intervention, with orlistat inducing 2.9% to 3.4% weight loss and naltrexone/bupropion inducing 4.8% weight loss below those of endoscopic sleeve gastroplasty. A final consideration with endoscopic bariatric and metabolic therapies, such as sleeve gastroplasty, is the possibility of weight regain, which often requires antiobesity medication support beyond 6 months after the procedure.

Key Learning Points

- The number of safe and effective options for the pharmacotherapy treatment of obesity is increasing rapidly. New and improved weight loss drugs continue to emerge, and several new multiagonist and multihormonal therapies will hopefully be approved for obesity in the near future and push the treatment envelope
- Understanding the individual mechanisms, tolerability, and efficacy of each of these weight-loss drugs is essential to inform how they may best be used not only as monotherapy, but also how they may be powerful adjuncts to endoscopic and surgical bariatric procedures.
- Some studies have already demonstrated the utility of the combination of bariatric surgery and pharmacotherapy for optimizing weight loss. With the increased use of less-invasive bariatric procedures, such as endoscopic surgeries, more studies are needed to evaluate the role of weight-loss drugs as adjunct therapy with such procedures.
- The optimal timing of adjunct obesity pharmacotherapy also requires further investigation to help provide patients with the most effective, tolerable, and long-lasting weight loss achievable.

Figure. Spectrum of Care for Obesity According to BMI



The spectrum of care for obesity by BMI reflects increasing overlap between AOMs and procedures, including bariatric endoscopy and bariatric surgery.
[Color—Print (Color Gallery page CG3) or web & ePub editions]

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