Combination Therapies
Anti-Obesity Medications and Endoscopic Bariatric Procedures

Megan E. White, MD[a], Vladimir Kushnir, MD[b,*]

KEYWORDS

• Obesity • Pharmacotherapy • Endoscopic bariatric treatment • Combination therapy

KEY POINTS

- Endoscopic bariatric treatment can bridge the gap between pharmacologic and surgical bariatric treatment.
- Combination of pharmacologic and endoscopic treatment options for obesity can provide improved weight loss benefits.
- Life-style interventions are key to long term success with both endoscopic and pharmacologic weight loss interventions.

BACKGROUND

Endoscopic Bariatric Technology (EBT) has rapidly developed over the past 2 decades due to the underutilization of surgery and historically limited effectiveness of pharmacotherapy for obesity and its metabolic complications. EBT relies on minimally invasive endoscopic interventions in the gastrointestinal tract to facilitate weight loss. While EBT provides a lesser degree of weight loss then surgery, it is less invasive, and thus, appealing to a broader patient population. EBT is currently recommended in patients who have tried and failed lifestyle or medical management or require adjunctive therapy to lifestyle or medical management due to comorbidities.[1] With the recent expansion of pharmacologic therapy for overweight and obesity, there is opportunity to combine pharmacologic therapy with endoscopic bariatric therapy to meet patient goals that may not be achieved with EBT alone.

[a] Division of Gastroenterology, Washington University School of Medicine, Washington University/Barnes Jewish Hospital, 660 South Euclid #8124, St Louis, MO 63110, USA; [b] Division of Gastroenterology, Washington University School of Medicine, Washington University, 660 South Euclid #8124, St Louis, MO 63110, USA
* Corresponding author.
E-mail address: Vkushnir@wustl.edu

Gastrointest Endoscopy Clin N Am 34 (2024) 743–756
https://doi.org/10.1016/j.giec.2024.06.003 giendo.theclinics.com

OVERVIEW OF ENDOSCOPIC BARIATRIC TECHNOLOGY

Intragastric balloons (IGB) are the oldest EBT and remain a popular choice for patients today. The first IGB prototype was created in 1985 called the Garren-Edwards bubble, which was quickly discontinued due to risk profile.[2] Since then, a multitude of IGBs have been created to improve both safety and efficacy. Most IGBs are placed endoscopically and filled with saline or gas and removed endoscopically after 6 months.[3,4] While placed, they increase satiation, delay gastric emptying, and restrict food ingestion.[3] On average, IGB result in 7% to 15% total body weight loss (TBWL) at 12 months.[5,6] The risk of severe complications is rare and includes migration, obstruction, and gastric perforation. Other side effects include pain, nausea, Gastroesophageal reflux disease and uncommonly gastric ulcers. Studies show positive effect on weight loss up to 12 months after removal. Long-term studies up to 5 years show weight regain 1 to 2 years after procedure with continued weight gain through the 5 year study protocol.[7,8] Both studies showed excess body weight loss (EBWL) of around 9% at 5 years from greater than 20% at time of balloon removal. Please refer to Diogo Turiani Hourneaux de Moura and colleagues' article, "Intragastric Balloons: Practical Considerations," in this issue for more information on intragastric balloons.

Endoscopic sleeve gastroplasty (ESG) is another common EBT that is meant to reduce the volume of the stomach similarly as laparoscopic sleeve gastrectomy (LSG). However, unlikely LSG, ESG slows gastric emptying, which increases the feeling of satiety.[9] The first ESG was conducted in 2013 and the Apollo Overstitch system was Food and Drug Administration (FDA)-approved in 2022 for body mass index (BMI) 30 to 50, based on the outcome of the MERIT study.[10] ESG is a partially reversible endoscopic suturing technique that restricts the stomach approximately 70%.[3,10,11] Patients commonly have abdominal pain and nausea especially in the first week following procedure, which typically improves rapidly thereafter. Severe complications include gastric leak (<1%) and gastric bleeding (<1%). While gastric restriction is the main cause of efficacy in ESG, there is also notable delayed gastric emptying.[12] On a physiologic level, there are some data to suggest a decrease in ghrelin, an orexigenic hormone released in the gastric fundus, after ESG, which may contribute to maintenance of weight loss.[12,13] Studies show TBWL at 12 months post ESG around 15% to 20%.[3,11,14] Five year follow-up data show maintenance of TBWL; however, in one study, 26% of patients were on adjuvant pharmacotherapy due to weight regain after ESG.[15,16] Of note, in large longitudinal studies of ESG, retightening or redo of the ESG for inadequate weight loss or weight regain was needed in up to 26% of patients.[3,10,15] The Primary Obesity Surgical Endoluminal (POSE) and POSE 2.0 system is a gastric plication procedure similar to the ESG but differs in the pattern of endoscopic suturing of the stomach as it specifically targets the fundus as opposed to the greater curvature with fundal sparing seen in ESG suturing technique.[17,18] This is not currently widely commercially available in the United States.

The duodenal bypass liner and duodenal resurfacing techniques were created to mimic gastric bypass surgery. The duodenojejunal bypass liner (DJBL) is a device that is implanted in the proximal small intestine.[19] This device is typically removed after 12 months. The DJBL is not currently FDA-approved in the United States. Duodenal resurfacing uses thermic energy to disrupt the duodenal mucosa. Both procedures block absorption of nutrition in the proximal small intestines and have been shown to improve metabolic diseases such as diabetes.[3,19] TBWL at time or removal was found to be 18.9% in one metanalysis, but 6 to 24 months after removal, that

dropped to 7.2% to 12%.[19,20] The aspire system is no long on the market but some patients still have their aspire device. This is a percutaneous gastrostomy tube that allows for drainage of 30% of calories following each meal (**Table 1**).[21]

COMBINATION OF PHARMACOTHERAPY AND ENDOSCOPIC BARIATRIC THERAPY

There are multiple FDA-approved pharmacologic therapies that can be used for obesity management. Most pharmacologic therapies provide between 5% and 10% TBWL. However, the recent introduction of incretin medications has revolutionized pharmacotherapy for obesity, with trials consistently demonstrating TBWL greater than 10% with these agents. Currently, pharmacologic treatment is recommended in patients with BMI greater than or equal to 27 with obesity related comorbidity or BMI greater than or equal to30 and should be continued if it meets appropriate weight loss standards of 5% TBWL at 3 months with tolerable side effect profile.[22] However, the major drawback of all pharmacologic interventions for obesity is rapid weight regain upon discontinuation of medications.[23] Moreover, long-term compliance with pharmacotherapy is poor, with 7% to 18% of patients discontinuing medications within 12 months in clinical trial.[24,25] In a more recent study looking at prescription refills, found that only 19% of patients were taking their anti-obesity medications at 12 months with the highest refill rate for semaglutide at 40% at 12 months.[26] Reasons for discontinuation include side effects, limited effectiveness, cost, and availability.[25,27]

Thus, there has been growing interest in combination of pharmacotherapy with anatomic interventions such as EBT and bariatric surgery. Combination therapy can be used for early inadequate weight loss, as a planned additive therapy to reach the patients goals, which would be otherwise unrealistic with EBT alone, or weight regain following EBT.

Phentermine is the oldest currently approved weight loss medication on the market but is currently only approved for short-term use (3 months). When combined with topiramate can be used long-term with good safety profile. Topiramate is also approved migraines and alcohol abuse making this medication combination especially favorable in these patient populations. There are multiple studies showing efficacy of phentermine

Table 1
Weight loss and risks of endoscopic bariatric technology

EBT	TBWL 6 mns	TBWL 12 mns	TBWL 5 Year	Risks/Side Effects
IGB[2]	13%	11%		Obstruction (0.8%), perforation (0.1%), pain, nausea, gastric ulcers
ESG[3,11,15]	8%–18%	15–16	15.9%	Gastric leak (0.5%), Gastric bleeding (0.5%), nausea, pain
POSE[17,18]	16%	5%–15%		Gastric bleeding, nausea, vomiting, pain
DBJL[19,20]		14.6%–18.9%	12%[a]	Nausea, vomiting, pain, obstruction, hepatic abscess (rare)
Aspire[21]		12.1%		Bleeding, infection, ulceration, indigestion, nausea, vomiting

[a] n dropped from 44 in original study to 15 at 4 year (2 year post explant).

and phentermine topiramate in bariatric surgery patients.[28–30] It is especially useful in patients with binge eating patterns, which can be common after bariatric surgery and EBT. A prospective study by Zilberstein and colleagues of 16 patients who underwent adjustable gastric banding (AGB) with post-operative binge eating behaviors found increase in EBWL from 20.9% to 34.1% after augmentation with topiramate.[31] A retrospective study by Schwartz colleagues was performed in patients who underwent either Roux-en-Y gastric bypass (RYGB) or LSG with phentermine or phentermine-topiramate lost 12% to 13% of excess body weight after 90 days of use.[30] Lastly, a study of patients undergoing LSG with BMI greater than 50 were assessed to see if peri- and post-operative use of phentermine-topiramate would improve weight loss outcomes. Patients were compared to historic controls. This study showed the mean BMI 2 years after LSG was 33.8 for patients on phentermine-topiramate versus 42 for historic controls.[32]

Orlistat has recently fallen out of favor due to poorer efficacy and malabsorption side effects. However, this medication is cheap and found over the counter so still has some utility for weight loss. It works via inhibition of gastric and pancreatic lipases causing poor fat absorption. This should be used very cautiously for patients at risk for malabsorption such as RYGB. A study by Zoss and colleagues on orlistat in AGB patients showed significant weight loss of 8 kg during an 8 month follow-up.[33]

Naltrexone-bupropion is also approved for weight loss. It is contraindicated in patients with severe hypertension, opioid use, or seizure disorders. Studies show improved inhibition and ability to resist cravings,[34] thus, it is especially good for food cravings and addictive behaviors. There are no studies directly assessing its use in the post-bariatric or EBT patients.

The newest medications to undergo approval are the incretin medications–Glucagon like peptide – 1 receptor agonists (GLP-1) and gastric inhibitory polypeptides (GIPs) receptor agonists. These include liraglutide (GLP-1) specifically at the 3 mg dose, semaglutide (GLP-1) specifically at the 2.4 mg dose and the newest, approved for weight loss November of 2023, is tirzepatide (GLP-1/GIP). While liraglutide has had modest weight loss benefits on par with previously approved anti-obesity medications, semaglutide and tirzepatide show staggering results with TBWL in the 15% to 20% (**Table 2**). The most recent incretin to be studied is Retatrutide, a GLP-1/GIP/Glucagon receptor, which is currently in phase 3 trials for weight loss. Preliminary phase 2 trials are very encouraging with weight loss on par with some bariatric surgeries.

Given the popularity of incretin medications, there have been significant enthusiasm and a growing body of evidence for use of these medications in conjunction with bariatric surgery and EBT. A small study by Caroline Hoff and colleagues of ESG alone or with semaglutide found significantly more weight loss in the semaglutide group that was on par with expected weight loss of an LSG.[39] A retrospective study by Badurdeen and colleagues on liraglutide use starting 5 months after ESG showed significant improvement in TBWL at 1 year after ESG of 20.5% in ESG alone and 24.7% in ESG plus liraglutide group.[13]

More limited data are available on the use of incretin medications in combination with IGB. Mosli and colleagues evaluated the use of liraglutide in patients treated with IGB; liraglutide was started 1 month after to balloon placement and continued until 1 month after balloon removal; they demonstrated improved weight loss with liraglutide plus IGB group over the IGB alone (18.5 vs 10.2 kg). However, after adjusting for cofounders, was no longer significant.[40] Interestingly, there was no increase in patient reported nausea, abdominal pain, heartburn, or early IGB removal in patients on liraglutide. Another study by Jense and colleagues found that 11.3% of patients undergoing IGB selected

Table 2
Summary of incretin medications in weight loss

Study	Medication	Number of Participants	Duration	Weight Loss (% TBWL)	>5% TBWL	>10% TBWL	FDA-Approved For Weight Loss
Pi-Sunyer et al,[35] 2015	Liraglutide 3.0 mg	3731	56 wk	8.0%	62.3%	33.1%	Yes at 3.0 mg
Garvey et al,[36] 2015	Liraglutide 3.0	396	56 wk	5.8%	51.8%	22.8%	Yes at 3.0 mg
Wilding et al,[24] 2021	Semaglutide 2.4 mg	1961	68 wk	14.9%	86.4%	69.1%	Yes at 2.4 mg
Jastreboff et al,[37] 2022	Tirzepatide	2539	72 wk				Yes
	5 mg			15%	85%	68.5%	
	10 mg			19.5%	89%	78.1%	
	15 mg			20.9%	91%	83.5%	
Jastreboff et al,[38] 2023	Retatrutide	338	48 wk				In phase 3 studies
	1 mg			8.7%			
	4 mg			17.1%	92%	75%	
	8 mg			22.8%	100%	91%	
	12 mg			24.2%	100%	93%	

combination therapy with an anti-obesity medication (89% chose liraglutide). Weight loss was found to be 12.6% TBWL at 12 weeks when IGB was combined with medication versus 11.6% TBWL with balloon alone.[41]

A study by Gala and colleagues looked at the real world data of patient prescribed anti-obesity medications (AOM) at any time within a year of their ESG.[42] They stratified by type GLP-1 versus non-GLP-1 AOM. After 24 months, there was no difference in TBWL between no AOM, GLP-1, and other AOMs. However, it is notable that this was a real world study and most patients prescribed AOMs were done due to weight recidivism or failure to lose weight to goal. Thus, this likely represents a positive outcome that patients who did not respond as intended to ESG could achieve intended response with addition of AOMs.

Multiple studies have been conducted on liraglutide post bariatric surgery (most commonly in RYGB or LSG), which show significant improvements in weight with liraglutide as compared with controls.[43–47] Interestingly, when compared to patients taking liraglutide who have not undergone bariatric surgery to patients on liraglutide who have undergone bariatric surgery, there was no difference in gastrointestinal side effects.[46] It is also notable that patients with prior bariatric surgery taking liraglutide versus placebo, there was also no significant increase in gastrointestinal side effects.[45] A study by Lautenbach and colleagues[48] with use of semaglutide in patients with prior RYGB or LSG with inadequate weight loss or weight regain showed 10.3% TBWL 6 months after the initiation of semaglutide. There was no difference in weight loss in patients with inadequate weight loss or weight regain or based on type of bariatric surgery (**Table 3**).

APPROACH TO COMBINATION OF PHARMACOLOGIC AND ENDOSCOPIC THERAPY

The decision to combine pharmacologic and endoscopic therapy for weight loss should be made on an individual basis with communication with the patient. It is important to understand patient goals and medical comorbidities when deciding on the ideal approach. The physician and patient need to be realistic about the expected weight loss with EBTs along with the side effects and indefinite use expected for pharmacologic therapy. Multiple studies have shown the additive effects of medications with bariatric surgery, which can be extrapolated to EBTs, as well as a few studies on the use of pharmacologic agents to augment EBTs. Various degrees of weight loss are associated with improvement in a variety of medical co-morbidities (**Table 4**). Pharmacologic therapy can be added for increased weight loss.

Timing and selection of pharmacologic therapy should be based on patients' comorbidities and desired weight loss. Both the total amount of weight loss and other indications or side effects of medications can be used to determine which medications are best in augmentation for each individual patient (**Table 5**).

If EBT alone is not expected to allow patient to reach desired weight loss, it may be prudent to plan augmentation in the peri-procedure period.[32,40] Alternatively, studies in bariatric surgery patients have found that augmentation at weight plateau led to more successful outcomes then when used after weight recidivism.[61–63] Therefore, it is important to assess patients throughout their weight loss journey and offer pharmacologic therapy at plateau if they have not reached desired weight loss rather than just after weight regain. Medications need to be timed to avoid excessive side effects. The incretin medications are known to cause gastrointestinal side effects and may need to consider holding or not starting these medications until 4 to 6 weeks after EBTs that are also expected to cause negative gastrointestinal side effects.[40] However, overall, these medications appear to be just as well-tolerated in the bariatric surgery

Table 3
Review of studies on pharmacotherapy augmentation after bariatric surgery or endoscopic bariatric procedures

Study	Bariatric Procedure	Medication	Number of Participants	Duration	Additional Weight Loss (kg)	Additional Weight Loss TWBL vs EBWL
Schwartz et al,[30] 2016	RYGB or LABG	Phentermine Phentermine-topiramate	52 13	90 d	6.35 3.81	12.8%EBWL 12.9% EBWL
Zoss et al,[33] 2002	LABG	Orlistat 120 mg TID	38	8 mn	8	
Wharton et al,[44] 2019	RYGB, LABG, LSG	Liraglutide 3 mg	117	1 year	6.3	5.5% TBWL
Suliman et al,[46] 2019	Any bariatric surgery	Liraglutide	188	16 wk	6	6.1% TBWL
Pajecki et al,[47] 2013	Any Bariatric surgery	Liraglutide	15	8–28 wk	7.5	
Gazda et al,[49] 2021	Any bariatric surgery	Any GLP-1	207	9 mn		6.9% TBWL
Jensen et al,[50] 2023	Any bariatric surgery	Liraglutide Semaglutide	50	6 mn		7.3% TBWL 9.8% TBWL
Lautenbach et al,[48] 2022	RYGB or LSG	Semaglutide	44	6 mn		10.3% TBWL
Mosli et al,[40] 2017	IGB	Liraglutide	108	12 mn	8 kg[a]	
Mehta et al,[51] 2023	IGB	Any anti-obesity medication (AOM)	102	12		2.9% TBWL
Badurdeen et al,[13] 2021	ESG	Liraglutide	52	12 mn		4% TBWL
Gala et al,[42] 2024	ESG	Any AOM	1506	24 mn		No difference

[a] After look at cofounding variables, no difference in mean weight loss between participants who used liraglutide.

Table 4
Weight loss required for disease remission or clinically significant improvement[52–55]

Disease	%TBWL
Diabetes prevention	2%–5%
Hypertriglyceridemia	2%–5%
Elevated systolic blood pressure	2%–5%
Polycystic ovarian syndrome	2%–10%
Metabolic Associated Steatotic Liver Disease	5%
Established diabetes	5%–10%
Elevated diastolic blood pressure	5%–10%
Hyperlipidemia	5%–10%
Urinary incontinence	5%–10%
Sexual dysfunction	5%–10%
Obstructive sleep apnea	10%
Metabolic liver disease – fibrosis regression	10%
Knee osteoarthritis	10%–20%

population as the non-bariatric surgery population.[45,46] Further, the specific class of medications should be picked based on patient comorbidities, eating patterns, and side effect profile. Overall, the combination of pharmacologic and endoscopic treatment for obesity can be very successful and provide not only desired weight loss for patients but also improve or ameliorate medical co-morbidities.

Multiple pharmacologic agents are available for diabetes including both FDA and non-FDA approved medications for weight loss. Combining a pharmacologic therapy for diabetes that also causes weight loss is a widely accepted augmentation strategy to both bariatric surgeries and EBTs.[13,63] GLP-1 agonists Liraglutide and Semaglutide are both approved for weight loss and diabetes although at different doses. However, weight loss is seen even at the approved diabetic doses to a lesser extent.[22] Tirzepatide is now approved in both diabetes and obesity. Other diabetic medications are available that are not FDA-approved for obesity but show modest weight loss. Both metformin and sodium-glucose co-transporter 2 (SGLT-2) inhibitors lead to very modest weight loss but are approved for diabetes. SGLT-2 inhibitors are also approved for cardiovascular disease.[64–66] While these medications have less weight loss efficacy, their price and side effect profile may be ideal for some patients.

Naltrexone-bupropion can be used in patients with mild depression, binge eating disorder, and alcohol and nicotine abuse. Its weight loss mechanism is thought to be due to decreasing food cravings.[67] This can be especially helpful in patients with high oral intake due to cravings, which can cause failure of adequate weight loss in ESG, sleeve gastrectomy, and gastric bypass due to dilation of the gastric sleeve or pouch. Naltrexone is an opioid receptor antagonist and should not be used in the direct peri-procedural period if opioids are expected to be needed for pain control.

Phentermine-topiramate can be used for patients with headaches but also the topiramate component has been shown to be helpful in binge eating disorder.[68] Topiramate; however, is not FDA-approved for binge eating disorder, and use with this indication would be considered off-label. Studies in sleeve gastrectomy have shown that patients with binge eating disorders or loss of control of eating often do worse post operation including less weight loss.[69] This can be extrapolated to patients with EBTs such as ESG. Another study of topiramate use in patient is laparoscopic

Table 5
Review of currently Food and Drug Administration-approved medications for weight loss

	% TBWL	% Achieving 5% TWBL [56]	% Achieving 10% TBWL [56]	Approved Conditions Other than Obesity	Side Effects	Contraindications
Phentermine[57]	7.4	96[a]	63[a]		Tachycardia, hypertension, tremor, anxiety, dry mouth, constipation	Cardiovascular disease, hyperthyroidism, Gluacoma
Phentermine-Topiramate[58]	9.8	67–70	47–48	Migraines, alcohol abuse	As above + insomnia, cognitive side effects	As above + nephrolithiasis, pregnancy
Orlistat[59]	9.6[b]	44–51	14–29		Abdominal pain, steatorrhea	Malabsorptive conditions
Naltrexone-buproprion[60]	6.1	45–51	19–28	Alcohol use disorder, nicotine use, mild depression	Headache, nausea, vomiting, constipation	Use of opioid narcotics, seizures (and conditions that lower seizure threshold)
Liraglutide (3 mg)[35,36,56]	8.4	50–73	25–37	Diabetes, cardiovascular risk reduction	Nausea, vomiting, diarrhea, constipation, abdominal pain	MEN-2, medullary thyroid cancer, pancreatitis, gastroparesis
Semaglutide (2.4 mg)	14.9	86.4	69.1	As above	As above	As above
Tirzepatide (15 mg)[37]	20.9	91	83.9	Diabetes	Nausea, vomiting, constipation, abdominal pain	MEN-2, medullary thyroid cancer

[a] High placebo weight loss in this study as well with > 20% with 5% or more TBWL.
[b] Only 3% TBWL in placebo controlled trials.

AGB with inadequate weight loss and binge eating patterns that were prescribed topiramate had improved EBWL from 20.9% to 34.1%.[31] Patients should be screened for eating disorders such as binge eating disorders prior to EBT but even in patients who have already undergone EBT, ongoing screening for eating disorders should be done and treated if appropriate.

SUMMARY

EBT has now been firmly established as a safe and effective treatment for patients with obesity. While EBT still lag surgery with regard to weight loss efficacy the combination of EBT with AOMs holds significant promise for obtaining weight loss comparably to that seen with weight loss surgery and can be used for patients with inadequate weight loss after EBT or weight regain after EBT. Moreover, EBT may help to reduce the typical weight regain, which occurs in patients who have lost weight with AOMs and wish to wean off medications.

CLINICS CARE POINTS

- The combination of endoscopic and pharmacologic interventions for obesity can provide greater weight loss then ether intervention alone, providing weight loss on par with surgical interventions.
- Understanding the pharmacology and side effect profile of anti-obesity medications is critical to maximizing effectiveness, minimize side effects and avoiding premature discontinuation.

DISCLOSURE

The authors have nothing to disclosures.

REFERENCES

1. ASGE Bariatric Endoscopy Task Force, Sullivan S, Kumar N, et al. ASGE position statement on endoscopic bariatric therapies in clinical practice. Gastrointest Endosc 2015;82(5):767–72.
2. Ibrahim Mohamed BK, Barajas-Gamboa JS, Rodriguez J. Endoscopic Bariatric Therapies: Current Status and Future Perspectives. Jsls 2022;26(1).
3. Goyal H, Kopel J, Perisetti A, et al. Endobariatric procedures for obesity: clinical indications and available options. Therapeutic Advances in Gastrointestinal Endoscopy 2021;14. 2631774520984627.
4. Kim SH, Chun HJ, Choi HS, et al. Current status of intragastric balloon for obesity treatment. World J Gastroenterol 2016;22(24):5495–504.
5. Kozłowska-Petriczko K, Pawlak KM, Wojciechowska K, et al. The Efficacy Comparison of Endoscopic Bariatric Therapies: 6-Month Versus 12-Month Intragastric Balloon Versus Endoscopic Sleeve Gastroplasty. Obes Surg 2023;33(2):498–505.
6. Shah R, Davitkov P, Abu Dayyeh BK, et al. AGA Technical Review on Intragastric Balloons in the Management of Obesity. Gastroenterology 2021;160(5):1811–30.
7. Ashrafian H, Monnich M, Braby TS, et al. Intragastric balloon outcomes in superobesity: a 16-year city center hospital series. Surg Obes Relat Dis 2018;14(11):1691–9.
8. Kotzampassi K, Grosomanidis V, Papakostas P, et al. 500 intragastric balloons: what happens 5 years thereafter? Obes Surg 2012;22(6):896–903.

9. Abu Dayyeh BK, Acosta A, Camilleri M, et al. Endoscopic Sleeve Gastroplasty Alters Gastric Physiology and Induces Loss of Body Weight in Obese Individuals. Clin Gastroenterol Hepatol 2017;15(1):37–43.e1.
10. Abu Dayyeh BK, Bazerbachi F, Vargas EJ, et al. Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. Lancet 2022;400(10350):441–51.
11. Hedjoudje A, Abu Dayyeh BK, Cheskin LJ, et al. Efficacy and Safety of Endoscopic Sleeve Gastroplasty: A Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol 2020;18(5):1043–53.e4.
12. Abu Dayyeh BK, Acosta A, Camilleri M, et al. Endoscopic Sleeve Gastroplasty Alters Gastric Physiology and Induces Loss of Body Weight in Obese Individuals. Clin Gastroenterol Hepatol 2017;15(1):37–43.e1.
13. Badurdeen D, Hoff AC, Hedjoudje A, et al. Endoscopic sleeve gastroplasty plus liraglutide versus endoscopic sleeve gastroplasty alone for weight loss. Gastrointest Endosc 2021;93(6):1316–24.e1.
14. Storm AC, Abu Dayyeh BK, Topazian M. Endobariatrics: A Primer. Clin Gastroenterol Hepatol 2018;16(11):1701–4.
15. Sharaiha RZ, Hajifathalian K, Kumar R, et al. Five-Year Outcomes of Endoscopic Sleeve Gastroplasty for the Treatment of Obesity. Clin Gastroenterol Hepatol 2021;19(5):1051–7.e2.
16. Bhandari M, Kosta S, Reddy M, et al. Four-year outcomes for endoscopic sleeve gastroplasty from a single centre in India. J Minim Access Surg 2023;19(1):101–6.
17. Sullivan S, Swain JM, Woodman G, et al. Randomized sham-controlled trial evaluating efficacy and safety of endoscopic gastric plication for primary obesity: The ESSENTIAL trial. Obesity (Silver Spring) 2017;25(2):294–301.
18. Lopez-Nava G, Asokkumar R, Turró Arau R, et al. Modified primary obesity surgery endoluminal (POSE-2) procedure for the treatment of obesity. VideoGIE 2020;5(3):91–3.
19. Betzel B, Cooiman MI, Aarts EO, et al. Clinical follow-up on weight loss, glycemic control, and safety aspects of 24 months of duodenal-jejunal bypass liner implantation. Surg Endosc 2020;34(1):209–15.
20. Jirapinyo P, Haas AV, Thompson CC. Effect of the Duodenal-Jejunal Bypass Liner on Glycemic Control in Patients With Type 2 Diabetes With Obesity: A Meta-analysis With Secondary Analysis on Weight Loss and Hormonal Changes. Diabetes Care 2018;41(5):1106–15.
21. 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.
22. Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metabol 2015;100(2):342–62.
23. Wilding JPH, Batterham RL, Davies M, et al. Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. Diabetes Obes Metabol 2022;24(8):1553–64.
24. Wilding JPH, Batterham RL, Calanna S, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med 2021;384(11):989–1002.
25. Khera R, Murad MH, Chandar AK, et al. Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events: A Systematic Review and Meta-analysis. JAMA 2016;315(22):2424–34.

26. Gasoyan H, Pfoh ER, Schulte R, et al. Early- and later-stage persistence with antiobesity medications: A retrospective cohort study. Obesity 2024;32(3):486–93.
27. Chakhtoura M, Haber R, Ghezzawi M, et al. Pharmacotherapy of obesity: an update on the available medications and drugs under investigation. eClinicalMedicine 2023;58.
28. Lucas E, Simmons O, Tchang B, et al. Pharmacologic management of weight regain following bariatric surgery. Front Endocrinol (Lausanne) 2022;13:1043595.
29. Edgerton C, Mehta M, Mou D, et al. Patterns of Weight Loss Medication Utilization and Outcomes Following Bariatric Surgery. J Gastrointest Surg 2021;25(2):369–77.
30. Schwartz J, Chaudhry UI, Suzo A, et al. Pharmacotherapy in Conjunction with a Diet and Exercise Program for the Treatment of Weight Recidivism or Weight Loss Plateau Post-bariatric Surgery: a Retrospective Review. Obes Surg 2016;26(2):452–8.
31. Zilberstein B, Pajecki D, Garcia de Brito AC, et al. Topiramate after adjustable gastric banding in patients with binge eating and difficulty losing weight. Obes Surg 2004;14(6):802–5.
32. Ard JD, Beavers DP, Hale E, et al. Use of phentermine-topiramate extended release in combination with sleeve gastrectomy in patients with BMI 50 kg/m(2) or more. Surg Obes Relat Dis 2019;15(7):1039–43.
33. Zoss I, Piec G, Horber FF. Impact of orlistat therapy on weight reduction in morbidly obese patients after implantation of the Swedish adjustable gastric band. Obes Surg 2002;12(1):113–7.
34. Roberts CA, Christiansen P, Halford JCG. Pharmaceutical approaches to weight management: behavioural mechanisms of action. Current Opinion in Physiology 2019;12:26–32.
35. 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.
36. Garvey WT, Birkenfeld AL, Dicker D, et al. Efficacy and safety of Liraglutide 3.0 mg in individuals with overweight or obesity and type 2 diabetes treated with basal insulin: the SCALE insulin randomized controlled trial. Diabetes Care 2020;43(5):1085–93.
37. Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med 2022;387(3):205–16.
38. Jastreboff AM, Kaplan LM, Frías JP, et al. Triple–Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial. N Engl J Med 2023;389(6):514–26.
39. Carolina Hoff A, Barrichello S, Badurdeen D, et al. ID: 3492486 Semaglutide in association to endoscopic sleeve gastroplasty: taking endoscopic batriatric procedures outcomes to the next level. Gastrointest Endosc 2021;93(6):AB6–7.
40. Mosli MM, Elyas M. *Does combining liraglutide with intragastric balloon insertion improve sustained weight reduction?* Saudi. J Gastroenterol 2017;23(2):117–22.
41. Jense MTF, Palm-Meinders IH, Sanders B, et al. The Swallowable Intragastric Balloon Combined with Lifestyle Coaching: Short-Term Results of a Safe and Effective Weight Loss Treatment for People Living with Overweight and Obesity. Obes Surg 2023;33(6):1668–75.
42. Gala K, Ghusn W, Brunaldi V, et al. Outcomes of concomitant antiobesity medication use with endoscopic sleeve gastroplasty in clinical US settings. Obesity Pillars 2024;11:100112.
43. Miras AD, Pérez-Pevida B, Aldhwayan M, et al. Adjunctive liraglutide treatment in patients with persistent or recurrent type 2 diabetes after metabolic surgery

(GRAVITAS): a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol 2019;7(7):549–59.
44. Wharton S, Kuk JL, Luszczynski M, et al. Liraglutide 3.0 mg for the management of insufficient weight loss or excessive weight regain post-bariatric surgery. Clin Obes 2019;9(4):e12323.
45. Thakur U, Bhansali A, Gupta R, et al. Liraglutide Augments Weight Loss After Laparoscopic Sleeve Gastrectomy: a Randomised, Double-Blind, Placebo-Control Study. Obes Surg 2021;31(1):84–92.
46. Suliman M, Buckley A, Al Tikriti A, et al. Routine clinical use of liraglutide 3 mg for the treatment of obesity: Outcomes in non-surgical and bariatric surgery patients. Diabetes Obes Metabol 2019;21(6):1498–501.
47. Pajecki D, Halpern A, Cercato C, et al. Short-term use of liraglutide in the management of patients with weight regain after bariatric surgery. Rev Col Bras Cir 2013;40(3):191–5.
48. Lautenbach A, Wernecke M, Huber TB, et al. The Potential of Semaglutide Once-Weekly in Patients Without Type 2 Diabetes with Weight Regain or Insufficient Weight Loss After Bariatric Surgery-a Retrospective Analysis. Obes Surg 2022;32(10):3280–8.
49. Gazda CL, Clark JD, Lingvay I, et al. Pharmacotherapies for Post-Bariatric Weight Regain: Real-World Comparative Outcomes. Obesity (Silver Spring) 2021;29(5):829–36.
50. Jensen AB, Renström F, Aczél S, et al. Efficacy of the Glucagon-Like Peptide-1 Receptor Agonists Liraglutide and Semaglutide for the Treatment of Weight Regain After Bariatric surgery: a Retrospective Observational Study. Obes Surg 2023;33(4):1017–25.
51. Mehta A, Shah S, Dawod E, et al. Impact of Adjunctive Pharmacotherapy With Intragastric Balloons for the Treatment of Obesity. The American Surgeon™ 2023;89(4):707–13.
52. Ryan DH, Yockey SR. Weight Loss and Improvement in Comorbidity: Differences at 5%, 10%, 15%, and Over. Curr Obes Rep 2017;6(2):187–94.
53. Wing RR, Lang W, Wadden TA, et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. Diabetes Care 2011;34(7):1481–6.
54. Glass LM, Dickson RC, Anderson JC, et al. Total body weight loss of $\geq$ 10 % is associated with improved hepatic fibrosis in patients with nonalcoholic steatohepatitis. Dig Dis Sci 2015;60(4):1024–30.
55. Messier SP, Resnik AE, Beavers DP, et al. Intentional Weight Loss in Overweight and Obese Patients With Knee Osteoarthritis: Is More Better? Arthritis Care Res (Hoboken) 2018;70(11):1569–75.
56. Ard J, Fitch A, Fruh S, et al. Weight Loss and Maintenance Related to the Mechanism of Action of Glucagon-Like Peptide 1 Receptor Agonists. Adv Ther 2021;38(6):2821–39.
57. Li Z, Hong K, Yip I, et al. Body weight loss with phentermine alone versus phentermine and fenfluramine with very-low-calorie diet in an outpatient obesity management program: a retrospective study. Curr Ther Res Clin Exp 2003;64(7):447–60.
58. Allison DB, Gadde KM, Garvey WT, et al. Controlled-release phentermine/topiramate in severely obese adults: a randomized controlled trial (EQUIP). Obesity (Silver Spring) 2012;20(2):330–42.
59. Drew BS, Dixon AF, Dixon JB. Obesity management: update on orlistat. Vasc Health Risk Manag 2007;3(6):817–21.

60. Greenway F, Fujioka K, Plodkowski RA, et al. Effect of naltrexone plus bupropion on weight loss in overweight and obese adults (COR-I): A multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2010;376:595–605.
61. Toth AT, Gomez G, Shukla AP, et al. Weight Loss Medications in Young Adults after Bariatric Surgery for Weight Regain or Inadequate Weight Loss: A Multi-Center Study. Children (Basel) 2018;5(9).
62. Stanford FC, Toth AT, Shukla AP, et al. Weight Loss Medications in Older Adults After Bariatric Surgery for Weight Regain or Inadequate Weight Loss: A Multicenter Study. Bariatr Surg Pract Patient Care 2018;13(4):171–8.
63. Stanford FC, Alfaris N, Gomez G, et al. The utility of weight loss medications after bariatric surgery for weight regain or inadequate weight loss: A multi-center study. Surg Obes Relat Dis 2017;13(3):491–500.
64. Pereira MJ, Eriksson JW. Emerging Role of SGLT-2 Inhibitors for the Treatment of Obesity. Drugs 2019;79(3):219–30.
65. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2022;145(18):e895–1032.
66. Yerevanian A, Soukas AA. Metformin: Mechanisms in Human Obesity and Weight Loss. Curr Obes Rep 2019;8(2):156–64.
67. Wang GJ, Zhao J, Tomasi D, et al. Effect of combined naltrexone and bupropion therapy on the brain's functional connectivity. Int J Obes (Lond) 2018;42(11):1890–9.
68. Guerdjikova AI, Williams S, Blom TJ, et al. Combination Phentermine-Topiramate Extended Release for the Treatment of Binge Eating Disorder: An Open-Label, Prospective Study. Innov Clin Neurosci 2018;15(5–6):17–21.
69. Anbara T. The impacts of eating disorders on sleeve gastrectomy outcomes. Surgery in Practice and Science 2023;13:100165.