Review

The role of bariatric metabolic endoscopy in 2026 and beyond

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ABSTRACT

The global burden of obesity continues to rise, with over one billion people affected worldwide. Obesity is a chronic, complex disease whereby excess adiposity leads to adverse health outcomes, and the associated metabolic dysfunction is closely linked to type 2 diabetes mellitus and other cardiometabolic complications. Incretin-based pharmacotherapies have transformed obesity management, but uncertainties remain regarding long-term durability, treatment adherence, weight regain after discontinuation and healthcare affordability. These challenges highlight the need for additional minimally invasive treatment strategies that bridge the gap between pharmacological interventions and bariatric surgery. Metabolic and bariatric endoscopy has emerged as an intermediary therapeutic domain, aiming to modulate gastrointestinal anatomy, nutrient flow and metabolic signalling through a range of endoscopic procedures and devices that are currently available or undergoing investigation. These approaches broadly target different components of the gut–metabolic axis, including gastric, small bowel and pancreatic pathways. In this narrative review, we summarise the current evidence across gastric-directed, small bowel-directed and pancreatic-directed endoscopic therapies and discuss their evolving position within the wider obesity treatment landscape. We then consider the trajectory of the field in the context of highly effective incretin-based pharmacotherapies and outline its potential role in the future of obesity care.

KEY MESSAGES

⇒ Bariatric metabolic endoscopy has emerged as a minimally invasive intermediary therapy between pharmacological treatment and bariatric surgery for the management of obesity and related metabolic disease.
⇒ Gastric-directed procedures such as endoscopic sleeve gastroplasty achieve clinically meaningful weight loss with favourable safety profiles and are increasingly incorporated into international obesity management guidelines.
⇒ Emerging gastric technologies, including automated gastroplasty systems, gastric fundal mucosal ablation and hybrid devices, aim to combine mechanical restriction with hormonal modulation but remain early in clinical evaluation.
⇒ Revisional endoscopic therapies, including transoral outlet reduction and revisional gastroplasty, offer strategies to manage weight regain after bariatric surgery with modest but durable weight loss.
⇒ Small bowel-directed interventions such as duodenal mucosal ablation and intestinal bypass devices target proximal intestinal signalling to improve glycaemic control and metabolic regulation.
⇒ In the era of effective incretin pharmacotherapy, bariatric metabolic endoscopy will likely complement medical therapy through three strategies: efficacy synergy, response rescue and compensation control.

INTRODUCTION

Our understanding and management of patients living with obesity and related diseases is changing rapidly amid a surging global burden with over one billion people now living with obesity worldwide.[1] Recent expert consensus has emphasised that obesity should be regarded as a disease of dysfunctional adipose tissue and impaired metabolic regulation, rather than solely a weight-based classification.[2] Within this framework, type 2 diabetes mellitus (T2DM) represents one of the most clinically significant downstream manifestations of adiposity-related organ dysfunction, with the vast majority of individuals with

T2DM meeting conventional body mass index (BMI) criteria for overweight or obesity. This has led to the rapid integration of glucagon-like peptide-1 receptor agonist (GLP-1RA)-based therapies for the treatment of obesity and related diseases.[3] Originally developed for glycaemic control, these agents are now central to the management of both obesity and T2DM, reflecting the close pathophysiological relationship between excess adiposity and disordered glucose metabolism.[4] The increasing array of these incretin-based pharmacotherapies has fundamentally reshaped the therapeutic landscape of obesity management. However, uncertainties remain regarding long-term treatment duration, real-world persistence, weight regain following discontinuation and health-system affordability.[5–8] Furthermore, pharmacotherapy alone is unlikely to address the full spectrum of disease burden, and there remains a need for intermediate, minimally invasive interventions that not only bridge the gap between lifestyle/drug interventions and bariatric surgery, but also offer patients a non-pharmacological alternative for weight reduction and/or glycaemic control.

Against this backdrop, the field of metabolic and bariatric endoscopy has expanded rapidly and positioned itself as an intermediary therapeutic domain.[9] Rather than replicating surgery in a less invasive format, contemporary endoscopic interventions are increasingly conceptualised as targeted modulators of gastrointestinal anatomy, nutrient flow and mucosal signalling through a variety of gastric-directed and small bowel-directed procedures using a range of novel endoscopic devices.[9 10] Bariatric endoscopic procedures are primarily aimed at inducing weight loss, whereas metabolic endoscopic procedures are aimed at improvements in glycaemic control independent of weight. However, as new procedures and indications for endoscopic approaches are emerging, this traditional distinction becomes less valid. Instead, current and investigational approaches can be best understood by their principal site and mechanism of action: gastric remodelling procedures that alter volume and motility, temporary intragastric space-occupying devices, proximal small-bowel mucosal interventions designed to modify nutrient sensing, endoluminal bypass systems that alter nutrient exposure, revisional techniques for postsurgical weight recurrence, and more recently, pancreatic-directed therapies to induce endogenous GLP-1 release.

To date, several consensus and guideline documents have been released by professional societies across the world to provide a position and/or recommendation(s) on the use of endoscopic interventions for the management of obesity. In 2024, the American Society of Gastrointestinal Endoscopy (ASGE) in collaboration with the European Society of Gastrointestinal Endoscopy (ESGE) provided the first guideline on the use of endoscopic procedures for the management of obesity, outlining recommendations for patient selection, procedural techniques and postprocedural care.[11] Despite growing international interest, the adoption of these endoscopic interventions has varied significantly across healthcare systems. In countries such as the USA, Brazil, India and parts of Europe (eg, Italy), endoscopic procedures have been more rapidly integrated into clinical practice, supported by structured pathways, reimbursement, commercial availability and increasing procedural experience. In the UK, the broad adoption of metabolic and bariatric endoscopic therapies has been comparatively limited, although with the recent endorsement of endoscopic gastroplasty by the National Institute for Health and Care Excellence (NICE).[12] As clinical evidence accumulates and international guidance begins to formalise standards for patient selection and governance, the role of these procedures within multidisciplinary obesity and diabetic care pathways requires careful evaluation. The central question is no longer whether endoscopic therapies can induce weight loss or improvements in glycaemic control, but how they should be positioned within an increasingly complex therapeutic ecosystem that now includes highly effective pharmacological agents and established surgical options. As the therapeutic landscape expands, the emphasis is shifting beyond demonstration of safety and efficacy towards considerations of cost-effectiveness, combination strategies, durability of response, and how best to define treatment success in modern obesity care.

In this narrative review, we look at the current state of metabolic bariatric endoscopy and highlight the most transformative emerging therapies (table 1). We then consider the trajectory of the field in the context of highly effective incretin-based pharmacotherapies and outline its potential role in the future of obesity care.

GASTRIC-DIRECTED THERAPIES

Gastroplasty

Gastroplasty refers to a surgical intervention designed for the management of obesity, carried out either through conventional surgical techniques or via endoscopic approaches. These methods involve full-thickness gastric tissue plication or suture placement along the greater curvature of the stomach, thereby reducing gastric capacity, limiting accommodation and inducing early satiety.[13] Traditional gastroplasty refers to restrictive bariatric surgical procedures that achieve weight loss primarily by reducing functional gastric capacity, thereby limiting oral intake and promoting early satiety.[14] These procedures do not involve intestinal bypass and therefore preserve normal nutrient absorption, distinguishing them from malabsorptive or mixed bariatric operations.

Historically, vertical banded gastroplasty (VBG), first described by Mason, represented the prototypical form of traditional gastroplasty, which involves creation of a small proximal gastric pouch along the

Table 1 A summary of modern endoscopic metabolic and bariatric procedures

Procedure	Device (company)	Description	Key trial(s)	Dev. phase	CE mark	Efficacy	Safety (SAE)	Combination strategies
Gastric-directed therapies								
↳ Endoscopic gastroplasty								
ESG	OverStitch Sx (Boston Scientific)	Full thickness suturing (U or Z-pattern)	MERIT RCT (2022)	Routine use	Yes	TBWL: 13%–18% over 6–60 months	~2%	Combination with GLP-1RA under investigation, timing of introduction unclear
POSE-1	Incisionless operating platform (USGI Medical)	Full thickness plications of gastric fundus and distal body	MILEPOST RCT (2017) ESSENTIAL RCT (2017)	No longer used	Yes	TBWL: 4.8% mean difference versus control over 12 months	0%–5%	Never evaluated
POSE-2	Incisionless operating platform (USGI Medical)	Full thickness plications of the gastric body sparing the fundus	Observational (2022)	Routine use	Yes	TBWL: 13.2%–17.5% over 12 months	0%–3%	Combination with GLP-1RA under investigation, timing of introduction unclear
Endomina	Endoscopic triangulation platform (EndoTools Therapeutics)	Full-thickness plication targeting distal stomach	RCT (2021)	Routine use	Yes	TBWL: up to 11% over 6–12 months	0%	Not yet evaluated
Automated gastroplasty	EndoZip (Nitinotes surgical)	Automated endoscopic suturing system producing standardised, operator-independent gastric plications	Early clinical evaluation (2025) EASE RCT (pending)	Under investigation	Yes	TBWL: up to 13.2% at 12 months	0%	Not yet evaluated
↳ GFMA								
GFMA	Hybrid Argon Plasma Coagulation (Erbe)	Selective ablation of ghrelin-producing enteroendocrine cells in the gastric fundus	Early feasibility (2024) MAINTAIN RCT (pending)	Under investigation	No (off-label use of CE-marked APC system)	TBWL: 7.7% at 6 months	No current safety signal	Evaluating benefit in combination with ESG. Evaluating benefit as weight management strategy after stopping GLP-1RA therapy
↳ Hybrid gastric/small bowel device—preclinical								
Hybrid bypass device	ForePass (Keyron)	Channelled intragastric balloon with integrated duodenal–jejunal bypass sleeve	–	Preclinical	No	No human data		Preclinical data versus semaglutide
↳ Post-RYGB: TORe								
TORe	OverStitch, IOP, APC (Boston Scientific, USGI medical, ERBE)	Endoscopic ablation (APC) with or without suturing or plication to narrow a dilated gastrojejunal anastomosis after RYGB	RESTORe RCT (2013)	Routine use	No (performed using CE-marked devices)	TBWL: 3.3%–8.1% over 6–60 months	0%–1%	Evaluating benefit of sequential GLP-1RA therapy
↳ Postsleeve gastrectomy: revisional ESG								
Revisional gastroplasty	Overstitch (Boston Scientific)	Full thickness endoscopic suturing of a dilated gastric sleeve or failed/dilated endoscopic gastroplasty to induce gastric restriction	Observational (2025)	Routine use (selected centres)	Yes	TBWL: up to 12.6% over 24 months	0%–1.2%	Evaluating revisional ESG versus GLP-1RA for weight recidivism
Small bowel-directed therapies								
↳ Small intestinal ablation								

Continued

Table 1 Continued

Procedure	Device (company)	Description	Key trial(s)	Dev. phase	CE mark	Efficacy	Safety (SAE)	Combination strategies
DMR	REVITA (Fractyl Laboratories)	Over-the-guidewire balloon-based hydrothermal ablation of the postampullary duodenal mucosa	REVITA-2 RCT (2022) INSPIRE (2023) REVEAL-1 (pending) REMAIN-1 (pending)	Under investigation	Yes	HbA1c: reduction by 0.8% up to 24 months	2.2%–3.6%	Shown to eliminate exogenous insulin in combination with Liraglutide Evaluating benefit as weight management strategy after stopping GLP-1RA therapy
Duodenal electroporation	ReCET (Endogenex)	Over-the-guidewire pulsed electric field electroporation of the postampullary duodenal mucosa	EMINENT-1 (2025) REGENT-1 (pending) EMINENT RCT (pending)	Under investigation	No	HbA1c: reduction by 1.5% up to 12 months	0%	Exploring combination with GLP-1RA to eliminate need for exogenous insulin
DMA	RFVA (Aqua Medical)	Through-the-scope vapour-based ablation of the postampullary duodenum	STEAM-T-2DM (2025)	Under investigation	No	HbA1c: reduction by 0.7% over 6 months	0%	No current investigation
PIMA	RFVA (Aqua Medical)	Through-the-scope vapour-based ablation of the postampullary duodenum and proximal jejunum	Early feasibility STEAM-IE,(pending)	Under investigation	No	HbA1c: reduction by 1.8% at 3 months	0%	Exploring combination with GLP-1RA to eliminate need for exogenous insulin
↳ DJBL								
DJBL	Endobarrier (Morphic Medical, formerly GI Dynamics)	Impermeable fluoropolymer sleeve (60 cm) anchored fluoroscopically in the duodenum. Explanted after 9 months	ENDO Trial RCT (2025) Endobarrier diabetes RCT (2022) European DJBL Registry (2023) STEP-1 RCT (pending)	Under investigation/ routine use (selected centres)	Yes	TBWL: 5.6% versus sham at 12 months HbA1c: 0.85% versus sham at 12 months	9.0%	No current investigation
↳ Magnetic compression duodeno-ileal diversion								
Magnetic duodeno-ileal anastomosis	MagDI System (GT Metabolic Solutions)	Hybrid endo-laparoscopic magnetic compression system creating duodeno-ileal diversion	Early clinical evaluation (2026)	Under investigation	No	TBWL: 10.4% up to 90 days	13.0%	No current investigation
Magnetic duodeno-ileal anastomosis	SNAP System (GI Windows)	Hybrid endo-laparoscopic magnetic compression system creating duodeno-ileal diversion	Early clinical evaluation (2025)	Under investigation	No	TBWL: 17.0%–31.0% up to 12 months	0%–21%	No current investigation
Pancreatic-directed therapies								
EUS-guided pancreatic gene therapy	Rejuva (Fractyl Laboratories)	EUS-guided delivery of AAV vector encoding GLP-1 analogue into pancreatic β cells—meal-responsive endogenous GLP-1	–	Preclinical	No	No human data		Speculative

*11 SAEs; at least 4 patients affected; exact patient-level incidence unclear.

AAV, adeno-associated virus; APC, argon plasma coagulation; CE, Conformité Européenne; DJBL, duodenal–jejunal bypass liner; DMA, duodenal mucosal ablation; DMR, duodenal mucosal resurfacing; ESG, endoscopic sleeve gastroplasty; EUS, endoscopic ultrasound; GFMA, gastric fundal mucosal ablation; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated haemoglobin; IOP, incisionless operating platform; PIMA, proximal intestinal mucosal ablation; POSE, primary obesity surgery endoluminal; RCT, randomised controlled trial; RFVA, radiofrequency vapour ablation; RYGB, Roux-en-Y gastric bypass; SAE, serious adverse event; TBWL, total body weight loss; TORe, transoral outlet reduction endoscopy.

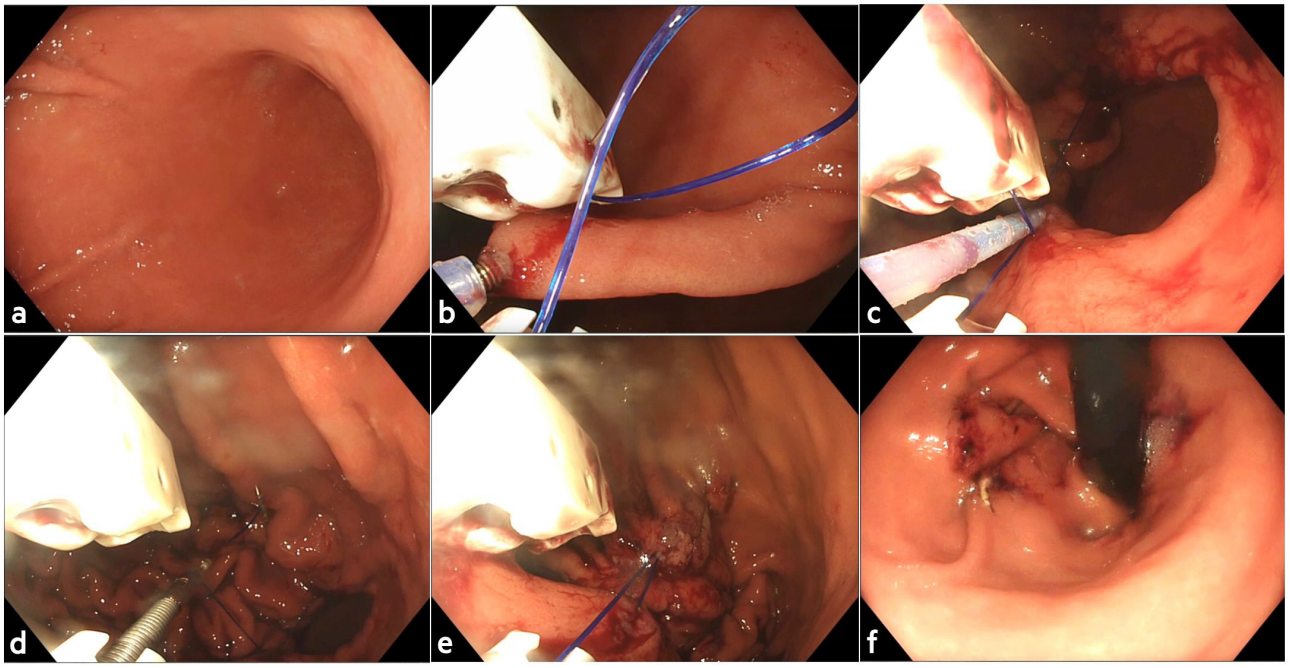

Figure 1 Endoscopic sleeve gastroplasty (ESG).

lesser curvature, reinforced with a non-adjustable band or mesh to restrict outlet size.[15] Although early weight loss outcomes were acceptable, long-term follow-up revealed significant limitations, including pouch dilation, staple line disruption, gastro-oesophageal reflux, vomiting and suboptimal durability of weight loss.[16] As a result, VBG has largely fallen out of favour in contemporary bariatric practice. Subsequent refinements in restrictive gastric surgery led to the development of procedures such as laparoscopic sleeve gastrectomy, which, although not strictly classified as gastroplasty, further emphasised the role of gastric volume reduction in obesity management. Traditional gastroplasty techniques demonstrated that mechanical restriction alone would induce meaningful short-term weight loss; however, absence of hormonal modulation and higher rates of long-term failure limited their widespread acceptance.[17] Nevertheless, traditional surgical gastroplasty remains a foundational concept in the evolution of bariatric surgery, contributing significantly to the understanding of gastric restriction as a therapeutic strategy for obesity.

Current interest in gastroplasty has shifted towards minimally invasive and endoscopic approaches that replicate the restrictive principles of traditional gastroplasty while reducing surgical morbidity (figure 1). Recent societal guidance has begun to formalise the role of endoscopic gastroplasty within obesity care pathways. In 2024, the International Federation for the Surgery of Obesity and Metabolic Disorders published an evidence-based position statement supporting the use of endoscopic sleeve gastroplasty (ESG), completed with the OverStitch device (Boston Scientific, Marlborough, Massachusetts, USA) as an effective treatment for obesity.[18] Based on pooled analyses, ESG was associated with sustained weight loss (% total body weight loss (TBWL) ~15%–18% across 6–60 months) and a low rate of serious adverse events (SAEs) (~1.25%). In the same year, NICE supported the use of ESG for patients living with obesity and a BMI ≥30 kg/m^2, and the joint ASGE/ESGE guideline recommended endoscopic gastric remodelling procedures, including ESG and related platforms, in combination with lifestyle modification for patients with BMI ≥30 kg/m^2 or ≥27 kg/m^2 with obesity-related comorbidity.[11] These recommendations remain conditional, reflecting moderate to low certainty evidence, but pooled analyses demonstrate clinically meaningful weight loss compared with lifestyle therapy alone. Collectively, these guidance documents support gastroplasty-based endoscopic therapies as a minimally invasive option within the broader spectrum of obesity management.

Automated procedures

The introduction of mechanical staplers marked a significant advancement in bariatric surgery by improving procedural precision,[19] reducing operative time, and minimising technical variability compared with hand-sewn techniques.[20] VBG represented the earliest and most widely described automated gastroplasty procedure. The automation of stapling enabled consistent pouch size and staple line integrity, contributing to early postoperative weight loss.[21] In 2025, using a similar concept of automation, a small prospective multicentre study treated 43 patients with an automated endoscopic suturing system (EndoZip, Nitinotes, Caesarea, Israel).[22] The average TBWL reached

13.2% at 12 months with more than three quarters of participants achieving a weight loss exceeding 5% alongside other reduction is biometric, biochemical and quality-of-life markers. Interim reports in another prospective, single-arm study evaluating automatic endoscopic gastroplasty showed consistent TBWL at 6 months (11.9%) with additional improvements in glycated haemoglobin (HbA1c) and ambulatory blood pressure control.[23] Procedure-related complications were uncommon and predominantly mild, with only one case of moderate bleeding managed endoscopically.

Although automated surgical gastroplasty, particularly VBG, was widely performed in the early 1990s, its use declined substantially by the mid-2010s owing to limited long-term efficacy, high complication rates and frequent need for revisional surgery.[24] Contemporary bariatric practice is now dominated by laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass (RYGB), which together account for the vast majority of procedures due to superior durability and metabolic outcomes.[24 25] Nevertheless, the core concept of standardised, operator-independent gastric restriction introduced by automated gastroplasty remains central to modern bariatric surgery and continues to inform the development of emerging endoscopic metabolic therapies.

ForePass device

The ForePass device (Keyron, London, UK) is a novel, fully endoscopic bariatric intervention developed to reproduce key metabolic effects observed with biliopancreatic diversion. The system combines a channelled intragastric balloon, which reduces functional gastric volume by approximately two-thirds, with a central conduit that directs a portion of ingested nutrients into a duodenal–jejunal bypass sleeve extending into the proximal jejunum. This configuration results in partial exclusion of the foregut and preferential delivery of nutrients to the mid-jejunum, thereby promoting early satiety while simultaneously modulating nutrient absorption and metabolic signalling without anatomical manipulation of the foregut.[26 27] Preclinical evaluation has demonstrated promising mechanistic and metabolic effects across animal models. In a 2024 study by Angelini *et al*[26] the device was implanted in a swine model for 4 weeks with eight treated animals compared with sham controls. ForePass-implanted pigs exhibited a 79% reduction in weight gain attributable to a combination of 22% lower food intake and increased faecal nutrient loss. Metabolic assessments revealed enhanced glucose disposal and insulin sensitivity alongside favourable shifts in faecal microbiota associated with metabolic health. Importantly, comprehensive pathological evaluation showed no macroscopic or microscopic injury to gastric or duodenal tissues, supporting the safety of the endoluminal configuration in this large-animal model. Complementing these findings, a 2025 study compared ForePass with semaglutide in diet-induced obese rats. ForePass produced substantially greater weight loss, with effects approximately eightfold larger than those observed with semaglutide. The device also conferred twofold greater improvements in glycaemic control and insulin sensitivity. Metabolomic profiling suggested distinct alterations in pathways related to glucose handling and energy balance, reinforcing its multifaceted metabolic impact.[27] Although these preclinical results are compelling, no peer-reviewed human outcome data have yet been published and preliminary assertions await validation in formal, controlled clinical trials.

Intragastric balloons

There is a wealth of evidence to support the use of intragastric balloons in the management of obesity, which are currently recommended as a therapeutic option by the joint ASGE/ESGE guidelines.[11] The modest weight loss, not insignificant adverse events and availability of more effective pharmacological and endoscopic options, however, has seen a fall in use, particularly within Europe. Intragastric balloons remain a valid option for patients seeking a non-pharmacological, non-surgical option, and prior small retrospective series showed the benefit of combining various intragastric balloons with liraglutide to induce a more profound degree of weight loss without increase in adverse events.[28–30] More recently, a small randomised controlled trial (RCT) (n=40) demonstrated that combining the Spatz intragastric balloon with semaglutide from month 2 significantly enhanced weight loss and reduced postremoval weight regain to 12 months.[31]

Gastric fundal mucosal ablation

Gastric fundal mucosal ablation (GFMA) is an emerging endoscopic bariatric intervention aimed at inducing weight loss through selective ablation of the gastric fundal mucosa, the primary site of ghrelin-producing enteroendocrine cells. By reducing ghrelin secretion, GFMA seeks to attenuate hunger signalling, promote early satiety and support sustained weight reduction.[32 33] The procedure is typically performed using hybrid argon plasma coagulation (HybridAPC) technology and has been explored both as a standalone therapy and as an adjunct to pharmacological or endoscopic bariatric interventions. Initial human evidence comes from early feasibility and pilot studies. Maselli *et al*[34] reported the first clinical experience with GFMA in adults using HybridAPC, demonstrating significant TBWL following selective fundal ablation with an acceptable safety profile. Although cohort size was limited, the study established technical feasibility and suggested a potential role for ghrelin-targeted endoscopic therapy in obesity management.

Further evaluation is ongoing through structured early phase trials. A phase I study conducted at the Mayo Clinic (NCT05486338; CLS-20542401) is assessing the safety and efficacy of GFMA in patients with obesity, with planned ablation of up to 70% of fundal mucosa and 6-month TBWL as the primary endpoint.[35] These results are awaited to clarify dose-response relationships and procedural tolerability. GFMA is also being explored as a weight-maintenance strategy following pharmacological weight loss. The MAINTAIN Trial (NCT06420700), a randomised controlled study currently in screening phases, is evaluating whether GFMA can prevent weight regain in patients who have achieved more than 10% weight loss with semaglutide, with follow-up extending to 12 months.[36] This approach reflects growing interest in combining endoscopic interventions with incretin-based therapies to enhance durability of weight loss. In parallel, large prospective registries are being established to assess real world outcomes. The Fundus Ablation Registry (NCT06428617) aims to enrol up to 200 patients aged 18–65 years to evaluate the safety profile, weight-loss trajectory and metabolic outcomes of GFMA. The ABLATE WEIGHT Study (NCT05578703) is investigating combined fundal ablation and ESG strategies to achieve synergistic effects on gastric restriction and hormonal modulation, although published results remain preclinical or interim.[37]

Despite its promising mechanistic rationale, GFMA remains investigational, with evidence currently limited to pilot studies, early phase trials and registries. As of January 2026, no large RCTs with long-term follow-up have been published. Further high-quality comparative studies are required to define optimal patient selection, procedural extent, durability of ghrelin suppression and its role relative to established endoscopic and pharmacological obesity therapies.

Revisional procedures

Revisional bariatric surgery has become increasingly common to address weight regain, suboptimal metabolic outcomes or complications following primary procedures. Revisional bariatric surgery accounts for approximately 5%–15% of all bariatric procedures.[38–40] The need for revision is highest after laparoscopic adjustable gastric banding (LAGB), occurring in 20%–60% of cases,[41–46] compared with 9%–17% following RYGB, and 9%–11% after sleeve gastrectomy.[41 45 47 48] Systematic reviews demonstrate that revisional bariatric surgery can achieve meaningful metabolic improvement and weight loss, although outcomes are generally modestly lower and complication rates higher than primary procedures. A meta-analysis by Koh *et al*[49] reported improvement in diabetes (92%; remission 50%), hypertension (81%; remission 33%), dyslipidaemia (37%) and obstructive sleep apnoea (86%). Similarly, Sharples *et al*[50] found excess weight loss of 44.5%–59.7% after revisional LAGB procedures with a morbidity of 13.2%, while network meta-analysis suggests RYGB and one-anastomosis gastric bypass are among the most effective revisional options following sleeve gastrectomy.[51]

In parallel with surgical approaches, revisional endoscopic therapies have emerged as minimally invasive strategies to address weight regain following bariatric surgery. The most widely studied procedure is transoral outlet reduction endoscopy, which reduces the diameter of a dilated gastrojejunal anastomosis after RYGB.[9] RCTs have demonstrated modest but significant weight loss compared with sham procedures, with TBWL of approximately 7%–10% at 6–12 months and low rates of SAEs (figure 2).[52–54] Prospective observational cohorts have also demonstrated durability of weight loss in the range of ∼8%–10% TBWL up to 2–3 years.[55 56] Revisional endoscopic gastroplasty has also been explored following sleeve gastrectomy or prior endoscopic gastroplasty to restore gastric restriction. Although evidence is limited to observational cohorts, these studies report TBWL of approximately 13%–14% at 6–12 months with very low reported SAE rates.[57–59] Collectively, these findings suggest that revisional endoscopic therapies may provide a safe and effective intermediary option between pharmacotherapy and revisional bariatric surgery in selected patients with weight regain.

SMALL BOWEL-DIRECTED THERAPIES

Bariatric surgery is the most effective intervention for sustained weight loss and glycaemic control.[60] While initially conceived as a restrictive or malabsorptive procedure, its profound metabolic effects are now recognised to extend beyond caloric restriction alone. After RYGB, improvements in glycaemic control occur early, often before significant weight loss, suggesting weight-independent mechanisms.[61 62] Surgical exclusion enhances GLP-1 secretion, improves β cell function, suppresses hepatic glucose production and increases insulin sensitivity.[63–65] Altered bile acid signalling via FXR-FGF19 and TGR5 pathways further contribute to improved glucose homoeostasis, reinforcing the concept of a gut-liver-pancreatic axis driving metabolic disease.[66 67] This axis appears dysregulated in obesity and T2DM with enhanced glucose transport, villous hypertrophy and impaired incretin responses that promote excessive glucose uptake and hyperglycaemia.[65 68–70] Collectively, these findings have helped highlight the proximal small intestine as a central modulator of glucose regulation and hormonal signalling. This understanding has directly informed the development of endoscopic and device-based therapies designed to replicate the metabolic benefits of surgery without anatomical resection. These include ablation-based techniques that remodel the intestinal mucosa in an attempt to restore metabolic signalling,

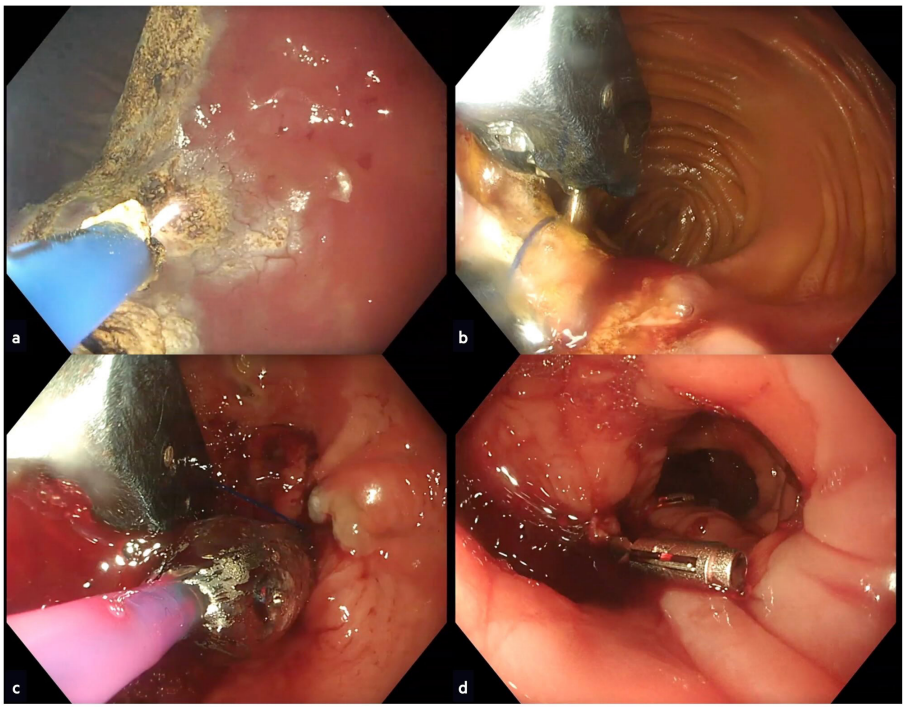

Figure 2 Transoral outlet reduction endoscopy (TORe).

and those that bypass the proximal intestines more akin to traditional metabolic surgery.

Small intestinal mucosal ablation

Duodenal mucosal ablation (DMA) is the prominent procedure within the field, which aims to reversibly destroy the mucosal lining of the postampullary duodenum to improve insulin sensitivity and promote reductions in HbA1c.[71–73] At present, there are three main endoscopic technologies under investigation that can be used as a DMA device: hydrothermal (REVITA system; Fractyl Laboratories, Lexington, Massachusetts, USA), electroporation (ReCET system; Endogenex, Plymouth, Minnesota, USA) and steam (Radiofrequency vapour ablation (RFVA); Aqua Medical, Pleasanton, California, USA; figure 3).[74–77] The REVITA and ReCET systems are over-the-guidewire procedures that require fluoroscopy for device placement into the small intestines, whereas RFVA is a through-the-scope device. The original REVITA procedure was known as duodenal mucosal resurfacing, but with the advent of new devices the term DMA is more encompassing of the field. A recent meta-analysis showed that across all devices, the reduction in HbA1c at 6 months is −1.13% (95% CI −1.37% to −0.89%; I^2 93%, p<0.001) and the pooled incidence of SAEs was 2% (95% CI 0.0% to 5.0%; I^2 10.2%).[71]

The ReCET procedure is currently being investigated in a randomised, sham-controlled, double-blind clinical trial across centres in the USA (NCT06267391) with 264 participants expected to be enrolled. This is on the back of encouraging open-label prospective trials in both Australia and the USA that showed meaningful reductions in HbA1c up to 24 weeks with no reported SAEs.[78 79] In parallel, investigators in the Netherlands have explored the metabolic effects of combining electroporation-based therapy with semaglutide in IR T2DM through the EMINENT programme. Prior work from this group demonstrated

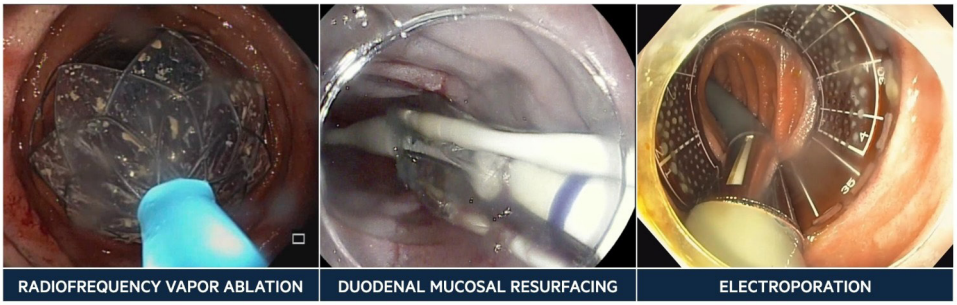

Figure 3 Duodenal mucosal ablation (DMA) technologies.

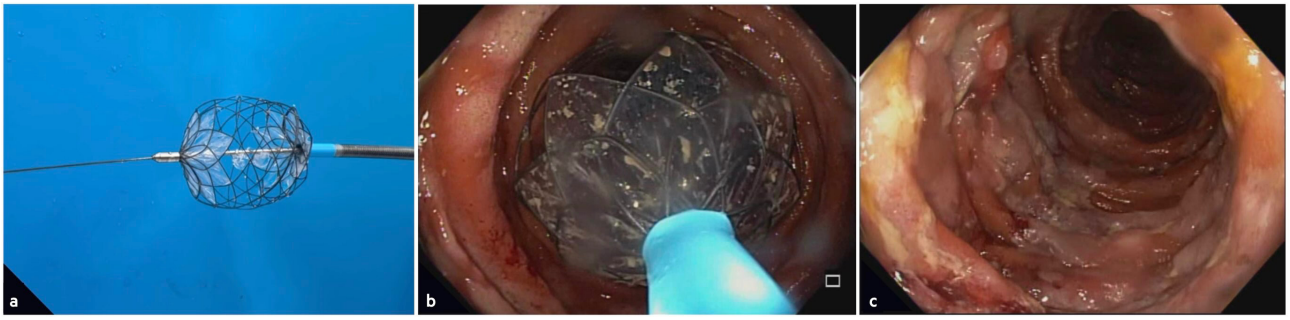

Figure 4 Radiofrequency vapour ablation (RFVA).

that DMA with REVITA in conjunction with liraglutide enabled withdrawal of exogenous insulin in more than half of treated patients, with durability observed over 18 month follow-up and only mild, predominantly gastrointestinal, adverse events.[80] At 12 months, the combination of ReCET with semaglutide enabled 12/14 patients (86%) to remain off exogenous insulin with additional improvements in other glycaemic and metabolic parameters.[81] However, as semaglutide was initiated shortly after the procedure, the independent contribution of electroporation to insulin discontinuation cannot be clearly delineated. To address this limitation, the EMINENT-2 Trial (NCT05984238) is a randomised, sham-controlled trial aiming to compare the combination of ReCET plus semaglutide, and thereby, clarify the additive value of duodenal electroporation within combination metabolic therapy.

RFVA using the second-generation mesh-tip catheter is being investigated in a series of prospective, open-label, clinical trials looking at a longer length of ablation up to 70 cm into the proximal jejunum. This longer ablation, known as proximal intestinal mucosal ablation (PIMA), is enabled by the through-the-scope technology and hypothesised to lead to a more enhanced and durable glycaemic response (figure 4).[82] Early reports show it can lead to reductions in HbA1c by 1.8% at 3 months in patients with inadequately controlled T2DM despite oral glucose lowering agents and without SAEs.[83] In addition, among insulin-requiring (IR) T2DM, PIMA was able to eliminate the need for exogenous insulin in a small cohort of patients who stopped a daily long-acting insulin (average dose 22.4 IU/day) prior to the procedure without requiring escalation to a GLP-1RA.[84] These early results suggest that the longer ablation may have a more beneficial effect than traditional DMA, with end of trial results soon to be reported.

The REVITA system represents the earliest investigation of DMA with encouraging results from initial open-label studies. However, the randomised, sham-controlled REVITA-2 failed to meet its primary endpoint of reduction in HbA1c at 6 months (−10.4 vs −7.1 mmoL/moL; p=0.147), although regional differences were observed, and in the European modified intention-to-treat subgroup, it resulted in a greater reduction in HbA1c compared with sham (−6.6 vs −3.3 mmoL/moL; p=0.033).[76] On the back of the promising findings from early studies evaluating REVITA in combination with liraglutide, Fractyl proceeded to the randomised sham-controlled study known as REVITALISE-1 (NCT04419779). This trial was designed to evaluate whether REVITA could meaningfully reduce or eliminate the need for exogenous insulin in people with T2DM as an independent therapy. However, in early 2025, after difficulty in recruiting with the rise in use of incretin-based therapies, the company announced a pause in recruitment. Instead, there was a new focus on the role of DMA in post-GLP-1 therapy weight maintenance. An initial pilot known as REVEAL-1 showed that among 20 individuals with obesity who had previously lost ≥15% of total body weight on tirzepatide, they were able to maintain weight loss (TBWL+1.5%; SEM 1.3%) up to 6 months postdiscontinuation following a single REVITA procedure without any procedure or device-related SAEs.[85] This has led to the randomised, double-blind, sham-controlled REMAIN-1 Study that suggests, on early midpoint results, DMA with REVITA may substantially reduce post-GLP-1 weight rebound and improve cardiometabolic measures compared with sham, with final results expected late 2026.[86]

Intestinal bypass devices

Duodenal jejunal bypass liners (DJBL) have been investigated since the late 2000s and involve fluoroscopic placement of a 60 cm impermeable fluoropolymer sleeve into the proximal small bowel to prevent nutrient contact with the mucosa.[9] The main DJBL under investigation is known as Endobarrier (Morphic Medical, Boston, Massachusetts, USA; formally GI Dynamics) and was developed in 2008. After a series of successful early phase open-label studies and RCTs, the US pivotal ENDO Trial, which was funded by GI dynamics (former company), aimed to investigate the use of Endobarrier in combination with moderate-intensity lifestyle against sham-endoscopy among patients living with T2DM and obesity.[87] Unfortunately, the trial was halted by the Food and Drug Administration (FDA) because of a hepatic abscess rate of 3.5%, which was above the predetermined threshold.[88] Ultimately, the

device never achieved FDA approval and in 2017 it lost its Conformité Européenne (CE) mark. An analysis performed by the sponsor determined that the high doses of protein pump inhibitors used in combination when implanted led to a biofilm on the device and high bacterial load.[11] In 2019, the FDA approved an Investigational Device Exemption to initiate a new multicentre RCT (STEP-1) which is currently recruiting in the USA (NCT: NCT04101669, Sponsor: Morphic Medical). As of July 2025, the device has regained its CE mark following a reapplication largely based on the large cohort of patients treated through the European DJBL registry.[89] These registry data show a HbA1c reduction of 1.3% (SD 1.5; n=646) and BMI reduction of 4.6 kg/m^2 (SD 3.6; n=808) at the time of explantation (originally 12 months, now moved to 9 months), and SAEs in 4.2%. However, an additional 75 patients developed obstruction or device migration that warranted early explantation that were not captured as SAEs. In 2025, the joint ASGE/ESGE bariatric guidelines recommended the use of DJBLs over lifestyle management alone for patients with T2D who are living with obesity pending regulatory approval,[11] and the final results of the ENDO Trial were published that showed among 320 randomised patients (212 DJBL, 108 sham); the between-group difference in HbA1c and TBWL at 12 months was −0.85% (95% CI −1.27% to −0.37%; p=0.0004) and −5.6% (95% CI −7.7% to −3.5%; p<0.0001), respectively.[90] The hepatic abscess rate in the intervention group was 3.3% (7/212) and device-related SAEs requiring early explant occurred in 9.0% (19/212). Therefore, while DJBL demonstrates reproducible metabolic efficacy in randomised and registry data, its safety profile and requirement for device removal mean its role within the contemporary treatment algorithm remains uncertain.

An alternative strategy for excluding the proximal small intestine involves creating a bypass through a deliberately formed anastomosis. One emerging approach uses self-assembling magnetic compression devices, typically delivered as paired magnetic rings or octagonal segments that couple across adjacent bowel loops to generate a side-to-side anastomosis.[91] These systems are placed using a hybrid endoscopic–laparoscopic technique, allowing controlled approximation of the duodenum and ileum without the need for formal surgical stapling. Early feasibility studies have demonstrated technical success in establishing a duodeno-ileal bypass with the SNAP system (GI windows) in patients experiencing weight regain after sleeve gastrectomy, offering a potential alternative to revisional RYGB.[92 93] More recently, a small prospective study among 19 patients postsleeve gastrectomy showed a TBWL of 31% (SD 11) up to 12 months with 11 SAEs recorded, including recurrent episodes of protein malnutrition.[94] Additionally, an Italian multicentre trial reported on their experience with the GT Metabolic Solutions Magnet System (MagDI System) among 28 patients.[95] Technical success was achieved in 96% with spontaneous magnet passage after approximately 37 days. At 90 days (n=23) the average TBWL was 10.4% with HbA1c decreasing from 6.0% to 5.5%. However, procedure-related SAEs occurred in three patients (ileal perforation, malnutrition requiring reversal and trocar-site hernia), underscoring the inherent risks of the hybrid laparoscopic approach and the metabolic consequences of creating a relatively distal duodeno-ileal diversion.

PANCREATIC-DIRECTED THERAPIES

In light of the widespread adoption of incretin-based GLP-1 receptor agonists, there is growing interest in pancreatic-directed gene therapies that may obviate the need for chronic injectable treatment. Rejuva (Fractyl Laboratories, Lexington, Massachusetts, USA) is a locally delivered adeno-associated viral gene therapy platform currently in preclinical development that introduces a GLP-1 analogue gene into the pancreas. The transgene is driven by an insulin promoter, restricting expression to pancreatic β cells and enabling meal-responsive, endogenous GLP-1 production. In murine models, this approach attenuated high-fat diet-induced weight gain and hyperglycaemia,[96] while porcine data have demonstrated the technical feasibility of endoscopic ultrasound-guided pancreatic delivery.[97]

WHAT IS THE ROLE IN THE ERA OF EFFECTIVE PHARMACEUTICAL AGENTS?

The therapeutic landscape of obesity and T2DM has been transformed by incretin-based pharmacotherapies, which now achieve weight reductions approaching those historically associated with bariatric surgery.[39] Next-generation agents including CagriSema, tirzepatide and the triple agonist retatrutide demonstrate greater efficacy in early and comparative trials compared with single-receptor agonists such as semaglutide.[98–101] These therapies also confer significant cardiovascular and renal protection in high-risk populations,[102–106] establishing pharmacotherapy as a cornerstone of modern cardiometabolic disease management. Consequently, the success of metabolic bariatric interventions will depend not on competing with these medications, but on integrating alongside them and demonstrating additive or complementary effects, including potential long-term effects on cardiometabolic outcomes that remain largely unexplored.

Nevertheless, several practical and biological factors temper the universal applicability of pharmacotherapy. Real world data demonstrate substantial attrition within the first 12–24 months of treatment.[8 107 108] Gastrointestinal intolerance remains the principal limitation and a major contributor to dose reduction or discontinuation in clinical practice.[39] Nausea, vomiting and diarrhoea are typically dose-dependent and

transient but can meaningfully affect adherence.[5 109] Beyond these predictable class effects, recognised but uncommon risks include gall bladder disease[110] and a small, uncertain pancreatitis signal.[111] Withdrawal studies consistently show partial or complete reversal of weight and metabolic improvements after cessation, reinforcing the chronic nature of therapy.[6 7] Cost and access remain significant constraints to the widespread implementation within publicly funded health systems. In the UK, NICE has recommended semaglutide and tirzepatide for defined patient groups; however, eligibility is restricted by BMI and comorbidity thresholds, and geographical variation in services creates inequity in access.[112 113] Although National Health Service pricing agreements can reduce headline acquisition costs, chronic pharmacotherapy for obesity represents a substantial recurring expenditure when considered at a population scale. Economic modelling shows that these therapies have cost-effectiveness profiles that are highly sensitive to assumptions regarding long-term benefit, baseline patient risk, treatment duration, persistence and drug price.[112–116] Given that weight and metabolic improvements frequently attenuate following discontinuation, sustained benefit may require prolonged or indefinite therapy, thereby amplifying the cumulative lifetime cost.

Taken together, while these novel therapies have redefined expectations of medical management, their financial aspects, tolerability limitations and requirement for sustained administration mean they do not eliminate the potential role of procedural strategies. Rather than representing competing paradigms, pharmacological and endoscopic therapies are likely to occupy complementary positions within a chronic disease management framework. Endoscopic metabolic interventions may provide a structurally durable or time-limited alternative for individuals unable to access or tolerate long-term pharmacotherapy and may also serve within combination or sequential strategies to enhance durability and optimise resource utilisation.

Emerging data are beginning to explore such integration. DMA has been evaluated both in combination with GLP-1RAs to facilitate insulin withdrawal and as a potential strategy to mitigate weight regain following pharmacotherapy discontinuation.[81 86] In addition, early real world series have reported enhanced weight loss with the addition of incretin-based therapy following endoscopic gastroplasty, suggesting additive or synergistic effects.[58 117–119] However, optimal sequencing, timing and patient selection remain unclear, with current evidence limited by observational, largely retrospective data. The integration of metabolic bariatric therapies with pharmacotherapy can be conceptualised across three strategic domains: (1) Efficacy synergy, (2) Response rescue and (3) Compensation control. In efficacy synergy, early combination therapy targets complementary metabolic pathways to maximise initial response. In response rescue, procedural intervention addresses biological heterogeneity in patients demonstrating suboptimal pharmacological response, thereby enhancing durability. In compensation control, the aim is to attenuate adaptive biological mechanisms that may limit long-term pharmacological efficacy. It is within these paradigms that metabolic bariatric endoscopy may define its future role in the management of obesity and related metabolic disease. Looking ahead within this framework, the field must prioritise rigorous comparative effectiveness studies, long-term durability assessment, and evaluation of hard cardiometabolic and cardiovascular outcomes to define the true clinical and health-system value of these endoscopic therapies.

CONCLUDING REMARKS

Bariatric metabolic endoscopy is a rapidly evolving subspeciality that has shown excellent initial efficacy and safety data in the treatment of obesity and related metabolic disease. With the increase in novel incretin-based therapies, these endoscopic techniques are likely to evolve as a complementary component of integrated weight management services, positioned alongside pharmacological and surgical approaches within a multidisciplinary treatment pathway. Ultimately, this will enable the delivery of personalised, durable and scalable treatments for patients living with obesity.

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