



Review

# Metabolic Endoscopy: Should Gastroenterologists Be Treating Type 2 Diabetes?

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**Abstract:** Type 2 diabetes (T2D) is one of the most significant and fast-growing health challenges of the 21st century. Despite the variety of available glucose-lowering agents, many patients do not attain or maintain adequate glycaemic control. Bariatric surgery demonstrates a profound anti-diabetic effect, which is almost immediate and weight-loss independent. The significant improvement in diabetes after bariatric surgery together with the endoscopic accessibility of the duodenum has led to the development of new metabolic endoscopic procedures that capitalise on the importance of the proximal small bowel in glycaemic control. Clinical trials have shown a clear efficacy signal, and now, several devices are undergoing evaluation as primary T2D treatments. Establishing where these procedures fit into the treatment algorithms for T2D and how they can be combined with modern pharmacotherapies is needed in a rapidly changing landscape. Ultimately, through metabolic endoscopy, gastroenterologists are on the cusp of providing safe and effective treatments for the multidisciplinary management of T2D.

**Keywords:** metabolic endoscopy; type 2 diabetes; obesity; duodenal mucosal ablation; bariatric surgery; bypass liners



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## 1. Introduction

Type 2 diabetes (T2D) is one of the most significant and fast-growing health challenges of the 21st century. In 2021, it was estimated that 1 in 11 adults in Europe were living with diabetes, and the UK prevalence of diabetes was 8.2% [1]. Collectively, T2D accounts for a total healthcare expenditure of >180 billion within Europe alone [1]. The upsurge in T2D is primarily driven by the rising rates of obesity, with an estimated 90% of patients with T2D being overweight or obese [2]. This is concerning given that diabetes is a chronic, multi-system disease associated with many long-term complications including blindness, chronic kidney disease, limb amputation, cardiovascular disease, and stroke [3]. Unfortunately, there is no simple fix to one of the biggest epidemics in human history. T2D is due to a complex interaction of genetic, metabolic, and environmental risk factors. Modifiable risk factors, including high body mass index (BMI), lower physical activity, and poor diet, are central to its development [4]. Obesity is the strongest risk factor for T2D because it promotes insulin resistance, which describes a process in which cells become less responsive to insulin. This causes pancreatic beta cells to secrete increasing quantities of insulin that ultimately leads to beta cell dysfunction and long-term complications. The management of T2D therefore requires holistic multi-modal multidisciplinary care.

Despite the variety of available glucose-lowering agents and the important advances in oral and injectable medications, many patients do not attain or maintain adequate glycaemic control. In fact, many patients eventually require escalation to insulin that can result in a perpetuating cycle of weight gain and increasing insulin dose. Therefore, despite an increase in the number of available anti-diabetic agents, the disease remains a major public health burden. We know from major diabetic studies that intensive control results in lower levels of glycated haemoglobin (HbA1c) and a lower risk of both microvascular and macrovascular complications [5,6]. However, many patients are unable to achieve these tight glycaemic targets and struggle to lose and maintain weight loss long-term. This is particularly true among patients with obesity, defined as a BMI  $\geq 30$  kg/m<sup>2</sup> (a lower threshold of 27.5 kg/m<sup>2</sup> is recommended for South Asian and Chinese populations), as the estimated annual rate of weight normalisation among obese individuals is less than 1% [7]. In Europe, just over 50% of patients were reported to achieve HbA1c levels  $< 7.0\%$  (53 mmol/mol), but over 25% of this population were on insulin [8]. Data from the DiRECT study showed that diabetes can be reversed after 12 months of an intensive low-calorie diet in 46%, which was correlated with the degree of weight loss (WL) [9]. However, we know that these types of dieting programmes, which have been promoted widely, can achieve short-term WL, and hence improved diabetic control. The problem is that for the vast majority, these diets will ultimately result in weight regain, often within the first year [10–12]. In fact, restrained eating and exercise for weight control are predictors of weight gain [13]. If dietary interventions and pharmacotherapy are proving suboptimal in many patients, we need to look at alternative methods of controlling blood glucose levels that include bariatric surgery and, more recently, metabolic endoscopy.

A growing area of interest is metabolic and bariatric endoscopy. This is a novel subspeciality of endoscopy that is performed by upper gastrointestinal surgeons, gastroenterologists, and/or bariatric surgeons. It encompasses a wide range of procedures that are primarily grouped as weight loss procedures (i.e., bariatric endoscopy) or metabolic procedures (i.e., metabolic endoscopy). Bariatric procedures include intragastric balloons, intragastric implants, and gastroplasty devices that are primarily aimed at weight loss by targeted manipulation of the gastric anatomy and physiology. Metabolic procedures, which are discussed within the review, are principally focused on the small bowel to treat T2D. In essence, these procedures have been developed to mimic the beneficial metabolic effects observed after gastric bypass surgery when nutrients are diverted away from the proximal small bowel. These effects are weight-independent and highlight the proximal small bowel as a potential key regulator in metabolic health.

In this narrative review, we outlay the most up to date information on the safety and efficacy of metabolic endoscopy for the management of T2D. We provide an overview of emerging duodenal technologies and collate results from recently reported clinical trials in the field of duodenal mucosal ablation. In addition, we provide novel insight into the proposed mechanism of these procedures and the future direction of the subspeciality including its limitations. For a broader overview assessing both metabolic and bariatric endoscopic procedures, we point the reader to an excellent overview article [14].

## 2. Bariatric Surgery, Type 2 Diabetes, and the Proximal Small Bowel

Bariatric surgery is the most effective treatment for patients with severe obesity leading to sustained WL, reduced mortality, and improvement in obesity-associated comorbidities [15]. The two main procedures are Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG); both are associated with sustained long-term WL [16–18]. Bariatric surgery is also an excellent treatment option for T2D, particularly following RYGB. Bariatric surgery is associated with multiple physiological changes including altered gut hormones, microbiome changes, and enhanced bile acid delivery [19]. These changes collectively result in WL and improved whole-body insulin sensitivity. In fact, the improvements in diabetes after RYGB are almost immediate and weight independent, which underscores the importance of the proximal small bowel as a critical signalling centre. The

exact mechanism of improved glucose control is currently uncertain. Hypotheses suggest either enhanced delivery to the distal small bowel (i.e., hindgut hypothesis) and/or the removal of an unknown inhibitory mechanism stimulated by proximal intestinal nutrient exclusion (i.e., foregut hypothesis) [20]. Either way, subsequent randomised controlled trials (RCT) have confirmed that surgical interventions that bypass the proximal small bowel are associated with a high, albeit heterogenous, rate of T2D remission that is reversible on re-exposure of nutrients via the remnant stomach [21–24]. Unfortunately, bariatric surgery is unable to address the magnitude of the T2D crisis due to resource and scalability, operative risks, irreversibility, patient selection, and patient preference.

### 3. Targeting the Proximal Small Bowel with Endoscopy

The significant improvement in glycaemic control after bariatric surgery together with the endoscopic accessibility of the duodenum led to the development of the new non-pharmacological, non-surgical treatments for T2D. These endoscopic treatments, which are collectively known as ‘metabolic endoscopy’, involve the use of novel devices to target the duodenum to mimic the anti-diabetic effect of gastric bypass surgery.

#### 3.1. Implantable Bypass Liners

The duodenal jejunal bypass liner, known as EndoBarrier™ (Morphic Medical, Boston, MA, USA; formerly GI Dynamics Inc.), is an early device that involves the endoscopic placement of a 60 cm fluoropolymer sleeve with fluoroscopic guidance into the proximal small bowel. The sleeve terminates in the proximal jejunum with nutrients from the stomach passing through the sleeve and bypassing the duodenum. In 2015, a meta-analysis among nine prospective trials showed that EndoBarrier™ led to a reduction in HbA1c by  $-1.7\%$  (95% CI:  $-2.5$  to  $-0.86$ ;  $p < 0.001$ ) and  $-1.5\%$  (95% CI:  $-2.2$  to  $-0.78$ ;  $p < 0.001$ ) at 24 and 52 weeks, respectively [25]. Unfortunately, safety concerns were raised during the US-based ENDO trial due to a high rate of hepatic abscesses (7 patients; 3.5%) leading to early discontinuation and the loss of its CE mark [26]. More recently, registry data from the Association of British Clinical Diabetologists has shown that among 1022 treated patients, there is a significant reduction in HbA1c ( $-1.3\%$ ; SD 1.5) between baseline and device removal at one year. Serious adverse events (SAEs) occurred in 4.2% with 11 liver abscesses [27]. Although these safety issues raise concerns, the experience with EndoBarrier™ showed that the small bowel can be targeted by endoscopy with clear evidence of an efficacy signal. Furthermore, research into the safety and efficacy of EndoBarrier™ continues with the randomised, double-blind, sham-controlled STEP-1 trial currently recruiting in the US (NCT04101669).

#### 3.2. Duodenal Mucosal Ablation

To prevent the issues that arise when a device is left in situ, researchers explored the possibility of targeting the duodenal mucosa through endoscopic ablation. Thermal ablation is a common therapeutic strategy in Barrett’s oesophagus whereby the abnormal columnar mucosa is destroyed and subsequently regenerates with normal squamous cells. Duodenal mucosal resurfacing (known as ‘DMR’) is a procedure that selectively ablates the duodenal mucosa through hydrothermal ablation. The first in-human study on 39 patients with T2D showed a clinically significant reduction in HbA1c following a single procedure with the Revita™ system (Fractyl Laboratories Inc., Lexington, MA, USA), although it was associated with three cases of duodenal stenosis that were successfully treated with balloon dilatation [28]. We subsequently performed an open-label prospective study in patients on oral hypoglycaemic agents and showed a reduction in HbA1c by  $10 \pm 2$  mmol/mol ( $p < 0.001$ ) at 24 weeks, which appeared sustained at 24 months with only one procedure-related adverse event (transient febrile illness) [29,30]. The follow-up randomised, double-blind, sham-controlled, multicentre trial involving 108 patients from Europe and Brazil showed no significant difference in the combined mean reduction in HbA1c ( $p = 0.15$ ) [31]. However, when stratifying for high fasting glucose ( $>10$  mmol/L), HbA1c reduction

with DMR was significant (−14.2 vs. −4.4;  $p = 0.002$ ), and a post-hoc analysis showed a significant difference when separating the European cohort (−6.6 vs. −3.3;  $p = 0.033$ ). There was one device-related SAE secondary to a jejunal perforation from manipulation of the endoscope, which required surgical repair. Mild AEs were common with hypoglycaemia observed in 25% and abdominal pain in 26.8%. REVITALISE-1 is the follow-up randomised, double-blind, sham-controlled trial that is currently recruiting in the USA and Europe (NCT04419779). The aim is to determine whether DMR can effectively eliminate the need for exogenous insulin among patients with insulin-requiring T2D that we know has an enormous impact on cost, quality of life, and morbidity.

### 3.3. Emerging Duodenal Ablation Technologies

Although DMR is still in its infancy, it remains an attractive option because it provides a minimally invasive treatment that targets insulin resistance—the root cause of T2D. The device has a high technical barrier, but as more accessible devices become available it could become a realistic, scalable option. The two important aspects of a duodenal ablation device are how to deliver the catheter into the proximal small bowel and the technology for delivering ablation. Wire-guided over-the-scope (OTS) delivery is a standard endoscopic technique but increases procedure time and difficulty with the need for fluoroscopy. A through-the-scope (TTS) system allows passage of the device through the working channel of the endoscope that increases ease, and ultimately, scalability. New ablation technologies with both OTS and TTS techniques are emerging that involve the use of laser, electroporation, or steam to selectively ablate the duodenal surface (Table 1).

**Table 1.** Emerging duodenal ablation technologies for type 2 diabetes.

Procedure	Technology	Delivery	Study	Design	Target Population	No.	HbA1c Reduction (mmol/mol)	Off Insulin (%)	Serious Adverse Events (%)	Follow-Up (Weeks)
Duodenal mucosal resurfacing with the REVITA system (Fractyl health)	Hydrothermal	Over-the-scope	REVITA-1 [32]	Open label	OAD	36	10.0	-	2.2	24
			REVITA-1 (extension) [29]	Open-label	OAD	27	9.0	-	0.0	108
			REVITA-2 [31]	RCT	OAD (treatment)	56	10.4	-	3.6	24
					OAD (control)	52	7.1	-	0.0	24
			GLP-1/DMR [33]	Open label	Insulin	16	4.4	53	0.0	78
REVITALISE-1	RCT	Insulin	560	-	-	-	48			
Duodenal Mucosal Regeneration with the ReCET procedure (Endogenex)	Electroporation	Over-the-scope	REGENT-1 (US)	Open label	OAD	20	-	-	-	48
			REGENT-1 (AUS)	Open label	OAD or insulin	-	-	-	-	48
			EMINENT-1 [34]	Open label	Insulin	14	6.6	86	0.0	24
			EMINENT-2	RCT	Insulin	32	-	-	-	24
Duodenal mucosal ablation with Radiofrequency vapor ablation (AQUA medical)	Steam	Through-the-scope	STEAM T-2DM	Open label	≥1 OAD	30	-	-	-	24
Duodenal submucosal laser ablation with DiaGone (Digma Medical)	Laser	Through-the-scope	First-in-human [35]	Open label	OAD	9	13.5	-	0.0	24

DMR—Duodenal mucosal resurfacing; GLP—Glucagon-like peptide 1 agonist; OAD—Oral anti-diabetic drug

■ Completed  
 ■ Recruiting

Electroporation is a process in which an external electric field is generated around a cell that causes cellular disruption and increased permeability. At high levels, this will result in irreversible cell death [36]. This type of non-thermal ablation technique is currently being investigated as part of the ReCET™ procedure (Endogenex Inc., Plymouth, MN, USA). The safety and feasibility of electroporation is being investigated in both the US (NCT05014204) and Australia (NCT04725890) as part of open-label clinical trials in patients on oral hypoglycaemic agents or insulin therapy. ReCET™ is still a relatively advanced procedure requiring wire-guided placement of the catheter. Concurrently, the EMINENT study in the Netherlands has been investigating the use of electroporation in combination with a glucagon-like peptide 1 (GLP-1) agonist among patients with insulin-requiring T2D. Previously, the same group showed that the combination of DMR and the GLP-1 agonist Liraglutide led to the elimination of exogenous insulin in >50% of patients that was maintained at 18 months [33]. On follow-up, there were 21 suspected treatment-related AEs that were predominantly mild GI symptoms with no SAEs. A recently presented abstract showed that the combination of ReCET™ and empirical semaglutide enabled 86% ( $n = 14$ ) of patients with insulin-requiring T2D to remain off insulin at one year with no device-related SAEs and a single episode of hypoglycaemia [34]. However, because semaglutide was given empirically at two weeks post-procedure, it is difficult to draw any conclusions on the independent effect of electroporation for the elimination of insulin. EMINENT-2 is currently undergoing recruitment (NCT05984238), which is a randomised, sham-controlled trial, comparing ReCET™/semaglutide against sham/semaglutide.

Another method of duodenal ablation involves the use of steam and radiofrequency energy. A radiofrequency vapor ablation (RFVA) catheter (AQUA Medical Inc., Santa Ana, CA, USA) is currently being investigated for the treatment of patients with T2D on oral hypoglycaemic agents within a first-in-human trial (NCT05887635). During the procedure, radiofrequency energy is used to convert water into heated water vapor that can then be delivered to tissue to induce thermal ablation. The device was first shown to be effective in the setting of Barrett's oesophagus [37] and its TTS system negates the need for an advanced endoscopy suite with access to fluoroscopy.

Finally, laser ablation using DiaGone™ (Digma Medical, Petah Tiqva, Israel) is another TTS device that is being investigated for the treatment of T2D. This procedure uses precise lasers to target the duodenal submucosa to modulate the neurohormonal axis of the gastrointestinal tract. Early data in abstract form showed that the procedure was technically successful in 100% ( $n = 18$ ) and resulted in an average HbA1c reduction of 13.5 mmol/mol at six months post-procedure among nine included patients with no adverse events [35,38]. However, the full paper has yet to be published with the six- and twelve-month follow-up.

### 3.4. Anastomotic Devices

Several procedures have been developed that create an anastomosis between the proximal and distal small bowel with the use of self-assembling magnets. The new anastomosis helps to redistribute the flow of nutrients in a similar manner to the gastrointestinal reconstruction seen in bariatric surgery. These devices include the Incisionless Anastomotic System (GI Windows, Westwood, MA, USA), Magnet Anastomosis System (GT Metabolic Solution, St Michael, MN, USA), and Magnamosis magnetic compression device (magnamosis). Early pilot data show that at 12 months, the reduction in HbA1c after the incisionless anastomotic system is 1.9% [39], and after the magnet anastomotic system, 2.0% [40]. However, results must be taken in context as both pilots only assessed outcomes for four patients and these procedures require laparoscopic assistance for the optimal placement of the magnet. Although no device-related SAEs occurred, mild gastrointestinal adverse events were common, and one magnet had to be retrieved endoscopically. In addition, to highlight the increased risk of adding procedures, one patient had damage to the gastric serosa by a laparoscopic trocar. Therefore, while efficacy is clear, we appear to have lost the concept of endoscopy being a minimally invasive procedure that mitigates against the risk of surgery, not an add-on therapy that may enhance risk and cost.

#### 4. Drug Therapy and Endoscopy

Collectively, these new metabolic devices form part of a wider subspeciality of gastroenterology known as ‘metabolic and bariatric endoscopy’ as we discussed in the introduction. These one-off interventions are highly attractive for patients who want to mitigate the risks of bariatric surgery, but are also intolerant to, or want to avoid, long-term medication. New pharmacological agents including GLP-1 receptor agonists and combined GLP-1/gastrointestinal peptide agonists are highly effective obesity and diabetic treatments [41,42]. However, they involve weekly injections, are associated with side effects, have supply and cost issues, and rely on patient concordance [43]. In addition, real-world efficacy data may be lower than clinical trials, and up to 45% discontinue therapy after one year [43]. We must remember that duodenal mucosal ablation is not a primary weight loss procedure, and therefore it may complement, rather than replace, pharmacotherapy in those wanting to avoid bariatric surgery or achieve a more profound glycaemic effect. Nevertheless, as more scalable devices become integrated into routine clinical care, these could even be combined with a ‘same-sitting’ bariatric endoscopic procedure, such as an endoscopic sleeve gastropasty (ESG), which may have the potential to avoid the need for pharmacotherapy all together.

Modern diabetes management should be about combining metabolic interventions (e.g., metformin, duodenal ablation) with weight loss interventions (e.g., GLP-1 receptor agonist, ESG) to drive remission. We need to be able to identify the most suitable patients for the most suitable interventions, which will likely require stratification based on BMI, co-morbidities, and patient choice. Ultimately, the field of metabolic health is headed towards combination therapy, similar to treatments for both cancer and autoinflammatory conditions, as we look to obtain diabetes remission and weight normalisation as realistic biological endpoints.

#### 5. Discussion

T2D is a complex disease with a myriad of treatment options available. The increasing interest in metabolic endoscopy means that gastroenterologists are well placed to offer endoscopic therapy as part of a broader treatment paradigm under the umbrella of the MDT. Duodenal bypass liners helped us understand that a minimally invasive endoscopic procedure can provide an effective treatment for T2D with HbA1c reduction between 1.3–1.7% at 3–12 months after explantation. However, the high rate of adverse events is notable given that we should be trying to mitigate against the risks of surgery. This is important when the 2020 report from the UK National Bariatric Surgery Registry showed bariatric surgery was associated with an overall complication rate of 2.4% and in-hospital mortality of 0.04% [44]. This has led to a growing interest in duodenal mucosal ablation, which provides a one-off, minimally invasive endoscopic procedure with subsequent regeneration of the duodenal mucosal surface. Although early data from the first in-human study with the REVITA device showed three cases of duodenal stenosis, more recent data across multiple ablation technologies confirms both good, and comparable, safety data with SAEs in 0–3.6%. This is especially true considering that ablation therapy for Barrett’s oesophagus, which is the standard of care for dysplastic tissue, is associated with a stricture rate of 5.6–10.2% [45,46]. Across all ablation techniques, duodenal mucosal ablation is associated with a reduction in HbA1c of 9.0–13.5 mmol/mol among patients on oral hypoglycaemic agents over variable follow-up. However, the first RCT in this area did not meet the primary outcome. On the surface, this highlights the need for more evidence to determine the true effect of these ablation devices. Results from both REVITALISE-1 and EMINENT-2 will help answer this question, which is currently lingering in the field. Nevertheless, these trials show the true nature of T2D, and the difficulties clinicians and patients face with the need for life-long pharmacotherapy with implications on cost, concordance, and side effects that may partly explain the improvements seen in the sham group of the RCT. If the true effect of the procedure can be clearly defined, then a device that can reduce a patient’s ‘pill burden’ is highly appealing.

One of the interesting differences between duodenal mucosal ablation and duodenal bypass liners is the improved efficacy with the latter device. Duodenal liners enable 60 cm of proximal small bowel to be bypassed, whereas duodenal ablation targets 9–15 cm of the post-ampullary duodenum. We know from meta-analysis data among patients undergoing RYGB that the length of the biliopancreatic limb correlates with the degree of weight loss and diabetic resolution [47]. Therefore, it is theorised that ablating a longer segment of small bowel could enhance the effect on glycaemia, but achieving a longer ablation is more endoscopically challenging. This raises the question that, in the context of an optimised circumferential mucosal ablation of the duodenum, there is likely to be a maximum glycaemic effect that this procedure can achieve that may be around 10 mmol/mol. Currently, there are very limited data investigating why we see this perceived benefit from duodenal mucosal ablation. Data from duodenal bypass liners show that the procedure can improve insulin sensitivity [48], but there is no clear evidence to support changes in incretins and no studies have assessed meal-stimulated incretin effects [26,49]. Therefore, in the absence of a marked incretin response, the improvement in glycaemic control could be related to how the proximal small bowel handles dietary glucose with subsequent changes to the gut–liver axis and a reduction in hepatic gluconeogenesis. However, many of these hypotheses are inferred from studies investigating bariatric surgery, which we know is associated with alterations in bile acid metabolism, the microbiome, utilisation of intestinal glucose, the incretin response, and hepato-portal glucose sensing [20,50,51]. To enhance our knowledge in the field, future endoscopy trials need to attempt to answer these questions surrounding the perceived mechanism of action and potentially unlock key mechanisms in glucose regulation.

Another important interest is the use of combination therapy with two recent trials showing the value of adding a GLP-1 agonist to duodenal mucosal ablation. Among two small cohorts involving 30 insulin-requiring patients with T2D, 53–86% were able to remove the need for exogenous insulin following duodenal mucosal ablation with DMR or ReCET after the addition of liraglutide or semaglutide, respectively. At present, it is difficult to discern how much independent influence the ablation device has over the improvement in glycaemic control, especially with the rising use of more powerful anti-obesity and diabetic agents. However, it does highlight how the procedure could be added into a treatment algorithm for these patients at a time point when there is more likelihood of reversibility before the inevitable beta-cell depletion and dependence on exogenous insulin. Mechanistically, the current absence of a marked incretin response to duodenal endoscopic therapy means the addition of the incretin GLP-1 could have a synergistic effect similar to the benefits seen with dual pharmacotherapy [52,53]. Instead of focusing on combining drug and endoscopic therapy, one question is whether duodenal mucosal ablation could be combined with an endoscopic bariatric procedure (e.g., gastroplasty) to provide a ‘same-session’ metabolic and weight loss intervention. Although still experimental, these types of treatment choices can become quite complex and need to consider the cost, availability, experience, patient-related co-morbidities, and ultimately patient choice. In the face of these complex choices, multidisciplinary-led care is essential to ensure both safety and efficacy for patients.

The question remains: if the efficacy of duodenal mucosal ablation can be robustly confirmed, then where does it sit within the treatment algorithm of T2D? We envisage three treatment strategies where it could be used: (1) reduction in oral hypoglycaemic burden, (2) elimination of exogenous insulin, (3) high-risk new-onset T2D. This last category is perhaps the most controversial, but given that the number one research priority for patients is whether T2D can be reversed or even cured [54], we feel there is a strong incentive to treat high-risk new-onset T2D with a more intensive treatment strategy that will undoubtedly involve combination therapy. To achieve this, new treatment algorithms would need to be structured within multidisciplinary teams due to both the complexity of metabolic disease, and the vast array of treatment options available to patients. Metabolic endoscopy still has its limitations that should not be overlooked. While the efficacy of duodenal bypass liners

has been confirmed in RCTs, the rates of adverse events mean it remains an unattractive option, and the independent effect of duodenal mucosal ablation needs to be further confirmed in high-quality clinical trials. Furthermore, if many anti-diabetic agents have prognostic implications, then these endoscopic procedures may become add-on therapy, rather than upfront replacement. Finally, patient selection remains a big challenge with little understanding of when and what patients should be offered and who will respond. Although many unknowns remain, the rising prevalence of T2D coupled with the increasing availability of novel endoscopic interventions means this exciting new subspecialty will remain for the foreseeable future.

## 6. Conclusions

With the rapid evolution of metabolic endoscopy, gastroenterologists will undoubtedly play a role within the diabetic MDT and the evolving treatment paradigm of T2D. Duodenal ablation technologies are some of the most exciting because they offer a minimally invasive, one-off intervention, with low adverse effects and efficacy akin to a single anti-diabetic agent in early clinical data. Anastomotic devices are still in their infancy and need to be further refined to make them a truly feasible option. We watch with interest the re-emergence of duodenal bypass liners that show reasonable real-world safety and efficacy data, but concern will always remain around the safety of devices left in situ. Within the field of metabolic endoscopy, many issues still exist including their unknown mechanisms, patient selection, efficacy of combination therapy, cost, and training. However, what is certain is that through metabolic endoscopy, gastroenterologists are on the cusp of providing safe and effective treatments for people living with type 2 diabetes.

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