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American Society for Gastrointestinal Endoscopy–European Society of Gastrointestinal Endoscopy guideline on primary endoscopic bariatric and metabolic therapies for adults with obesity

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ABSTRACT

This joint ASGE-ESGE guideline provides an evidence-based summary and recommendations regarding the role of endoscopic bariatric and metabolic therapies (EBMTs) in the management of obesity. The document was developed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework. It evaluates the efficacy and safety of EBMT devices and procedures that currently have CE mark or FDA-clearance/approval, or that had been approved within five years of document development. The guideline suggests the use of EBMTs plus lifestyle modification in patients with a BMI of ≥30 kg/m^2, or with a BMI of 27.0–29.9 kg/m^2 with at least 1 obesity-related comorbidity. Furthermore, it suggests the utilization of intragastric balloons and devices for endoscopic gastric remodeling (EGR) in conjunction with lifestyle modification for this patient population.

ABBREVIATIONS

AE	adverse event
AOM	antiobesity medication
ASGE	American Society for Gastrointestinal Endoscopy
AT	aspiration therapy
BMI	body mass index
CE	Conformité Européenne
CI	confidence interval
DJBL	duodenal-jejunal bypass liner
DMR	duodenal mucosal resurfacing
EBMT	endoscopic bariatric and metabolic therapy
EGR	endoscopic gastric remodeling
ESG	endoscopic sleeve gastroplasty
ESGE	European Society of Gastrointestinal Endoscopy
FDA	U.S. Food and Drug Administration
GLP-1Ras	glucagon-like peptide 1 receptor agonists
IGB	intragastric balloon
IOP	Incisionless Operating Platform
LM	lifestyle modification
MD	mean difference
PPI	proton pump inhibitor
RCT	randomized controlled trial
SAE	serious adverse event
T2DM	type 2 diabetes mellitus
TPS	transpyloric shuttle
TWL	total weight loss

The rising burden of obesity [1–4] and its related comorbidities, such as type 2 diabetes mellitus [5] (T2DM) and metabolic dysfunction–associated steatotic liver disease [6, 7], constitute a major public health issue globally. It is predicted that by 2030 the number of people suffering from obesity will have doubled since 2010, reaching over 1 billion adults worldwide [8]. Obesity is a significant risk factor for all-cause mortality [9], driven mainly by cardiovascular diseases and cancer. Therefore, expanding treatment options for obesity is paramount.

Traditionally, the primary modalities for the treatment of obesity include lifestyle modification (LM), antiobesity medications (AOMs), and bariatric and metabolic surgery. Weight loss

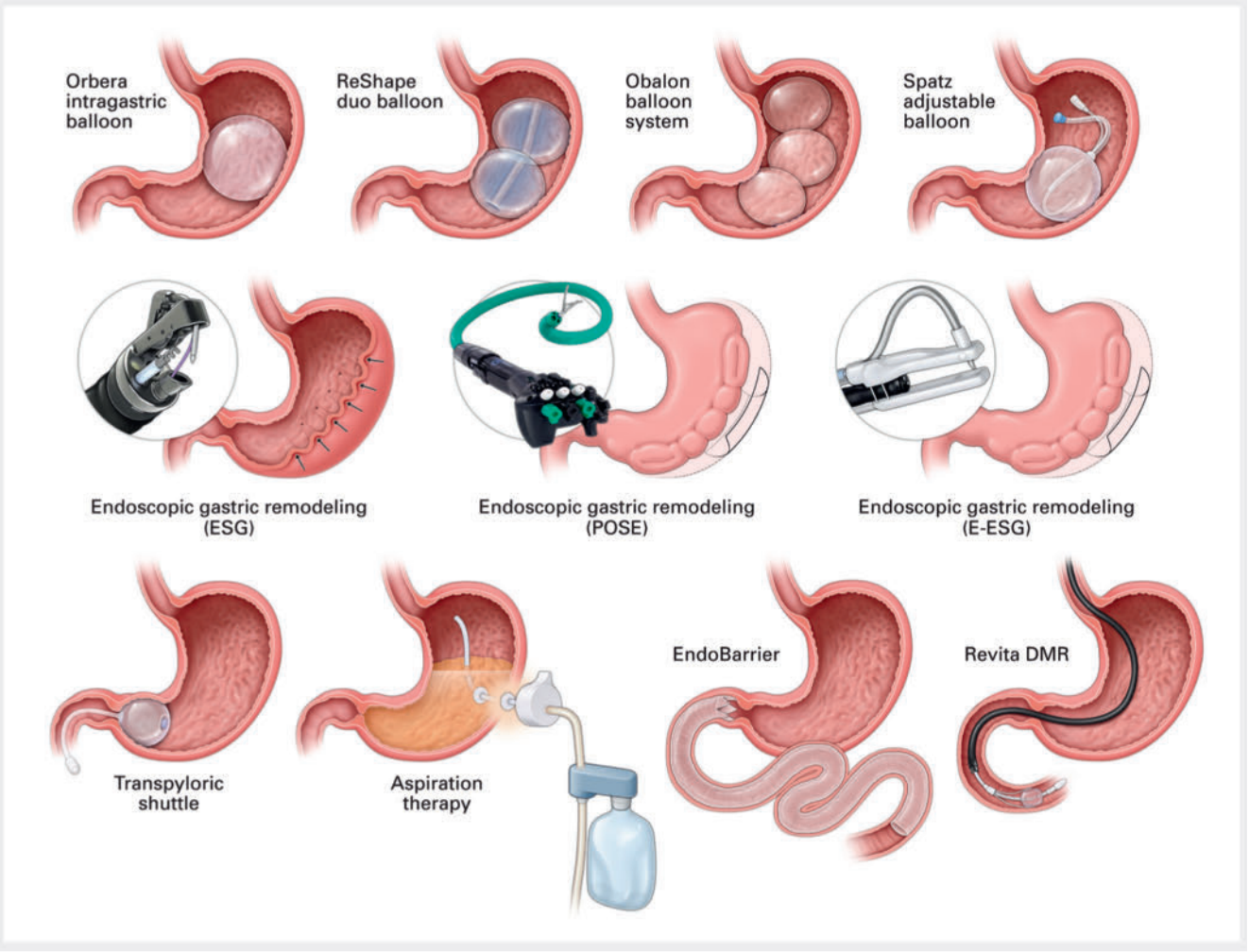
▶ **Table 1** ASGE–ESGE recommendations on primary endoscopic bariatric and metabolic therapies for the management of obesity.

Recommendations	Strength of recommendation	Quality of evidence
1. In adults with overweight or obesity, the ASGE–ESGE suggests the use of endoscopic bariatric and metabolic therapies plus LM over LM alone for patients with a BMI ≥ 30 kg/m2 with or without an obesity-related comorbidity or a BMI of 27 to 29.9 kg/m2 with at least 1 obesity-related comorbidity.	Conditional	Very low
2. In adults with obesity, the ASGE–ESGE suggests the use of an IGB plus LM over LM alone.	Conditional	Moderate
3. In adults with obesity undergoing IGB placement, the ASGE–ESGE suggests the use of antiemetics periprocedurally.	Conditional	Very low
4. In adults with obesity undergoing IGB placement, the ASGE–ESGE suggests the use of pain medications periprocedurally.	Conditional	Very low
5. In adults with obesity undergoing IGB placement, the ASGE–ESGE suggests the use of proton pump inhibitors while the IGB is in place.	Conditional	Very low
6. In adults with obesity, the ASGE–ESGE suggests treatment with EGR plus LM over LM alone.	Conditional	Moderate
7. In adults with obesity undergoing EGR, the ASGE–ESGE suggests the use of antiemetics periprocedurally.	Conditional	Very low
8. In adults with obesity undergoing EGR, the ASGE–ESGE suggests the use of pain medications periprocedurally.	Conditional	Very low
9. In adults with obesity undergoing EGR, the ASGE–ESGE suggests the use of prophylactic antibiotics periprocedurally.	Conditional	Very low
10. In adults with obesity undergoing EGR, the ASGE–ESGE suggests the use of short-term proton pump inhibitors periprocedurally.	Conditional	Very low
11. In adults with obesity, the ASGE–ESGE suggests treatment with aspiration therapy plus LM over LM alone.	Conditional	Low
12. In adults with obesity, the ASGE–ESGE recommends treatment with a transpyloric shuttle only in the context of a clinical trial.	No recommendation	Knowledge gap
13. In adults with obesity and concomitant type 2 diabetes mellitus, the ASGE–ESGE suggests treatment with a duodenal-jejunal bypass liner plus LM over LM alone.	Conditional	Moderate
14. In adults with type 2 diabetes mellitus, the ASGE–ESGE recommends treatment with duodenal mucosal resurfacing only in the context of a clinical trial.	No recommendation	Knowledge gap

ASGE, American Society for Gastrointestinal Endoscopy; *ESGE*, European Society of Gastrointestinal Endoscopy; *LM*, lifestyle modification; *IGB*, intragastric balloon; *EGR*, endoscopic gastric remodeling.

through LM is the first-line treatment for obesity. Nevertheless, even high-intensity LM encompassing calorie restriction, increased physical activity, and a structured behavior change program (≥ 14 sessions in the first 6 months of therapy) is associated with only minimal to moderate weight loss [10], with most patients unable to sustain a long-term weight loss of at least 5 % [11]. Barriers such as ongoing cost and time commitment also contribute to limited sustained weight loss with LM [12]. Newer AOMs, in particular glucagon-like peptide 1 receptor agonists (GLP-1RAs), which induce greater weight loss compared with previous AOMs, are increasingly being prescribed for patients with an inadequate response to LM [13–16]. Despite their efficacy, the use of GLP-1RAs is somewhat limited because of costs, drug shortages, insurance coverage, and intolerance [17]. Additionally, long-term efficacy and safety are unclear, including concerns regarding potentially irreversible GI motility disorders [18]. Finally, bariatric and metabolic surgery is considered the most effective treatment for class II and class III obesity [19, 20] and its related comorbidities [21–23]. Nevertheless, because of a variety of reasons, including cost, patient access, and potentially perceived invasiveness, less than 2 % of eligible patients currently choose to undergo surgery per year [24].

Endoscopic bariatric and metabolic therapies (EBMTs) have been developed and refined over the past 3 decades and are now increasingly performed worldwide. EBMTs are classically divided into gastric and small-bowel devices and procedures, with the former focusing primarily on weight loss with secondary effects on metabolic conditions and the latter focusing on metabolic conditions with or without weight loss [25, 26]. However, despite the increasing popularity of EBMTs over recent years, to date, there is no overarching guideline focusing on the field. This evidence-based guideline was jointly prepared by the American Society for Gastrointestinal Endoscopy (ASGE) and the European Society of Gastrointestinal Endoscopy (ESGE) and sought to address the efficacy and safety endpoints of gas-



▶ **Fig. 1** Gastric and small bowel endoscopic bariatric and metabolic therapies. ESG: endoscopic sleeve gastroplasty, POSE: primary obesity surgery endoluminal, DMR: duodenal mucosal resurfacing.

tric and small-bowel EBMTs as well as periprocedural care (▶ **Table 1**).

Target Goals for EBMTs

The amount of weight loss is the most important predictor for improvement in obesity-related comorbidities such as cardiovascular disease [27, 28], metabolic disorders (T2DM) [29], metabolic dysfunction–associated steatotic liver disease [30], and cancer [31]. Specifically, an improvement in comorbidity clinical endpoints starts at a weight loss of ≥ 5 %, which is associated with a decrease in serum glucose, insulin, triglyceride, and alanine transaminase [32]. In the Diabetes Prevention Program study, patients at risk for developing T2DM who were randomized to intensive LM and achieved ≥ 7 % total weight loss (TWL) at 12 months experienced a significant reduction in the cumulative incidence of T2DM [33]. In a post-hoc analysis of the Look AHEAD randomized clinical trial (RCT), which evaluated the effect of the amount of weight loss on cardiometabolic risk factors (n = 1428), patients with ≥ 8 % TWL at 1 year had the greatest reduction in hemoglobin A1c (HbA1c). They also sustained the most reduction in HbA1c at 4 years without or with partial recurrent weight gain (–.57 % and –.32 %, respectively) compared with those who achieved < 8 % TWL [34]. Similarly, another post-hoc analysis of this RCT found that patients who experienced ≥ 10 % TWL had a significant reduction in cardiovascular disease–related and all-cause mortalities [28]. For metabolic dysfunction–associated steatohepatitis [35], a study with paired liver biopsy samples before and at 52 weeks after LM (n = 261) found a dose-responsive improvement in metabolic dysfunction–associated steatohepatitis histologic features. Specifically, in patients with ≥ 10 % TWL, 90 % had resolution of metabolic dysfunction–associated steatohepatitis and 45 % had regression in liver fibrosis [30].

Target goals for EBMTs depend on the type of intervention. Specifically, for gastric interventions (intragastric balloons [IGBs], endoscopic gastric remodeling [EGR], aspiration therapy [AT], and transpyloric shuttle [TPS]), the primary efficacy endpoint is weight loss. For small-bowel interventions (duodenal-jejunal bypass liner [DJBL] and duodenal mucosal resurfa-

cing [DMR]), glycemic improvement is the primary efficacy endpoint, with weight loss as a co-primary or secondary endpoint for DJBL. Given the scope of this document with all relevant interventions included, cardiometabolic improvements were not analyzed independently. Nevertheless, the pooled weight loss of each intervention was assessed and compared with the 5 % to 10 % TWL threshold. If an intervention was associated with ≥ 5 % TWL, this suggested an improvement in cardiometabolic outcomes based on the findings described above.

Methods

This document represents the official recommendations of the ASGE and ESGE. It was developed by the primary EBMT guideline panel and approved by the ASGE and ESGE governing boards. The guideline was developed using the Grading of Recommendations Assessment, Development and Evaluation framework. The relevant clinical questions were developed a priori and listed in the PICO format, which outlined the specific patient population (P), intervention (I), comparator (C), and outcome (O) for each question (**Supplementary Table 1**, available online).

This document focused on EBMTs categorized by procedure type and not by specific device. Specifically, EBMTs that were approved or cleared by the U.S. Food and Drug Administration (FDA) or had a Conformité Européenne (CE) mark at the time of a literature search and 5 years before were included. The included procedures were IGB (Orbera IGB, Orbera365 IGB, Obalon IGB, Reshape IGB, and Spatz IGB), EGR (endoscopic sleeve gastroplasty [ESG] using the Overstitch Endoscopic Suturing System (Apollo Endosurgery, Austin, Tex, USA), primary obesity surgical endoluminal [POSE] using the Incisionless Operating Platform (IOP, USGI Medical, San Clemente, Calif, USA), and endoscopic gastric plication using the Endomina system (Endo Tools Therapeutics, Gosselies, Belgium)), aspiration therapy (AT) using the AspireAssist System (Aspire Bariatrics, King of Prussia, Penn, USA), Transpyloric Shuttle (TPS, BARONova INC, Goleta, Calif, USA), Duodenal Jejunal Bypass Liner (DJBL, GI Dynamics, Lexington, KY, USA) and duodenal mucosal resurfacing (DMR) using the Revita (Fractyl Health, Lexington, Mass, USA) (▶ **Fig. 1**). Evidence was presented to a panel of experts representing various stakeholders including bariatric endoscopy, bariatric surgery, obesity medicine, bariatric psychology, and nutrition. A patient advocate was also included. All panel members were required to disclose potential financial and intellectual conflicts of interest, which were addressed according to ASGE policies.

In developing these recommendations, we took into consideration the magnitude and certainty of evidence of benefits and harms of each intervention, feasibility, patient values and preferences, acceptability, resource requirement, cost, cost-effectiveness, and the impact on health equity. The final wording of the recommendation including direction and strength was approved by all members of the panel and the ASGE and ESGE governing boards. According to the Grading of Recommendations Assessment, Development and Evaluation approach, recommendations are labeled as "strong" or "conditional" and are phrased as "we recommend" or "we suggest," accordingly (▶ **Table 2** and ▶ **Table 3**). Further details of the methodology used for this guideline including, and results from all meta-analyses are presented in Appendix 1 (available online).

Results and Summary of Recommendations

A summary of all recommendations is provided in ▶ **Table 1**.

RECOMMENDATION 1

In adults with overweight or obesity, the ASGE–ESGE suggests the use of EBMTs plus LM over LM alone for patients with a body mass index (BMI) of ≥ 30 kg/m^2 or BMI of 27.0 to 29.9 kg/m^2 with at least 1 obesity-related comorbidity. *(Conditional recommendation, very low certainty)*

Implementation considerations

- For patients with a BMI of 27.0 to 29.9 kg/m^2 with at least 1 obesity-related comorbidity, data were available for IGB, EGR, and DJBL.
- For patients with class III obesity, data were available for IGB, EGR, AT, and DJBL.

Summary of the evidence

For the subgroup with BMIs of 27.0 to 29.9 kg/m^2, 6 observational studies were used to inform this PICO (IGB studies [55, 56], EGR study [57], and DJBL studies [58, 60]). Of these, 6 studies were used to assess safety [55–60], 4 studies for percentage of TWL [55–57, 59], and 3 studies for the change in HbA1c [58–60]. All studies on IGB and EGR only included patients who were overweight (BMI of 25.0–29.9 kg/m^2 or 27.0–29.9 kg/m^2). All DJBL studies included patients who were both overweight (starting BMI of 27.0 or 28.0 kg/m^2) and had obesi-

▶ **Table 2** Interpretation of the certainty in evidence of effects using the Grading of Recommendations Assessment, Development and Evaluation framework

Certainty	Description
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

From Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011;64:401–6.

▶ **Table 3** Interpretation of strong and conditional recommendations using the Grading of Recommendations Assessment, Development and Evaluation framework

Implications	Strong recommendation	Conditional recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	Most individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for individual patients consistent with their values and preferences. Use shared decision-making. Decision aids may be useful in helping patients make decisions consistent with their individual risks, values, and preferences.
For policymakers	The recommendation can be adapted as policy or performance measure in most situations.	Policymaking will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision-making is appropriate.

From Schünemann HJ, Mustafa RA, Brozek J, et al. GRADE guidelines: 22. The GRADE approach for tests and strategies-from test accuracy to patient-important outcomes and recommendations. J Clin Epidemiol 2019;111:69–82; Grunvald E, Shah R, Hernaez R, et al. AGA clinical practice guideline on pharmacological interventions for adults with obesity. Gastroenterology 2022;163:1198–225.

ty. Mean age ranged from 38 to 52 years and BMI from 29.7 to 43.1 kg/m^2. All studies prescribed concomitant LM, except for Moore et al [56], where the intensity of LM varied across sites given the nature of real-world experience (**Supplementary Table 2**, available online).

For the subgroup with classes I and II obesity, 17 RCTs were used to inform this PICO (IGB studies [39–44], EGR studies [45–47, 62], AT studies [48, 52], TPS studies [49], DJBL studies [50, 51, 63], and DMR studies [64]). Of these, 15 studies were used to assess safety [39, 40,42–46,49–52,61–64],14 studies for percentage of TWL [39–47, 49–52, 64], and 2 studies for the change in HbA1c [50, 51]. All IGB, EGR, and TPS studies only included patients with classes I and II obesity. Otherwise, the remainder included a combination of different classes of obesity (classes II and III for AT; classes I, II, and III for DJBL; and overweight and classes I and II for DMR). Mean age ranged from 38 to 58 years and BMI from 31.5 to 42.0 kg/m^2. Most studies compared EBMTs with LM alone, whereas Sullivan et al [44], Ponce et al [43], Sullivan et al [47], Rothstein et al [49], Thompson et al [50], and Mingrone et al [64] compared EBMTs with sham (**Supplementary Table 3**, available online).

For the subgroup with class III obesity, 31 observational studies and RCTs (interventional arms only) were used to inform this PICO (IGB studies [55, 56, 61, 65–73], EGR studies [57, 74], AT studies [48, 52, 75], and DJBL studies [50, 51, 58, 59, 63, 76–84]). Of these, 26 studies were used to assess safety [48, 50–52, 57–59, 63, 67–84], 20 studies for percentage of TWL [48, 50–52,55–57,59,61,65–69,71–75,81], and 10 studies for the changes in HbA1c [50, 51,58,59,79–84]. All IGB and EGR studies only included patients with class III obesity, whereas AT and DJBL studies included both class III and other classes of obesity (class II ± class I). Mean age ranged from 33 to 58 years and BMI from 34.6 to 69.1 kg/m^2. All studies prescribed concomitant LM, except for Moore et al [56], where the intensity of LM varied across sites given the nature of real-world experience (**Supplementary Table 4**, available online).

Benefits

For the subgroup with BMIs of 27.0 to 29.9 kg/m^2, 4 observational studies (n = 692) informed the outcomes of percentage of TWL at 6 months (for IGB) or 12 months (for EGR and DJBL) and 3 studies (n = 436) for HbA1c reduction at 12 months (for DJBL) [55–60]. The pooled weight loss at 6 to 12 months was 11.9 % TWL (95 % confidence interval [CI], 7.7–16.0) (**Supplementary Fig. 1**, available online) and pooled HbA1c reduction at 12 months was 1.0 % (95 % CI, .6–1.5) (**Supplementary Fig. 2**, available online).

For the subgroup with classes I and II obesity, 14 RCTs (n = 2787) informed the outcomes of percentage of TWL at 12 months [39–47, 49–52, 64] and 2 studies (n = 490) for HbA1c reduction at 12 months [50, 51]. A total of 1636 subjects were in the EBMT plus LM group and 1151 in the LM group. The mean difference (MD), which represented the difference between the pooled percentage of TWL in the EBMT arm minus the control arm, at IGB removal or 12 months after EGR, AT, DJBL, or TPS was 7.1 % (95 % CI, 5.4–8.8) in favor of EBMT (**Supplementary Fig. 3**, available online). The mean TWL of the EBMT arm ranged from 5.0 % to 18.6 % at IGB removal or 12 months for EGR, DJBL, AT, or TPS. The MD, which represented the difference between the pooled HbA1c reduction in the EBMT arm minus the control arm, at 12 months was .7 % (95 % CI, .4–1.1) in favor of EBMT (**Supplementary Fig. 4**, available online). The mean HbA1c reduction of the EBMT arms ranged from 1.1 % to 1.5 % at 12 months.

For the subgroup with class III obesity, 20 observational studies (n = 2776) informed the outcomes of percentage of TWL at 6 to 12 months [48, 50–52, 55–57, 59, 61, 65–69, 71–75, 81] and 10 studies (n = 815) for HbA1c reduction at 12 months [50, 51, 58, 59, 79–84]. The pooled TWL at 6 to 12 months was 13.1 % (95 % CI, 10.8–15.4) (**Supplementary Fig. 5**, available online) and pooled HbA1c reduction at 12 months was 1.3 % (95 % CI, 1,0–1.6) (**Supplementary Fig. 6**, available online).

Harms

For the subgroup with BMIs of 27.0 to 29.9 kg/m^2, 6 observational studies informed the outcome of serious adverse events (SAEs; n = 7416) [55–60]. SAEs were defined by the investigators and reported in the original studies. The pooled estimate for SAEs showed an event rate of 2.7 % (95 % CI, 1.2–6.0) (**Supplementary Fig. 7**, available online).

For the subgroup with classes I and II obesity, 16 RCTs informed the outcome of SAEs (n = 1464) [39, 40, 42–46, 49–52, 62–64]. The pooled estimate for SAEs showed an absolute risk of 14 additional SAEs per 1000 subjects [6, 30] in the EBMT group (111/2135) compared with the control group (6/1464) (**Supplementary Fig. 8**, available online).

For the subgroup with class III obesity, 26 studies informed the outcome of SAEs (n = 2042) [48, 50–52, 57–59, 63, 67–84]. The pooled estimate for SAEs showed an event rate of 6.9 % (95 % CI, 5.7–8.2) (**Supplementary Fig. 9**, available online).

Certainty of evidence assessment

The certainty in the evidence of effects of EBMTs in the subgroup with BMIs of 27.0 to 29.9 kg/m^2 with at least 1 comorbidity, subgroup with classes I to II obesity, and subgroup with class III obesity was very low, low, and very low, respectively (**Supplementary Table 5**, available online). Therefore, the overall certainty in the evidence of this PICO (ie, the effects of EBMTs for patients with a BMI of ≥ 30 kg/m^2 or 27.0–29.9 kg/m^2 with ≥ 1 comorbidity) was deemed to be very low.

In the subgroup with BMI of 27.0 to 29.9 kg/m^2, for the weight loss outcome, there was a concern for confounding bias in some studies as well as inconsistency and indirectness because some studies reported the amount of weight loss in both the overweight and obesity groups combined. For the HbA1c outcome, there was a concern for inconsistency, indirectness (because of a mixed overweight and obesity population in some studies), and imprecision (because of a small total number of patients). For harms, there was a very low certainty in evidence given the inconsistency, indirectness (because of a mixed overweight and obesity population in some studies), and imprecision (because of a small number of SAEs) (**Supplementary Table 6**, available online).

In the subgroup with classes I and II obesity, there was inconsistency in the amount of weight loss, which was likely explained by the heterogeneity among different EBMT devices and/or procedures pooled. For the HbA1c outcome, there was imprecision because the CI crossed the line of no difference. For harms, the certainty of evidence was downgraded twice for imprecision because of a low event rate and wide CI (**Supplementary Table 7**, available online).

In the subgroup with class III obesity, for the weight loss outcome, there was a concern for confounding bias in some studies as well as inconsistency and indirectness because some studies reported the amount of weight loss of both class III obesity and other classes combined. For the HbA1c outcome, there was a concern for inconsistency and indirectness with some studies reporting the outcomes of both class III obesity and other classes combined. For harms, there was a very low certainty in evidence given the inconsistency, indirectness, and imprecision because of a small number of SAEs (**Supplementary Table 8**, available online).

Discussion

To assess the patient populations in which EBMTs should be considered, we divided the potential populations into 3 categories based on BMI: BMI of 27.0 to 29.9 kg/m^2 with at least 1 obesity-related comorbidity, classes I and II obesity, and class III obesity. Because most EBMTs included in this guideline were approved or cleared for classes I and II obesity, only RCTs were included for this population. In contrast, for the BMI of 27.0 to 29.9 kg/m^2 and class III obesity subgroups, no RCTs specifically assessed the effect of EBMTs in these 2 populations. Therefore, observational studies were evaluated.

For the overweight category, whereas Moore et al [56] and Barrichello et al [57] included patients with BMIs of 25.0 to 29.9 kg/m^2, most studies included patients starting at BMIs of 27 or 28 kg/m^2 [55–60]. Additionally, half of the studies included patients with at least 1 obesity-related comorbidity (T2DM). Therefore, the panel decided to use a conservative cutoff for this patient population with a starting BMI of 27 kg/m^2 with at least 1 comorbidity. For the class III obesity category, all IGB and EGR studies [55–57, 61, 65–74] only included patients with class III obesity, whereas AT and DJBL studies [48, 50–52, 58, 59, 75, 79–84] included both class III and class II ± class I obesity. Although some studies had a cutoff for the highest BMI at 50 or 55 kg/m^2 [48, 50–52, 55–59, 61, 63, 69, 70, 74, 76–84], some did not and recruited patients with BMIs up to 70 or 78 kg/m^2 [65–68, 71–73, 75, 82]. The panel accepted the heterogeneity in this patient population. However, given that EBMTs may be used for either primary therapy or bridge therapy before bariatric surgery, the panel agreed to not having an upper limit of BMI for consideration of EBMTs.

The amount of weight loss after EBMT was determined to be moderate for all BMI subgroups. Specifically, the amount of weight loss was 11.9 % (95 % CI, 7.7–16.0) and 13.1 % (95 % CI, 10.8–15.4) TWL in the BMI of 27.0 to 29.9 kg/m^2 and class III obesity subgroups, respectively. For the subgroup with classes I and II obesity, the MD, representing the difference between the pooled percentage of TWL in the EBMT arm minus the control arm, was 6.3 % (95 % CI, 5.3–7.3) in favor of EBMT, with the absolute percentage of TWL in the EBMT arm ranging from 5.0 % to 18.6 % at 12 months. For the BMI of 27.0 to 29.9 kg/m^2 and class III obesity studies, the lower CI of percentage of TWL was 7.7 % and 10.8 %, respectively. Given the pooled average of 3.2 % TWL for the historical control subjects from all EBMT RCTs (**Supplementary Fig. 10**, available online), the MD of the amount of weight loss between the EBMT and control groups in these 2 populations should remain above the 3 % TWL minimal important difference threshold (MDs of 4.5 % and 7.6 % TWL, respectively). Similarly, for the subgroup with classes I and II obesity, not only did the lower CI of the overall MD lie above the 3 % TWL minimal important difference threshold, but our sensitivity analysis also showed that the lower CI of the MD of every EBMT also lay above this threshold (**Supplementary Fig. 3**). Additionally, all studies but IGB reported the

weight loss outcome at 12 months. For IGB, all studies reported percentage of TWL at the time of IGB removal (6–8 months). Although Nunes et al [85] reported percentage of TWL in the subgroups with overweight and class III obesity at 12 months (ie, 6 months after IGB removal), this study evaluated the effect of IGB plus a very-low-calorie diet, which likely biased the magnitude of weight loss [86]. Therefore, this study was excluded. The effect of IGB on weight loss after IGB removal in the subgroups with overweight and class III obesity therefore remains to be assessed. The panel also noted inconsistency in the amount of weight loss, especially for class III obesity. This was believed to be because of a heterogeneity of the patient populations, with some studies including patients with BMIs up to 55 kg/m^2 for a primary therapy as an alternative to bariatric surgery [48, 50–52, 55–59, 61, 63, 69, 70, 74, 76–84] and others including patients with BMIs up to 78 kg/m^2 for bridge therapy before bariatric surgery [65–68, 71–73, 75, 82]. The certainty of evidence was downgraded because of this inconsistency.

The SAE rate was 2.7 % (95 % CI, 1.2–6.0) and 6.9 % (95 % CI, 5.7–8.2) for the BMI of 27.0 to 29.9 kg/m^2 and class III obesity subgroups, respectively. For the subgroup with classes I and II obesity, the risk ratio of SAEs in the EBMT arm compared with the control arm was 4.4 (95 % CI, 2.4–8.2), which was equivalent to 14 additional events per 1000 subjects. The SAE rate in the EBMT arm ranged from 0 % to 10.6 %. Of note, the panel found that the wide CIs for pooled SAE rates were likely because of the difference in SAE definitions used by the authors, especially for DJBL studies. For example, although most DJBL studies defined SAEs as those resulting in early device explantation, Stratmann et al [82] only reported the rate of early device explantation and Roehlen et al [77] only reported the rate of SAEs without reporting the number of early device explantations. In contrast, early removal of IGBs has not been considered as a SAE in most trials, and specifically in the United States, RCTs would not meet the FDA categorization of SAE by itself.

Currently, the number of studies evaluating the cost-effectiveness of EBMTs is limited. Saumoy et al [87] and Kelly et al [88] demonstrated that ESG was cost-effective compared with LM alone in class II obesity in the United States and United Kingdom, respectively. Haseeb et al [89] showed that ESG was cost-effective compared with GLP-1RA and sleeve gastrectomy in class II obesity in the United States. Although currently no study has specifically evaluated the cost-effectiveness of EBMTs in other obesity classes or in an overweight population, the panel agreed that EBMTs would most likely be cost-effective, especially when compared with LM, in these other BMI categories.

The panel considered the current state of EBMTs to be associated with reduced equity for all BMI subgroups. This is solely because of the lack of insurance coverage for EBMTs in most countries. This leads to inequity between those patients who are able to afford the procedures and those who are not and potentially between the nonminority and minority. The panel noted that with universal insurance coverage, EBMTs will improve equity by providing better access to safe and effective care for more patients who suffer from obesity or overweight with at least 1 obesity-related comorbidity.

RECOMMENDATION 2

In adults with obesity, the ASGE–ESGE suggests the use of an IGB plus LM over LM alone.

(*Conditional recommendation, moderate certainty*)

Rationale

A conditional recommendation is driven primarily by moderate variability in patient values and preferences. Specifically, although the IGB is generally acceptable among most patients suffering from obesity, some may prefer a less-invasive treatment approach (ie, LM) despite a lower weight loss than seen with the IGB. Therefore, treatment options should be discussed to encourage shared decision-making.

Summary of the evidence

We identified a recently published guideline on IGB, which conducted a systematic review and meta-analysis with a comprehensive search strategy (MEDLINE, Embase, and Cochrane Library) from inception to January 2020 [36, 90]. We updated the search to March 2021 and found no additional RCTs that met our inclusion and exclusion criteria. Therefore, 7 RCTs assessing the safety and efficacy of IGB were used to inform this PICO [39–44, 91]. All 7 studies reported percentage of TWL at the time of IGB removal (6–8 months), and 2 studies reported percentage of TWL at 12 months [40, 41]. Mean age and BMI of the intervention arm ranged from 38.7 to 44.4 years and from 30.3 to 53.9 kg/m^2, respectively. The interventional arm of all studies underwent concomitant LM. The control arms of Sullivan et al [44] and Ponce et al [43] underwent a sham procedure with concomitant LM, whereas the rest of the studies underwent LM alone (**Supplementary Table 9**, available online).

Benefits

Seven RCTs informed the outcome of percentage of TWL at the time of IGB removal (6–8 months) [39–44, 91], and 2 RCTs informed the outcome of percentage of TWL at 12 months [40, 41]. Seven hundred seventy-nine subjects were in the IGB plus LM group and 654 in the LM group. The MD, representing the difference between the pooled percentage of TWL in the IGB arm minus the control arm at the time of IGB removal (6–8 months), was 6.9 % TWL (95 % CI, 4.1–9.7) in favor of the intervention (**Supplementary Fig. 11**, available online). This represented a 3.1 times greater weight loss in the IGB arm compared with the control arm (pooled weight loss of 10.7 % TWL in the IGB arm vs 3.4 % TWL in the control arm). The MD for percentage of TWL at 12 months was 4.4 % TWL (95 % CI, 2.9–6.0) (**Supplementary Fig. 12**). This represented a 2.4 times greater weight loss in the IGB arm compared with the control arm (pooled weight loss of 7.9 % TWL in the IGB arm vs 3.3 % TWL in the control arm).

Harms

Seven RCTs informed the outcome of SAEs [39–44, 91]. SAEs were defined by the investigators and reported in the original studies. The pooled estimate for SAEs showed an absolute risk of 32 additional SAEs per 1000 subjects (95 % CI, 7–114) in the IGB group (58/1028) compared with the control group (0/798) (**Supplementary Fig. 13**, available online). Selected examples of SAEs from studies that reported particular SAE outcomes included esophageal mucosal injury (4/473), gastric ulcer/bleeding (5/650), severe dehydration (5/704), aspiration pneumonia (2/42), perforation (2/653), gastric outlet/bowel obstruction (1/802), and mortality (0/741) (**Supplementary Table 10**, available online).

Certainty of evidence assessment

The overall certainty in the evidence of effects for IGB was moderate (**Supplementary Tables 11** and **12** and **Supplementary Fig. 14**, available online). For benefits at 6 months, we found imprecision with weight loss because of the wide CI and some inconsistency that was not deemed of serious concern by itself, and no additional downgrading was performed. For benefits at 12 months, imprecision was found because of a small sample size and CI that crossed the line of no difference. For harms, there was moderate certainty in evidence given a small number of SAEs with a wide CI.

Discussion

The first IGB approved for use was the Garren-Edwards Gastric Bubble (American Edwards Laboratories, Irvine, Calif, USA) in 1985, an air-filled balloon made of polyurethane in a cylindrical shape that was removed from the market in 1988 because of SAEs and lack of effective weight loss [92–94]. Current IGBs have been designed to mitigate AEs and have demonstrated weight loss efficacy in sham-controlled trials as noted in the summary of evidence. The next generation of IGBs approved in the United States and Europe came in 2015 and 2017, respectively, but IGBs have been used around the world since the 1990 s.

The mechanism of action of IGBs for weight loss is likely multifactorial. Early data suggested that at least 400 mL of space occupation in the stomach was required to reduce meal volume [95]. Subsequent analysis of gastric emptying has demonstrated that the effects of fluid-filled IGBs are also in part because of a reduction in the rate of gastric emptying during balloon implantation [96]. These mechanisms may help explain the recurrent weight gain that can occur after balloon removal, because the currently understood mechanisms for weight loss require balloon presence.

The magnitude of weight loss with IGB at 6 months was determined to be moderate, with a wide CI based on the mix of sham-controlled and open-label RCTs included in the analysis. An analysis comparing open-label and sham IGB RCTs found that the sham study design lowered weight loss compared with open-label studies [97]. Combining open-label and sham-controlled studies in this analysis may underestimate the true effect of IGB in a clinical setting; however, this is the most conservative approach. Additionally, the panel noted that weight loss was lower at 12 months (6 months after IGB removal) than at IGB removal. Although weight loss at the 12-month time point was still significant, patients considering IGB therapy should be made aware of the likely regain of some weight within 6 months of IGB removal. Studies have evaluated repeated use of IGB for longer term obesity treatment [98, 99], but repeated IGB therapy was not evaluated in this recommendation.

SAEs were also discussed by the panel. The SAE rate was 5.6 %, but safety varied across the gas-filled compared with fluid-filled balloons [39, 40, 43, 44]. Of note, most SAEs were related to short-term accommodative symptoms including nausea and vomiting, leading to dehydration and abdominal pain. Although these did meet the FDA criteria for SAEs, they were short-lived and resolved without sequelae, leading the panel to determine the reported rates of SAEs were acceptable.

The panel also found current reduced equity related to IGB treatment. This is solely because of the lack of insurance coverage of IGB in most countries. This leads to inequity between those patients who are able to pay out of pocket for IGB treatment and those patients who are not. The panel noted that insurance coverage is crucial to reduce inequity and improve access to recommended obesity treatments. The panel found that acceptability of IGBs was high with the caveat of some recurrent weight gain 6 months after IGB removal and noted that some patients favor the shorter duration of treatment with no permanent changes to the anatomy of the GI tract.

RECOMMENDATION 3

In adults undergoing IGB placement, the ASGE–ESGE suggests the use of antiemetics periprocedurally.
(*Conditional recommendation, very low certainty*)

Further details regarding the rationale for this recommendation including the results of systematic reviews, expert survey, and evidence profile are presented in Appendix 2 (available online).

RECOMMENDATION 4

In adults undergoing IGB placement, the ASGE–ESGE suggests the use of pain medications periprocedurally.
(*Conditional recommendation, very low certainty*)

Further details regarding the rationale for this recommendation including the results of systematic reviews, expert survey, and evidence profile are presented in Appendix 3 (available online).

RECOMMENDATION 5
In adults undergoing IGB placement, the ASGE–ESGE suggests the use of proton pump inhibitors (PPIs) while the IGB is in place over no PPIs.
(*Conditional recommendation, very low certainty*)

Further details regarding the rationale for this recommendation including the results of systematic reviews, expert survey, and evidence profile are presented in Appendix 4 (available online).

RECOMMENDATION 6
In adults with obesity, the ASGE–ESGE suggests treatment with EGR plus LM over LM alone.
(*Conditional recommendation, moderate certainty*)

Implementation consideration

- EGR may be performed using the Overstitch Endoscopic Suturing System (Apollo Endosurgery), Incisionless Operating Platform (IOP; USGI Medical), or Endomina System (Endo Tools Therapeutics). Prolene sutures are placed in the stomach to reduce its volume in all cases. The procedures have been generally referred to as endoscopic gastric plication or ESG, originally described with the Overstitch Endoscopic Suturing System. The primary obesity surgery endoluminal (POSE) procedure specifically referred to a procedure with the IOP; however, these also have been referred to as plication ESG in the literature. Evidence is insufficient to specifically recommend 1 device over another. The choice of device is based on clinical context, patient values, availability, and operator experience.

Rationale

A conditional recommendation is driven primarily by moderate variability in patient values and preferences. Specifically, although EGR is generally acceptable among most patients suffering from obesity, some may prefer a less-invasive treatment approach (ie, LM) despite lower weight loss than seen with the EGR. Therefore, treatment options should be discussed to encourage shared decision-making. In addition, insurance coverage is frequently lacking. A greater number of patients would elect to get EGR if it were universally covered by insurance. Furthermore, insurance coverage would reduce healthcare inequity.

Summary of the evidence

Four RCTs assessing the safety and efficacy of EGR were used to inform this PICO [45–47, 62]. Of these, 4 studies were used to assess safety [45–47, 62], and 3 studies were used to assess efficacy [45–47, 62]. In Huberty et al [62], the control arm was offered a crossover to the intervention arm at 6 months; therefore, the efficacy, which is the difference in mean weight loss between 2 two arms at 12 months, was not able to be assessed. Of the 4 studies, 1 study [45] used the Overstitch suturing device, 2 studies [46, 47] used the IOP plication system, and 1 study [62] used the Endomina plication system to perform EGR. Mean age and BMI of the intervention arm ranged from 38 to 47 years and from 34.8 to 36.2 kg/m^2, respectively (**Supplementary Table 9**). The intervention arm of all studies underwent concomitant LM (moderate intensity for all studies except for Sullivan et al [47], which underwent concomitant low-intensity LM). The control arm of Sullivan et al [47] underwent a sham procedure with concomitant low-intensity LM, whereas in the remaining studies moderate-intensity LM alone was used (**Supplementary Table 9**).

Benefits

Three RCTs informed the outcome of percentage of TWL at 12 months [45–47]. Three hundred forty subjects were in the EGR plus LM group and 245 in the LM group. The MD, representing the difference between the pooled percentage of TWL in the EGR arm minus the control arm at 12 months, was 8.0 % TWL (95 % CI, 3.4–12.6) in favor of the intervention (**Supplementary Fig. 15**, available online). This represented a 4.4 times greater weight loss in the EGR arm compared with the control arm (pooled weight loss of 10.5 % TWL in the EGR arm vs 2.4 % TWL in the control arm).

A separate meta-analysis including only observational studies was conducted. Twenty-one studies with 5250 patients reported percentage of TWL at 12 months after EGR and were included [57, 74, 100–116, 133, 134]. Of these, 16 studies (4880 patients) used the Overstitch suturing device, 4 studies (319 patients) used the IOP plication system, and 1 study (51 patients) used the Endomina plication system to perform EGR. Mean age ranged from 34 to 56 years and BMI from 32.5 to 49.9 kg/m^2. At 12 months, the pooled average weight loss was 17.3 % TWL (95 % CI, 16.2–18.4) (**Supplementary Fig. 16A**, available online). A subgroup analysis based on the device demonstrated the efficacy of EGR performed using the Overstitch endoscopic suturing device, IOP, and Endomina plication system to be 18.2 % TWL, 16.5 % TWL and 7.0 % TWL, respectively, at 12 months (**Supplementary Fig. 16B**).

Harms

Four RCTs informed the outcome of SAEs [45–47, 62]. SAEs were defined by the investigators and reported in the original studies. The pooled estimate for SAEs showed a relative risk of 5.6 (95 % CI, 1.1–30.1) when comparing the EGR group (14/435) with the control group (1/253) (**Supplementary Fig. 17**, available online). Selected examples of SAEs from the ESG study included abdominal abscess treated with endoscopy (1/131), upper GI bleeding managed conservatively (1/131), and malnutrition treated with endoscopic reversal of the ESG (1/131). Selected examples of SAEs from the largest plication ESG study included extraluminal bleeding treated with laparoscopy (1/221), hepatic abscess treated with percutaneous drainage (1/221), and abdominal pain, nausea, or vomiting requiring pro-

longed hospitalization (9/221) (**Supplementary Table 13**, available online).

Certainty of evidence assessment

The overall certainty in the evidence of effects for EGR was moderate (**Supplementary Tables 11** and **14** and **Supplementary Fig. 18**, available online). For benefits, we found indirectness for weight loss, making us rate the certainty in evidence down to moderate. Specifically, whereas Abu Dayyeh et al [45] used the current technique with placing stitches in the gastric body to reduce its volume, Miller et al [46] and Sullivan et al [47] used the former technique, which focused on placing plications in the fundus. This difference in techniques likely explained inconsistency and imprecision of the MD in weight loss. Additionally, the control group in Sullivan et al [47] underwent a sham procedure with concomitant low-intensity LM, which has been shown to be associated with a smaller MD in weight loss compared with a non-sham control group. For harms, there was moderate certainty in evidence given a small number of SAEs with a wide CI.

Discussion

This analysis included several types of devices for gastric remodeling including the Overstitch suturing device, IOP plication device, and Endomina plication device. Although these devices create tissue plications differently, the result is similar. All procedures reduce the width and length of the stomach and are believed to delay gastric emptying [74, 123, 124]. Currently, the Overstitch has a CE mark and FDA De Novo marketing authorization for the treatment of obesity, whereas the IOP and Endomina have a CE mark and FDA 510(k) clearance for tissue approximation of the GI tract.

For EGR, the MD in weight loss, representing the difference between the pooled percentage of TWL in the EGR arm minus the control arm, at 12 months was 8.0% TWL (95% CI, 3.4–12.6) in favor of the intervention. The certainty of this evidence was rated moderate. Variability was seen across the 3 RCTs on EGR likely because of several factors. First, the trial with the lowest weight loss in the intervention arm was a sham-controlled study (4.95% ± 7.04% TWL). Within that trial, a lead-in group of 34 subjects who were unblinded to their treatment achieved 40% more weight loss than the treatment patients who were blinded to study assignment [47]. Additionally, the same technique was used in a different trial included in the analysis. Treatment patients achieved significantly more weight loss in this open-label RCT (13.0%; 95% CI, 10.3–15.8) [46], supporting the hypothesis that the sham study design artificially reduces weight loss in the treatment arm of an EBMT study. Including the randomized sham-controlled study therefore may have artificially lowered the weight loss compared with what can be expected in clinical practice but is the most conservative analysis.

Four RCTs with at least 6 months of data were included in the safety analysis with a low SAE rate of 3.2%. Additionally, some of these SAEs were because of accommodative symptoms of nausea and vomiting causing dehydration and abdominal pain, which were short-lived and resolved without sequelae.

Similar to IGBs, the panel agreed that EGR currently reduces equity solely because it is not covered by the national health system or insurance in most countries. Therefore, in most countries only patients who can pay out of pocket have access to this therapy. Equity would substantially increase by expanding options and accessibility to a wider range of patients with obesity, including the under-represented minority patients with obesity, and if this procedure was covered universally by national health systems and insurance companies. The panel also agreed that acceptability of endoscopic suturing/plication remodeling of the stomach is high among patients seeking obesity treatment.

RECOMMENDATION 7
In adults undergoing EGR, the ASGE–ESGE suggests the use of antiemetics periprocedurally.
(*Conditional recommendation, very low certainty*)

Further details regarding the rationale for this recommendation including the results of systematic reviews, expert survey, and evidence profile are presented in Appendix 5 (available online).

RECOMMENDATION 8
In adults undergoing EGR, the ASGE–ESGE suggests the use of pain medications periprocedurally.
(*Conditional recommendation, very low certainty*)

Further details regarding the rationale for this recommendation including the results of systematic reviews, expert survey, and evidence profile are presented in Appendix 6 (available online).

RECOMMENDATION 9
In adults undergoing EGR, the ASGE–ESGE suggests the use of short-term antibiotics periprocedurally.
(*Conditional recommendation, very low certainty*)

Further details regarding the rationale for this recommendation including the results of systematic reviews, expert survey and evidence profile are presented in Appendix 7 (available online).

RECOMMENDATION 10
In adults undergoing EGR, the ASGE–ESGE suggests the use of short-term PPIs after the procedure over no PPIs.
(*Conditional recommendation, very low certainty*)

Further details regarding the rationale for this recommendation including the results of systematic reviews, expert survey and evidence profile are presented in Appendix 8 (available online).

RECOMMENDATION 11
In adults with obesity, the ASGE–ESGE suggests treatment with AT plus LM over LM alone depending on device availability.
(*Conditional recommendation, low certainty*)

Further details regarding the rationale for this recommendation including the results of systematic reviews, meta-analyses, and evidence profile are presented in Appendix 9 (available online).

RECOMMENDATION 12
In adults with obesity, the ASGE–ESGE recommends treatment with TPS only in the context of a clinical trial.
(*No recommendation, knowledge gap*)

Summary of the evidence

One RCT assessing the safety and efficacy of TPS was used to inform this PICO [49]. The study included subjects with class I obesity with at least 1 comorbidity and class II obesity with or without a comorbidity. Mean age and BMI of the intervention arm were 43 years and 36.8 kg/m^2, respectively. The intervention arm underwent concomitant moderate-intensity LM, whereas the control arm underwent a sham procedure with concomitant moderate-intensity LM (**Supplementary Table 9**).

Benefits

One RCT informed the outcome of percentage of TWL at 12 months [49]. One hundred eighty-one subjects were in the TPS plus LM group and 89 in the sham plus LM group (**Supplementary Table 9**). The MD, representing the difference between the mean percentage of TWL in the TPS arm minus the control arm at 12 months, was 6.7 % TWL (95 % CI, 4.5–8.9) in favor of the intervention (**Supplemental Fig. 19**, available online).

Harms

One RCT informed the outcome SAEs [49]. SAEs were defined by the investigators and reported in the original study. The SAEs showed an absolute risk of 18 additional SAEs per 1000 subjects (95 % CI, 3–380) in the TPS group (6/213) compared with the control group (0/89) (**Supplementary Fig. 20**, available online). These SAEs included esophageal rupture requiring a surgical repair (1/213), upper abdominal pain/device impaction (1/213), vomiting/device impaction (1/213), gastric ulcer/device impaction (1/213), device intolerance (1/213), and device impaction (1/213) (**Supplementary Table 15**, available online).

Certainty of evidence assessment

The overall certainty in the evidence of effects for TPS was low (**Supplementary Tables 11** and **16**, available online). Risk of bias was judged as not serious (**Supplementary Fig. 21**, available online). The only limitation of the efficacy evidence was imprecision because of a small number of patients included in the study. For harms, there was a low certainty in the evidence given a small number of SAEs with a wide CI that crossed the line of no difference.

Discussion

The TPS is a gastric device with FDA approval in the United States; however, it has not yet been commercialized. Unlike the IGB, it is not a space-occupying device. The mechanism of action is related to the device causing intermittent gastric outlet obstruction with the larger portion of the device, bobbing between the antrum and pylorus with gastric contractions. Because the larger portion of the device is filled with silicone, it does not have a risk of deflation and has FDA approval for 12 months of dwell time. However, only 1 RCT was available for analysis of the current generation of the TPS [49]. One previous pilot study was performed evaluating an earlier design of the device, but that device was associated with a high rate of ulceration that occurred in 50 % of patients [127] and necessitated the design change to its current form. The U.S. multicenter randomized sham-controlled trial demonstrated significant weight loss over sham and a low SAE rate of 2.8 %, but there were only 213 patients who received the device either in the active arm or an open-label extension arm and 89 control patients. Moreover, because the device has not been commercialized, only a few members of the panel had any experience with the device, and this experience was limited to the study setting. Because of the insufficient real-world experience with the device, the panel recommended using this device for treating obesity only in the context of a clinical trial.

RECOMMENDATION 13
In adults with obesity and T2DM, the ASGE–ESGE suggests treatment with the DJBL plus LM over LM alone.
(*Conditional recommendation, moderate certainty*)

Implementation considerations

- The DJBL is an EBMT device for the treatment of T2DM and obesity. The current generation is designed for a 12-month implant duration period.

Summary of the evidence

Three RCTs assessing the safety and efficacy of the DJBL were used to inform this PICO [50, 51, 63]. Of these, 3 studies were used to assess safety [50, 51, 63], and 2 studies were used to assess efficacy [50, 51]. In Koehestanie et al [63], the DJBL was implanted for 6 months. Therefore, the efficacy, which is the difference in HbA1c reduction and percentage of TWL between the 2 arms at 12 months, was not able to be assessed. Otherwise, both Thompson et al [50] and Ruban et al [51] had the DJBL implanted for 12 months. All studies included subjects with obesity and concomitant T2DM. Mean age, BMI, and HbA1c of the intervention arm ranged from 49.5 to 53 years, 34.6 to 38.4 kg/m^2, and 8.3 % to 8.9 %, respectively. In Thompson et al [50], the intervention arm underwent DJBL implantation and concomitant low-intensity LM, whereas the control arm underwent low-intensity LM alone (**Supplementary Table 9**).

Benefits

Two RCTs informed the outcomes of HbA1c reduction and percentage of TWL at 12 months [91, 93]. Two hundred ninety-eight subjects were in the DJBL plus LM group and 192 in the LM group. The MD, representing the difference between the pooled HbA1c reduction in the DJBL arm minus the control arm at 12 months, was .73 % (95 % CI, .39–1.06) in favor of the intervention (**Supplementary Fig. 4**, available online). The MD, representing the difference between the pooled percentage of TWL in the DJBL arm minus the control arm at 12 months, was 5.4 % TWL (95 % CI, 4.1–6.7) in favor of the intervention (**Supplementary Fig. 22**).

A separate meta-analysis including the active arm of the RCTs and observational studies of DJBL studies of the same patient population (obesity with concomitant T2DM) was previously conducted [128]. Fourteen studies with 412 DJBL patients were included with a median implantation duration of 33 weeks (range, 12–52). Mean age ranged from 36 to 54 years, BMI from 30.0 to 48.9 kg/m^2, and HbA1c from 6.7 % to 9.2 %. At the time of DJBL explantation, the pooled HbA1c reduction and weight loss were 1.3 % (95 % CI, 1.0–1.6) and 18.9 % TWL (95 % CI, 7.2–30.6), respectively.

Harms

Three RCTs informed the outcome of SAEs [50, 51, 63], which were defined as events that resulted in early explant. In Ruban et al [51], the rate of early explant was not reported. Therefore, the worldwide registry was reviewed, and the SAEs were categorized based on the AGREE classification and need for early explantation. The pooled estimate for SAEs showed an absolute risk of 24 additional SAEs per 1000 subjects (95 % CI, 8–59) in the DJBL group (26/331) compared with the control group (0/232) (**Supplementary Fig. 23**, available online). Selected examples of SAEs from the U.S. pivotal study (ENDO trial) included intolerance (8/212), hemorrhage (6/212), hepatic abscess (5/212), DJBL obstruction (3/212), pancreatitis (2/212), intestinal perforation (1/212), and ulceration (1/212) (**Supplementary Table 17**, available online).

Certainty of evidence assessment

The overall certainty in the evidence of effects for DJBL implantation was moderate (**Supplementary Tables 11** and **18** and **Supplementary Fig. 24**, available online). For benefits, because the lower 95 % confidence limit for HbA1c reduction crossed the minimal clinically important difference of .5 %, the evidence was rated down for imprecision. The certainty of evidence for percentage of TWL, otherwise, was rated as high. For harms, there was moderate certainty in the evidence given a small number of SAEs with a wide CI.

Discussion

As noted in the Introduction, the small bowel plays a role in glucose homeostasis, and treatments targeting the small bowel likely have effects that are independent of weight loss. In an effort to mimic the effects of Roux-en-Y gastric bypass where the duodenum and part of the jejunum are bypassed, more than 1 device has been developed to bypass the jejunum with or without bypassing other portions of the GI tract. Only 1 of these devices, the DJBL, has been studied in RCTs and was previously approved for use in Europe with a CE mark that was obtained in 2010. The CE mark was lost in 2017 because of administrative issues and not related to a concern about safety or efficacy, and efforts are underway to regain approval in Europe. A previous U.S. multicenter randomized sham-controlled trial was stopped early by the company because of concerns of hepatic abscesses despite meeting the primary endpoints, but a new multicenter RCT for FDA approval is ongoing as of the time of writing of this guideline. The DJBL is also being studied for approval in India.

The magnitude of HbA1c improvement at 12 months in patients with obesity and concomitant T2DM was evaluated in 2 RCTs with an additional improvement of .73 % (95 % CI, .39–1.06) above the control. A previous meta-analysis that included a combination of 14 observational and RCTs with data on glycemic control between 12 and 48 weeks of implantation found an absolute improvement in HbA1c of 1.3 % (95 % CI, 1.0–1.6) compared with baseline [128]. In a subgroup analysis of the RCTs with implantation between 12 and 48 weeks, the additional improvement in HbA1c in the interventional arm was .90 % (95 % CI, .5–1.3) above the control arm, consistent with the present analysis despite the shorter duration of device implantation. Although small-bowel therapies are categorized separately from gastric devices because of their weight loss–independent effects, the DJBL also has an effect on weight loss. The present analysis demonstrated a difference of 5.4 % TWL (95 % CI, 4.1–6.7) in the device arm over the control arm.

The rate of SAEs evaluated across 3 RCTs with at least 6 months of device implantation time was 8.5 %, with a wide CI. The panel noted that the original U.S. multicenter RCT was stopped early by the company because of a higher than anticipated rate of hepatic abscesses. An analysis performed by the

sponsor found that the high doses of PPIs used for bleeding prophylaxis in the United States, but not in other countries, contributed to a biofilm on the device with a high bacterial load. The U.S. multicenter RCT ongoing at the time of writing of this guideline has several infection mitigation strategies to reduce hepatic abscesses. Furthermore, given the risks of suboptimal T2DM management and that only about half of patients with T2DM are able to achieve glycemic control on medications [129], the panel believed the benefits of the DJBL outweighed the risks.

The panel found no negative effects on equity at the present time solely because the device is not commercially available at this time. However, if it were commercially available and not covered by national health systems or insurance companies, it would decrease equity because of lack of affordability by many patients. Physicians with experience using the device reported patient acceptability of the device was high both because of the lowering of the HbA1c during implantation and the durability of HbA1c change up to 6 months after device removal [128].

RECOMMENDATION 14

In adults with T2DM, the ASGE–ESGE recommends treatment with DMR only in the context of a clinical trial. (*No recommendation, knowledge gap*)

Summary of the evidence

One RCT assessing the safety and efficacy of DMR was used to inform this PICO [64]. The study included subjects with T2DM and BMIs between 24 and 40 kg/m^2. Mean age, BMI, and HbA1c of the intervention arm were 58 years, 31.5 kg/m^2, and 8.2 %, respectively. The intervention arm underwent concomitant low-intensity LM, whereas the control arm underwent a sham procedure with concomitant low-intensity LM (**Supplementary Table 9**).

Benefits

One RCT informed the outcome of HbA1c reduction at 6 months [64]. Fifty-six subjects were in the DMR plus LM group and 52 in the sham plus LM group. The MD, representing the difference between the mean HbA1c reduction in the DMR arm minus the control arm at 6 months, was .3 % (95 % CI, –1.1 to 1.7) in favor of the intervention (**Supplemental Fig. 25**, available online).

Harms

One RCT informed the outcome of SAEs [64], which were defined by the investigators and reported in the original study. The SAEs showed an absolute risk of 15 additional events per 1000 subjects (95 % CI, 3–375) in the DMR group (2/56) compared with the control group (0/52) (**Supplementary Fig. 26**, available online). These SAEs included precautionary hospitalization for hematochezia later found to be because of external hemorrhoids (1/56) and jejunal perforation requiring surgical repair (1/56) (**Supplementary Table 19**, available online).

Certainty of evidence assessment

The overall certainty in the evidence of effects for DMR was low (**Supplementary Tables 11** and **20**, available online). Risk of bias was judged as not serious (**Supplementary Fig. 27**, available online). The only limitation of the efficacy evidence was imprecision because of a small number of patients and the lower 95 % confidence limit for HbA1c reduction crossing the minimal clinically important difference of .5 %. For harms, there was low certainty given inconsistency because the data were derived from 1 RCT only and imprecision because of a small number of SAEs with a wide CI.

Discussion

DMR is one of several potential therapies that directly treat the abnormally hypertrophied small-bowel mucosa that is hypothesized to drive the enteral contribution to poor glycemic control. The Revita DMR is the only DMR therapy that has undergone an RCT at this time. A few issues were found with the RCT. The trial was small, with 108 patients randomized to either the active or control arm, and was performed at sites in Europe and Brazil, which were found to be too heterogenous to be combined into 1 analysis and were stratified by region. Moreover, glycemic control was only reported out to 24 weeks. In a meta-analysis of single-arm studies, the absolute change in HbA1c from baseline was 1.72 % (95 % CI, .25–3.19) at 3 months and .94 % (95 % CI, .68–1.21) at 6 months, with a small change in weight that was not sufficient to explain the improvement in HbA1c [130]. One single-arm study reported a change in HbA1c of −10 ± 2 mmol/mol at 12 months in 36 patients [131]. Finally, another small single-arm study performed in biopsy sample–proven nonalcoholic steatohepatitis patients [132] (11 patients, 82 % of patients with T2DM) found neither significant reduction of HbA1c nor weight loss reduction.

However, because of the limited number of patients in the RCT, patient heterogeneity between regions, and only a 24-week study duration, the panel believed the data were insufficient to make a recommendation for or against DMR in a clinical setting and that the device should be used in a trial setting only. At the time of the writing of this guideline, a U.S. and European multicenter RCT evaluating the effect of DMR on glycemic control is ongoing. This study may provide the additional data needed to determine whether recommendations should be made for or against this therapy for the treatment of T2DM.

Discussion

Management strategies for obesity have significantly expanded over the past decades to include AOMs, EBMTs, and bariatric surgery. From an EBMT standpoint, several devices have been developed and received FDA clearance or approval and/or a CE mark. Nevertheless, at the time of writing of this guideline, only IGBs and EGR devices are commercially available and routinely used in clinical practice. Of note, in this document, different IGBs and devices for performing EGR were grouped together for analyses regardless of the manufacturer of the balloon or suturing/plication device given their similar mechanisms. This

was similar to how previous guidelines grouped all types of IGBs or sleeve gastrectomy together regardless of the brand of the balloon or stapler. It is also important to offer EBMTs in conjunction with LM consisting of dietary interventions, physical activity, and behavioral therapy to achieve and maintain weight loss. Furthermore, a multidisciplinary approach for the treatment of obesity is crucial where bariatric endoscopists work closely and collaboratively with dietitians, exercise physiologists, behavioral experts, obesity medicine experts, and bariatric surgeons to optimize outcomes. Finally, as noted in the Discussions for both IGB and EGR, reduced equity because of a lack of widespread national health coverage or commercial insurance is a major factor leading to the conditional recommendation. Improved equity, in particular for under-represented minorities, will require widespread coverage of these procedures to increase patient access.

Regarding durability, although EGR procedures have been shown to be effective up to at least 5 years [133], it is important to acknowledge that, similar to most obesity treatments, inadequate weight loss and recurrent weight gain after EBMTs may occur. Multiple options are available for management of this condition, including repeat procedures, adding AOMs, intensifying LM therapy, or switching to a different device or procedure. These options, however, are not evaluated in this guideline. It is also important to note that EBMTs do not prevent patients from undergoing bariatric surgery, if needed in the future [134].

There are several key evidence gaps in the field of EBMTs. First, data appear to be limited on the long-term effect of EBMTs on comorbidities, including cardiovascular events, cancer risk, and mortality. Nevertheless, weight loss has been shown to improve these endpoints independent of how the weight loss was achieved. Therefore, it is likely that the weight loss achieved by EBMTs could be sufficient to improve comorbidity outcomes. Second, future studies evaluating the effect of combination therapy of different EBMTs or of an EBMT with another obesity intervention (such as AOMs) are warranted. Additionally, with an increasing number of EBMTs being developed and becoming available, it is important to understand how to personalize these interventions for each patient based on his or her characteristics and comorbidities. Furthermore, data on periprocedural care before and after EBMTs are limited. In this document, expert surveys were conducted to achieve the best practice consensus. Nevertheless, future studies on these topics would help further guide periprocedural care around EBMT procedures. Last but not least, studies evaluating cost-effectiveness are important to understanding the healthcare system benefit of these therapies, and further research on this area is needed.

The present guideline serves as a corollary to several contemporary guidelines on the topic of obesity management. Specifically, in 2013 the American Heart Association, American College of Cardiology, and The Obesity Society published the "Guideline for the Management of Overweight and Obesity in Adults" focusing on LM and bariatric surgery [10]. In 2015, the Obesity Society and European Society of Endocrinology published "Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline" focusing on AOMs that were available at that time [135]. With newer GLP-1RAs being available, the American Gastroenterological Association recently published "Clinical Practice Guideline on Pharmacological Interventions for Adults with Obesity," focusing on all available AOMs including these newer injection agents [17]. In 2021, the American Gastroenterological Association also published the "AGA Clinical Practice Guidelines on Intragastric Balloons in the Management of Obesity." [36] The present guideline expands on the American Gastroenterological Association guideline on IGB by also evaluating other EBMTs that have had FDA clearance or approval or a CE mark. Most recently, in 2022, the American Society for Metabolic and Bariatric Surgery and International Federation for the Surgery of Obesity and Metabolic Disorders published "Indications for Metabolic and Bariatric Surgery," focusing on BMI indications and long-term results of bariatric surgery [136].

In summary, EBMTs are an evolving category of obesity treatments. IGBs and devices for EGR are recommended for use by the ASGE–ESGE in conjunction with LM and are currently commercially available. These therapies should be performed with the appropriate peri- and postprocedural management as outlined in this guideline to optimize clinical outcomes. Additionally, AT and DJBL therapies would be recommended for use if they were to return to the market, and further recommendations regarding TPS, DMR, and other procedures will be made once real-world data are available.

Conflict of interest

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Supplementary material

APPENDIX 1

Methods

Overview. This document represents the official recommendations of the ASGE and ESGE. It was developed by the primary EBMT guideline panel and approved by the ASGE and ESGE governing boards. The guideline was developed using the Grading of Recommendations Assessment, Development and Evaluation framework and complies with best practices in guideline development as outlined by the National Academy of Medicine (formerly Institute of Medicine).

Panel composition, meetings, and conflict of interest. Members of the guideline panel were selected by the Association of Bariatric Endoscopy, ASGE Standard of Practice Committee, and ESGE Guidelines Committee based on their clinical and methodologic expertise and were approved by the ASGE and ESGE governing boards. The panel consisted of (1) clinicians with expertise in bariatric endoscopy (*ASGE*: co-leader of the guideline: Pichamol Jirapinyo; co-chair of the guideline: Shelby Sullivan; guideline panel members: Christopher Chapman, Vivek Kumbhari, Vladmir Kushnir, Rahul Pannala, Allison Schulman, and Christopher Thompson; *ESGE*: co-chair of the guideline: Vincent Huberty; guideline panel members: Marc Barthet, Ivo Boskoski, Gianfranco Donatelli, Stefan Goelder, Bu Hayee, Tomas Hucl, Roberta Maselli, and Arpad Patai), (2) clinicians with expertise in bariatric surgery (*ASGE*: Aurora Pryor; *ESGE*: Francois Pattou), (3) clinicians with expertise in obesity medicine (*ASGE*: Caroline Apovian; *ESGE*: Vincent Huberty), (4) experts in bariatric psychology (*ASGE*: Paul Davidson; *ESGE*: Maria Casagrande), (5) registered dietitians with expertise in bariatric endoscopy (*ASGE*: Janelle Esker; *ESGE*: Shira Zelber-Sagi), (6) clinicians with expertise in methodology (*ASGE*: co-leader of the guideline: Pichamol Jirapinyo; guideline panel member: Nirav Thosani; *ESGE*: co-leader of the guideline: Alia Hadefi; ESGE guidelines committee chair: Konstantinos Triantafyllou), (7) librarians (*ASGE*: Paul Bain; *ESGE*: Valérie Durieux), and (8) patient representative from the Obesity Action Coalition (Kristal Hartmann).

During guideline development, 5 virtual meetings for the entire guideline panel were conducted on May 15, 2021 (formulation of clinical questions), September 25, 2021 (finalization of clinical questions, determining outcomes of interest, and formation of subgroup taskforces for literature screening and data collection), May 23, 2022 (reviewing results of meta-analyses), October 16, 2022, and February 19, 2023 (formulation of guideline recommendations). All panel members disclosed and updated their conflicts of interest 3 times: before the first guideline panel meeting, before the fourth guideline panel meeting when recommendations were being formulated, and before publishing. Conflicts of interest were managed according to ASGE and ESGE policies (available at https://www.asge.org/docs/default-source/default-document-library/coi-full-policy-for-asge-and-publications_edd_2-10-20.pdf). The panel members with conflicts of interest did not vote to formulate the guideline recommendation(s) in the specific EBMT category in which they had conflicts. Specifically, Pichamol Jirapinyo, Stefan Goelder, Ivo Boskoski, Christopher Chapman, Roberta Maselli, and Allison Schulman had conflicts of interest within specific IGB categories and did not vote for IGB-related recommendations; Pichamol Jirapinyo, Stefan Goelder, Christopher Chapman, Roberta Maselli, Allison Schulman, Marc Barthet, Ivo Boskoski, Vincent Huberty, and Shelby Sullivan had conflicts of interest within specific EGR categories and did not vote for EGR-related recommendations; and Shelby Sullivan had conflicts of interest with DMR and did not vote on this recommendation. All conflicts of interest disclosures were maintained by the ASGE and ESGE offices.

Formulation of clinical questions. The relevant clinical questions were developed a priori and listed in the PICO format, which outlined the specific patient population (P), intervention (I), comparator (C), and outcome (O) for each question Supplementary Table 1. The document focused on EBMTs categorized by procedure type and not by specific device, similar to how sleeve gastrectomy or gastric bypass would be studied regardless of type of stapler or equipment used. Specifically, EBMTs that were approved or cleared by the FDA or had a CE mark at the time of a literature search and 5 years before (ie, any EBMTs with FDA approval or clearance or CE mark as of March 2016 to March 2021) were included. The included procedures were IGB (Orbera IGB, Orbera365 IGB, Obalon IGB, Reshape IGB, and Spatz IGB), EGR (ESG, primary obesity surgical endoluminal procedure, and endoscopic gastric plication using the Endomina system, AT, TPS, DJBL, and DMR (Fig. 1). Other FDA-approved devices for weight loss not requiring endoscopy, such as Plenity (Gelesis, Boston, Mass, USA) or vagal blocking devices, were not included.

Devices or procedures identified as substantially equivalent were grouped together for analyses. The determination of substantial equivalence used several sources of supporting evidence. For the IGB grouping, a previous guideline by the American Gastroenterological Association grouped all IGBs together.[36] Similarly, the American Society for Metabolic and Bariatric Surgery also grouped IGBs together for a position statement[37] and currently groups all IGBs together for the purposes of data collection in the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program. Moreover, the FDA classifies IGBs as Class III devices that require a Premarket Approval application to demonstrate safety and efficacy. Therefore, all IGBs were grouped together for the PICO questions evaluating IGBs and IGB periprocedural care.

Supplementary material

Similar to IGBs, EGR procedures were determined to be substantially equivalent. In all these procedures, the implant causing the weight loss is the suture. Although the Apollo Overstitch (Boston Scientific, Marlborough, Mass, USA) currently has approval for the indication of weight loss under the name Apollo ESG, it was previously used in the United States under a 510k approval for endoscopic placement of sutures and approximation of tissue. This is similar to the 510k clearance for the IOP (USGI Medical, San Clemente, Calif, USA) used for the primary obesity surgical endoluminal procedure, which has an indication for approximation of soft tissue in minimally invasive gastroenterology procedures. The Endomina System (Endo Tools Therapeutics, Gosselies, Belgium) was directly compared with the Overstitch System as its predicate for FDA 510k approval. The FDA determined the Endomina to be substantially equivalent to the Apollo Overstitch based on nonclinical performance data, biocompatibility, and animal testing.[38] Therefore, these devices used to perform EGR were grouped together.

Outcomes of interest and determination of minimally important difference thresholds. The outcomes deemed to be critically important for decision-making were percentage of TWL, change in HbA1c (for small-bowel EBMTs only), and SAE rate. The minimal clinically important difference for weight loss efficacy was determined a priori to be an MD, which represented the difference between the pooled percentage of TWL in the EBMT arm minus the control arm, of 3% TWL. To determine this minimal clinically important difference, a meta-analysis of the control arms of the RCTs on EBMTs plus LM versus LM alone was conducted,[39-52] demonstrating the pooled weight loss of LM alone to be 3.2% TWL (95% CI, 2.5-4.0) (Supplementary Fig. 10). For RCTs in the United States, the responder rate threshold was 5% TWL, and this threshold has been shown to be associated with improvements in obesity-related comorbidities as discussed above.[32] Requiring therapies to achieve an MD of at least 3% TWL ensures percentage of TWL in the therapy arm to exceed the threshold of 5% TWL. The minimal clinically important difference for glycemic control efficacy was determined a priori to be an MD, which represented the difference between the pooled HbA1c reduction in the EBMT arm minus the control arm, of .5%, as traditionally used in T2DM clinical trials. For EBMT devices, studies with the DJBL defined early removal as an SAE, whereas all other devices followed FDA classification of SAE or Clavien-Dindo classification, and SAEs were defined according to the authors of the original studies. If the studies did not grade the severity of AEs, the Clavien-Dindo classification was used, with class III (AEs requiring endoscopic, radiologic, or surgical intervention), class IV (AEs requiring intensive care or resulting in organ dysfunction), and class V (AEs resulting in death) categorized as SAEs.[53]

Search strategy. For PICO questions regarding patient populations where EBMTs should be considered and questions regarding benefits and harms for each EBMT category, we identified studies examining EMBTs by searching the electronic databases MEDLINE (Ovid), Embase (Elsevier, 1974-), Web of Science Core Collection (Clarivate), and the Cochrane Central Register of Controlled Trials (Wiley). The search was designed and conducted by a medical librarian with input from the expert panel. An extensive search strategy was used to find articles that related to EBMTs without specifying outcomes of interest to minimize missed articles. The searches were carried out on March 29, 2021 without a language restriction. Only EBMTs that had FDA clearance or approval or a CE mark as of March 2016 to March 2021 were included. We updated the search on August 1, 2022 for all included interventions. The search strategies for all databases are shown in Supplementary Table 21. The reference lists of previously published systematic reviews, meta-analyses, and guidelines were also reviewed manually to ensure that relevant articles were not missed. Additionally, the expert panel reviewed the final list of included studies to identify any recently completed studies.

For the PICO questions regarding periprocedural care, we searched MEDLINE (OvidSP interface) and Scopus from 1990 to December 2022. The search was designed and conducted by a medical librarian with input from the expert panel. The search strategies for all databases are shown in Supplementary Table 22. The reference lists of previously published systematic reviews, meta-analyses, and guidelines were also reviewed to find additional relevant studies. Only published articles in English were considered.

Study selection, data collection and analysis. Systematic reviews and meta-analyses were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Inclusion and exclusion criteria were based on the formulated PICO questions (Supplementary Table 21).

For the PICO question regarding patient populations where EMBTs should be considered, we divided patient populations into 3 groups: BMI of 27.0 to 29.9 kg/m^2 with at least 1 obesity-related comorbidity, BMI of 30 to 39.9 kg/m^2 (classes I and II obesity), and BMI of $\geq$40 kg/m^2 (class III obesity). For classes I and II obesity, because most EBMTs were approved or cleared for this subgroup, only RCTs were included. For the subgroups with BMIs of 27.0 to 29.9 kg/m^2 and class III obesity, RCTs, observational studies, and case series of at least 10 patients were included. For RCTs, data from the interventional arm were extracted and combined with data from observational studies and case series. If a study reported the safety and efficacy of EBMTs of at least 2 BMI subgroups combined, the study was included but that outcome was downgraded for indirectness (Supplementary Fig. 28).

Supplementary material

For PICO questions regarding benefits and harms of EBMTs, only RCTs that assessed EBMTs plus LM over LM alone or LM plus sham were assessed for inclusion. Studies comparing EBMTs with other EBMTs, AOMs, or bariatric surgery were excluded. Both published studies and conference abstracts were included. For gastric interventions, studies that evaluated the effect of EBMTs on patients with obesity regardless of comorbidities were included. For small-bowel interventions, only studies that evaluated the effect of DJBL implantation on patients with T2DM and concomitant obesity and the effect of DMR on patients with T2DM were included. Regarding follow-up duration, no minimum cutoff was applied during the screening process. However, only studies with a 12-month follow-up were included in the final analysis, with 2 exceptions. First, because the primary outcomes of most IGB and DMR studies were evaluated at 6 months, studies with a follow-up of at least 6 months were also included for their efficacy analysis. Second, because AEs for EGR and DJBL implantation usually occurred periprocedurally, studies with a follow-up of at least 6 months were also included for their safety analysis (Supplementary Fig. 29).

For PICO questions regarding periprocedural care, only IGB and EGR studies were evaluated because they are the most widely performed EBMT procedures. Inclusion criteria were RCTs, observational studies, or case series that assessed the effect of antiemetics, pain medications, PPIs, or antibiotics on the safety outcomes of included EBMTs. Studies were excluded if they were review articles, conference abstracts, or included fewer than 10 patients. After screening the literature, only 2 studies assessing antiemetic regimens that were available in Europe but not in the United States met the above inclusion and exclusion criteria. Therefore, an expert survey of the guideline panel was conducted with a 30-day window to respond (Supplementary Fig. 30).

Study selection consisted of 2 steps. The first step was a calibration phase to ensure that the subgroup of panel members, who were responsible for screening, interpreted the PICO questions and used the exclusion criteria in the same manner. The librarian uploaded 75 abstracts to Abstrakr.[54] Each member of the screening subgroup reviewed all uploaded articles. After the group had reviewed this subset of studies, any discordant responses between reviewers and any remaining uncertainties about the title and abstract review process were discussed with the co-leaders of the guideline.[54] The second step was a title and abstract review, followed by a full text review, which was conducted by the same subgroup of panel members using Covidence (Covidence, Melbourne, Australia). Disagreements were resolved by means of discussion and, if necessary, by the co-leaders of the guideline. If the patient cohorts overlapped, the study with a larger number of patients was selected to preserve the independence of the observations. If it was unclear if the patient cohorts overlapped, the corresponding authors were contacted for clarification. Data collection was then conducted by a separate subgroup of panel members. The following data were extracted: study characteristics (author, year of publication, country, study design, and number of subjects in each arm), patient demographics (age, sex, baseline weight, and BMI), follow-up time points, and benefit and harm outcomes (percentage of TWL, change in HbA1c, and SAE rate). Corresponding authors were contacted for additional information if needed.

Continuous variables were reported using MD with 95% CIs and categorical variables as relative risk. Traditional forest plots with 2-sided 95% CIs were constructed. For studies that only provided CIs or interquartile ranges and that we were unable to obtain standard deviations or standard errors of the means from the authors, a normal distribution was assumed to calculate standard deviation and standard error of the mean. Heterogeneity among studies was assessed using the χ^2 test and I^2 statistic. Significant heterogeneity was defined as $P < .05$ using the χ^2 test or $I^2 > 50\%$. A random-effect model was used except when statistical heterogeneity was not significant. Differences in subgroups were assessed using a χ^2 test for interaction with a $P < .05$ defined as statistically significant. The analyses were performed using Review Manager (RevMan) version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014; Cochrane, London, United Kingdom) and Comprehensive Meta-Analysis version 3 software (Biostat, Englewood, NJ, USA).

Certainty of the evidence. The certainty of evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation approach. In this approach, the evidence of each outcome is graded into 4 categories—high, moderate, low, or very low (Table 2). Evidence derived from RCTs, observational studies, and survey studies starts at high certainty, low certainty, and very low certainty, respectively. The certainty of evidence can be rated down for risk of bias, inconsistency, indirectness, imprecision, or publication bias. For observational studies, the certainty of evidence can be rated up when there is a large magnitude of effect or a dose-response relationship. The risk of bias was assessed using the Cochrane Risk of Bias Tools. The evidence profiles were created for each PICO question using the GRADEpro Guideline Development Tool (https://gradepro.org).

Evidence to recommendations. The methodology team and the co-leaders and co-chairs of the guideline committee convened virtually on July 24, 2022 to analyze, interpret, and synthesize the evidence profiles and presented the findings to the entire guideline panel at virtual meetings on October 16, 2022 and February 19, 2023 to formulate the guideline recommendations. The evidence-to-decision framework was used to formulate recommendations using the GRADEpro Guideline Development Tool (https://gradepro.org). For each PICO question, the

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magnitude and certainty of evidence of benefits and harms of each intervention was assessed and balanced with patient values and preferences, feasibility, acceptability, resource requirements, cost, cost-effectiveness, and the impact on health equity. Once consensus on the above domains was reached, the strength of recommendation and certainty of evidence were determined for each clinical question. According to the Grading of Recommendations Assessment, Development and Evaluation approach, recommendations are labeled as "strong" or "conditional" and are phrased as "we recommend" or "we suggest," accordingly (Table 3).

Review process. The guideline draft was prepared by the guideline co-leaders and co-chairs and was distributed to the guideline panel members for review. The draft was then opened to public comment for 30 days. All comments were reviewed and addressed in an internal response document and were used to revise the guideline as needed.

APPENDIX 2

Recommendation 3: In adults undergoing IGB placement, the ASGE–ESGE suggests the use of antiemetics periprocedurally.

(*Conditional recommendation, very low certainty*)

Rationale

Two RCTs[117,118] assessing the effect of antiemetics on postoperative nausea and vomiting after IGB placement were found. The first trial[117] focused on ondansetron plus midazolam versus ondansetron alone. This study showed that combination therapy trended toward outperforming ondansetron alone (relative risk, .62; 95% CI, .33-1.13). The second trial[118] assessed the incidence of postoperative nausea and vomiting with different antiemetic and antispasmotic regimens and found that the incidence was lower in the tropisetron group compared with the alizapride group. No significant difference was observed between the tropisetron group and the tropisetron plus droperidol group. Nevertheless, given that direct evidence was scarce, most of the above antiemetic agents are available in Europe but not in North America, and the nature of postoperative nausea and vomiting after IGB was likely different from that of bariatric surgery, the decision was made to conduct an expert survey among the panel members.

Of the 17 panel members with clinical expertise in bariatric endoscopy, 15 (88%) had placed at least 10 fluid-filled IGBs and responded to this PICO question. The total number of fluid-filled IGBs placed by our group of experts was 2587 (range of 10-1000 per endoscopist). Of the 15 experts, all (100%) routinely gave antiemetics before IGB placement to mitigate postoperative nausea and vomiting. The most common antiemetics administered before the procedure were ondansetron (93%), aprepitant (73%), dexamethasone (60%), and scopolamine patch (60%). With this regimen, 31.6% of patients were estimated to have experienced postoperative nausea and vomiting, and 7.7% required an emergency department visit for postoperative nausea and vomiting within the first 72 hours. After IGB placement, 14 of 15 experts (93%) routinely prescribed antiemetics on discharge, whereas 1 expert (7%) only prescribed antiemetics on an as-needed basis. The most commonly prescribed antiemetics on discharge were ondansetron (86%), scopolamine patch (64%), aprepitant (36%), and lorazepam (36%). With this regimen, 24.5% of patients were estimated to have experienced postoperative nausea and vomiting, and 9.2% required an emergency department visit for postoperative nausea and vomiting within the first 30 days. Of all patients who were prescribed the above antiemetics after IGB placement, 12.1% experienced AEs or intolerance (Supplementary Table 23).

Based on the expert survey, prescribing antiemetics periprocedurally and postprocedurally at the time of IGB placement reduced not only the incidence of postoperative nausea and vomiting, but also the rate of emergency department visits within the first 30 days, which likely led to increased tolerability and decreased early IGB removal rates. A previous network meta-analysis of antiemetic use to prevent postoperative nausea and vomiting after general anesthesia found that Neurokinin 1 (NK1) receptor antagonists (such as aprepitant) were the most effective drug class and that selective serotonin receptor (5-HT3) antagonists (such as ondansetron) were the most studied drug class,[119] which is consistent with our survey findings. Regarding harms, this meta-analysis demonstrated that ondansetron may increase headache (relative risk, 1.16; 95% CI, 1.06-1.28) and may reduce sedation (relative risk, .87; 95% CI, .79-.96) compared with placebo (very low to low certainty of evidence). Another retrospective observational study[120] did not find any episodes of torsades de pointes or death after the perioperative administration of low-dose ondansetron. Taken together, these studies suggest that these antiemetics likely have minimal harm.

Regarding certainty of evidence assessment, the 2 RCTs that assessed the effect of antiemetics on postoperative nausea and vomiting after IGB placement (ondansetron plus midazolam vs ondansetron and alizapride vs tropisetron vs tropisetron plus droperidol) were graded as very low certainty. Specifically, they were downgraded for risk of bias, indirectness (given that the comparator group of both studies was ondansetron and alizapride, respectively, rather than no antiemetics), and imprecision (given the low postoperative nausea and vomiting rate and small total sample size) (Supplementary Table 24). Additional data on this topic were also obtained from an expert survey. Therefore, the overall quality of evidence for this PICO question was deemed to be very low certainty.

Supplementary material

APPENDIX 3

Recommendation 4: In adults undergoing IGB placement, the ASGE–ESGE suggests the use of pain medications periprocedurally.

(*Conditional recommendation, very low certainty*)

Rationale

Because no studies assessing the effect of pain medications on postprocedural pain after IGB placement were found on literature screening, an expert survey was conducted. Of the 15 experts, 12 (80%) reported routinely prescribing pain medications after IGB placement, with acetaminophen (67%), hyoscyamine (58%), and opioids (42%) being the most commonly prescribed pain medications. With the above regimen, 27.5% of patients were estimated to have experienced pain, and 3.1% required an emergency department visit for pain management within 30 days after IGB placement. Given that a previous meta-analysis demonstrated that postprocedural pain occurred in approximately 55% to 73% after IGB placement,[121] prescribing the above pain regimen appeared to be effective at reducing the incidence of postprocedural pain.

Regarding harms, the experts reported that according to their experience, 2.7% of patients who received the above pain regimen would likely experience AEs or intolerance. However, a study showed that 10% of opioid-naive bariatric surgical patients become addicted to opioids from a periprocedural dose after surgery (Supplementary Table 23). Therefore, caution should be advised regarding the use of opioids, which should be used only sparingly.[122] Because of the lack of evidence comparing different pain medications, no recommendation regarding a specific pain regimen was made. The choice of regimen is based on institutional policy, clinical context, and availability. Regarding the certainty of evidence assessment, given the lack of studies that directly assessed the use of pain medications at the time of IGB placement and because data were obtained from an expert survey, the certainty of evidence was graded as very low.

APPENDIX 4

Recommendation 5: In adults undergoing IGB placement, the ASGE–ESGE suggests the use of PPIs while the IGB is in place over no PPIs.

(*Conditional recommendation, very low certainty*)

Rationale

No studies compared outcomes between PPI use versus no PPI use in patients who underwent IGB placement. In the 7 included RCTs on IGB,[39-44,91] 5 treated all patients with PPIs,[39,41-44] 1 had varying numbers of patients on PPIs during IGB therapy,[40] and 1 did not state whether or not patients were treated with PPIs.[91] Because most patients in the included RCTs were prescribed PPIs during IGB therapy and the gastric ulcer/bleeding SAE rate was low (<1%) in the treatment group, this was deemed to be indirect evidence for the PICO question of PPIs versuss no PPIs. All 15 experts (100%) reported prescribing PPIs for their patients throughout the entire IGB therapy.

Regarding certainty of evidence assessment, because comparative studies of PPIs versus no PPIs were lacking, we treated the data derived from the included RCTs as those derived from single-arm observational studies of IGB patients who received PPIs throughout the treatment. Therefore, the evidence was rated as low certainty, and we downgraded for indirectness.

APPENDIX 5

Recommendation 7: In adults undergoing EGR, the ASGE–ESGE suggests the use of antiemetics periprocedurally.

(*Conditional recommendation, very low certainty*)

Rationale

No studies assessing the use of antiemetics after EGR were found on literature screening. Therefore, an expert survey was conducted among the panel members. Of the 17 panel members with clinical expertise in bariatric endoscopy, 16 (94%) had performed at least 10 EGR procedures and responded to this PICO question. The total number of EGR procedures performed by our group of experts was 2700 (range of 20-700 cases per endoscopist). Of the 16 experts, 14 (88%) prescribed antiemetics before the procedure to mitigate postoperative nausea and vomiting. The most common antiemetics administered were ondansetron (79%), dexamethasone (64%), aprepitant (57%), and scopolamine patch (50%). With this regimen, it was estimated that 19.5% of patients experienced postoperative nausea and vomiting, and 2.9% had an emergency department visit for postoperative nausea and vomiting within 72 hours. After EGR, 14 of 16 experts (88%) routinely prescribed antiemetics on patient discharge. The most commonly prescribed antiemetics after the procedure were ondansetron (64%), scopolamine patch (57%), aprepitant (36%), and metoclopramide (29%). With this regimen, it was estimated that 13.3% of patients experienced postoperative nausea and vomiting, and 2.9% had an emergency department visit for postoperative nausea and vomiting within 30 days. Of the patients who were prescribed the above antiemetics, 5.3% experienced AEs or intolerance to the medications (Supplementary Table 25).

Based on the expert survey, administering antiemetics periprocedurally appeared to be associated with an acceptable rate of postoperative nausea and vomiting and

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emergency department visit for postoperative nausea and vomiting within 30 days. The antiemetic agents used varied slightly, likely because of differences in institutional policy and availability, but overall were similar to those used during IGB placement. In the most recent RCT on ESG (the MERIT trial),[45] all subjects in the study arm were given intravenous ondansetron and dexamethasone during the procedure. They were then discharged home on oral ondansetron, promethazine, and lorazepam on an as-needed basis to control postoperative nausea and vomiting. With this regimen, the rate of severe nausea was 20%, severe vomiting 10%, severe postoperative nausea and vomiting 5%, and hospital admission for accommodative symptoms 4%.[45] Regarding the certainty of evidence assessment, because studies that directly assessed the use of antiemetics for EGR were lacking and because data were obtained from an expert survey, the certainty of evidence was graded as very low.

APPENDIX 6

Recommendation 8: In adults undergoing EGR, the ASGE–ESGE suggests the use of pain medications periprocedurally.

(*Conditional recommendation, very low certainty*)

Rationale

No studies assessing the effect of pain medications on postprocedural pain after EGR were found on literature screening. Therefore, an expert survey was conducted. Of 16 experts, 14 (88%) reported prescribing pain medications after EGR at the time of discharge. The most commonly prescribed pain medications were acetaminophen (57%), opioids (36%), and nonsteroidal anti-inflammatory drugs (14%). With the above regimen, it was estimated that 15.1% of patients experienced pain and 2% returned to the emergency department for pain control within 30 days. Of all patients who were prescribed pain medications after EGR, it was estimated that 4.1% experienced AEs or intolerance to the medications (Supplementary Table 25). Given that in the literature approximately 10% of opioid-naive bariatric surgical patients become addicted to opioids from a periprocedural dose, caution should be advised regarding the use of opioids, which should only be used sparingly.[122]

Postprocedural pain after EGR is likely multifactorial. Possible contributing factors include gas pain, stitching through the serosa, inflammation, and transient ischemia. In the MERIT trial,[45] all subjects in the treatment arm were prescribed a low-dose liquid narcotic on an as-needed basis on discharge. With this regimen, the incidence of severe abdominal pain was 15%, which was similar to the findings from our expert survey. Regarding the certainty of evidence assessment, because studies that directly assessed the use of pain medications for EGR were lacking and because data were obtained from an expert survey, the certainty of evidence was graded as very low.

APPENDIX 7

Recommendation 9: In adults undergoing EGR, the ASGE–ESGE suggests the use of short-term antibiotics periprocedurally.

(*Conditional recommendation, very low certainty*)

Rationale

No studies assessing the effect of antibiotic usage on postprocedural infections after EGR were found on literature screening. Therefore, an expert survey was conducted. Of 16 experts, 10 (63%) routinely prescribed antibiotics for EGR. The average number of cases performed in the group who routinely prescribed antibiotics was 230 per endoscopist (range, 20-70), whereas the average number of cases performed in the group who did not routinely prescribe antibiotics was 67 per endoscopist (range, 20-200). The most commonly prescribed antibiotics were ciprofloxacin ± metronidazole (50%), amoxicillin-clavulanate acid or ampicillin-sulbactam (30%), and cephalosporin (20%). Of the 10 experts who routinely prescribed antibiotics, 6 (60%) gave a dose of intravenous antibiotics periprocedurally only, whereas 4 (40%) prescribed a dose of antibiotics periprocedurally as well as a 3-day course of oral antibiotics on discharge. With this antibiotic regimen, it was estimated that .2% of patients who underwent EGR experienced an infection and .8% experienced AEs or intolerance to the antibiotics prescribed (Supplementary Table 25).

In the MERIT trial,[45] all subjects in the treatment arm received a dose of intravenous antibiotics (ciprofloxacin, ceftriaxone, or piperacillin-tazobactam) periprocedurally. The decision to prescribe oral antibiotics postprocedurally at the time of discharge was at the discretion of the investigators at each site. The rate of postprocedural infection was .67%, with 1 treatment subject experiencing an abdominal abscess, which was successfully managed endoscopically.

As shown in our expert survey, practices varied regarding the duration of antibiotics given. Most (60%) administered only 1 dose of intravenous antibiotics at the time of the EGR procedure. In contrast, the remaining 40% gave additional 3-day dosages of oral antibiotics on patient discharge. Further studies to assess the benefits and risks of additional postprocedural antibiotics are warranted. It is possible that 1 dose of intravenous antibiotics at the time of EGR may suffice, given the literature on bariatric surgery that supports the use of 1 dose of periprocedural antibiotics.[125] Regarding the certainty of evidence assessment, given the lack of studies that directly assessed the use of antibiotics for EGR and that data were obtained

Supplementary material

from an expert survey, the certainty of evidence was graded as very low.

APPENDIX 8

Recommendation 10: In adults undergoing EGR, the ASGE–ESGE suggests the use of short-term PPIs after the procedure over no PPIs.
(*Conditional recommendation, very low certainty*)

Rationale

No studies comparing outcomes between EGR patients who received PPIs versus those who did not were found during the literature search. In 4 RCTs,[45-47,62] 2 studies treated all subjects in the EGR arm with PPIs,[45,62] and 2 did not state whether or not patients were treated with PPIs.[46,47] Specifically, in the MERIT trial,[45] all subjects in the treatment arm were prescribed PPIs 40 mg daily for 12 months. The rate of GI bleeding was of .67%, with 1 case of upper GI bleeding managed conservatively without transfusion. In Huberty et al,[62] the treatment group received PPIs 40 mg daily for 3 months after the procedure. No cases of GI bleeding (0%) occurred during the 12-month follow-up.

Because most patients in the included RCTs were prescribed PPIs after EGR and because of the low gastric ulcer/bleeding SAE rate (<1%) in the treatment group, this was deemed to be indirect evidence for the PICO question of PPIs versus no PPIs. Regarding the certainty of evidence assessment, because of the lack of comparative studies of PPIs versus no PPIs, we treated the data derived from the included RCTs as those derived from single-arm observational studies of EGR patients who received PPIs after the procedure. Therefore, the evidence was rated as low certainty, and we downgraded it to very low certainty for indirectness.

APPENDIX 9

Recommendation 11: In adults with obesity, the ASGE–ESGE suggests treatment with AT plus LM over LM alone depending on device availability.
(*Conditional recommendation, low certainty*)

Implementation considerations

- Evidence on AT was limited to patients with class II and class III obesity.
- This device is not currently commercially available.

Summary of the evidence

Two RCTs assessing the safety and efficacy of AT were used to inform this PICO.[48,52] Mean age and BMI of the intervention arm ranged from 39 to 42 years and from 42 to 42.6 kg/m^2, respectively. The intervention arm of both studies underwent concomitant moderate-intensity LM, whereas the control arm of both studies underwent moderate-intensity LM alone (Supplementary Table 9).

Benefits

Two RCTs informed the outcome of percentage of TWL at 12 months.[48,52] One hundred twenty-two subjects were in the AT plus LM group and 67 in the LM group. The MD, representing the difference between the pooled percentage of TWL in the AT arm minus the control arm, at 12 months was 10.4% (95% CI, 6.4-14.4) in favor of the intervention (Supplementary Fig. 31).

A separate meta-analysis including the active arm of the RCTs and observational studies was previously conducted.[126] Four studies with 373 AT patients were included. Mean age ranged from 39 to 46 years and BMI from 42.4 to 43.6 kg/m^2. At 12 months, the pooled average weight loss was 16.6% TWL (95% CI, 12.8-20.4).

Harms

Two RCTs informed the SAE outcomes.[48,52] SAEs were defined by the investigators and reported in the original studies. The pooled estimate for SAEs showed an absolute risk of 16 additional SAEs per 1000 subjects (95% CI, 3-354) in the AT group (4/122) when compared with the control group (0/67) (Supplementary Fig. 32). Selected examples of SAEs from the U.S. pivotal PATHWAY trial[52] included mild peritonitis treated with intravenous antibiotics (1/122), severe abdominal pain requiring hospitalization and intravenous pain medication (1/122), a prepyloric ulcer (1/122), and a product malfunction, requiring A-tube replacement (1/122) (Supplementary Table 26).

Certainty of evidence assessment

The overall certainty in the evidence of effects for AT was low (Supplementary Tables 11 and 27). Risk of bias on the individual study level and the body of evidence was judged as not serious (Supplementary Fig. 33). The only limitation of the efficacy evidence was imprecision because of the small number of patients included in the studies. For harms, there was a low certainty in the evidence because of a small number of SAEs with a wide CI that crossed the line of no difference.

Discussion

AT is performed using the AspireAssist System, which previously had both an FDA approval and CE mark and was commercially available when the Grading of Recommendations Assessment, Development and Evaluation process was initiated. Because of financial constraints, the device is no longer commercially available. The panel acknowledged that the procedure was beneficial for select patients and a possibility that it would return to the market. Therefore, the device was included in this guideline.

Supplementary material

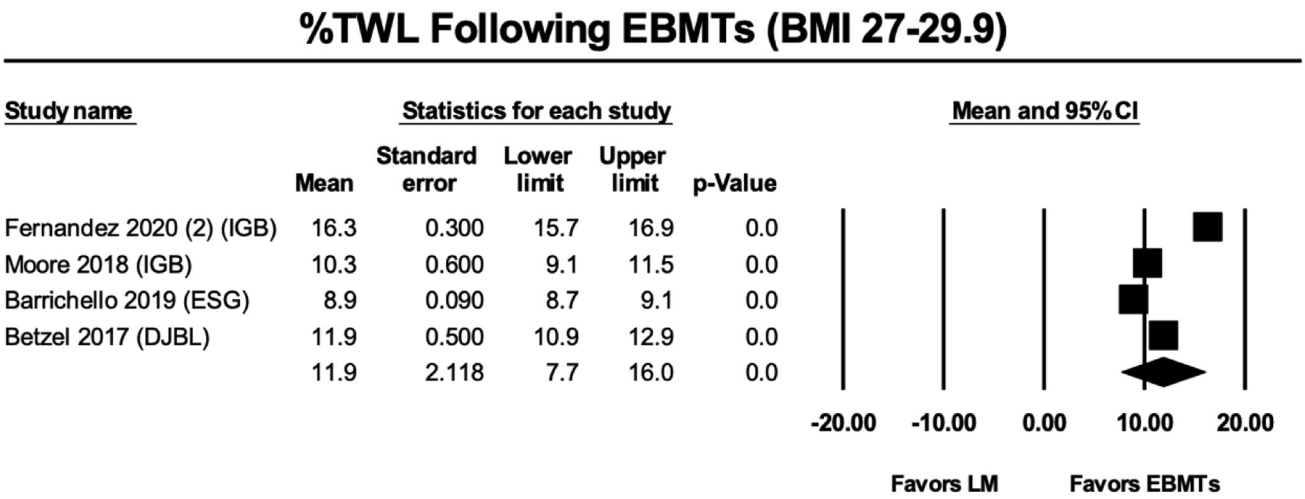
Multiple factors likely contribute to the weight loss seen with this device. The most apparent is removal of calories that were eaten in a meal. In the U.S. pilot trial, an analysis was performed to estimate the amount of weight loss attributed to the removed calories with a meal test using known meal calories and standard wait times between the completion of the meal and commencing aspiration. The authors found that 15% to 30% of the calories eaten in a meal were aspirated depending on how long patients waited between the end of the meal and commencing aspiration. However, this likely accounted for only ~50% of the weight loss seen in the trial. Meal-time behaviors that were required for adequate aspiration may explain additional weight loss, including small bites, thoroughly chewing each bite, and drinking water with meals, which likely led to a reduction in food intake. The U.S. multicenter pivotal RCT also found that patients aspirated 2.5 times per day in the first 14 weeks of the trial but only 2 times per day for the remainder of the study, further supporting the hypothesis that patients ate smaller volumes of food during treatment with AT.[52]

The magnitude of weight loss of AT was significant at 10.4% TWL over the control group; however, this was based on only 2 RCTs and a total sample size of <200 patients. A meta-analysis of 373 patients treated with AT that included both RCTs listed in this analysis and observational studies supported the weight loss efficacy seen in this analysis.[126] Weight loss was maintained in the patients who kept the device, but the rate and amount of recurrent weight gain after device removal is still unclear. This is an important point because although the therapy can be used long term, <25% of patients still had their device at 4 years.

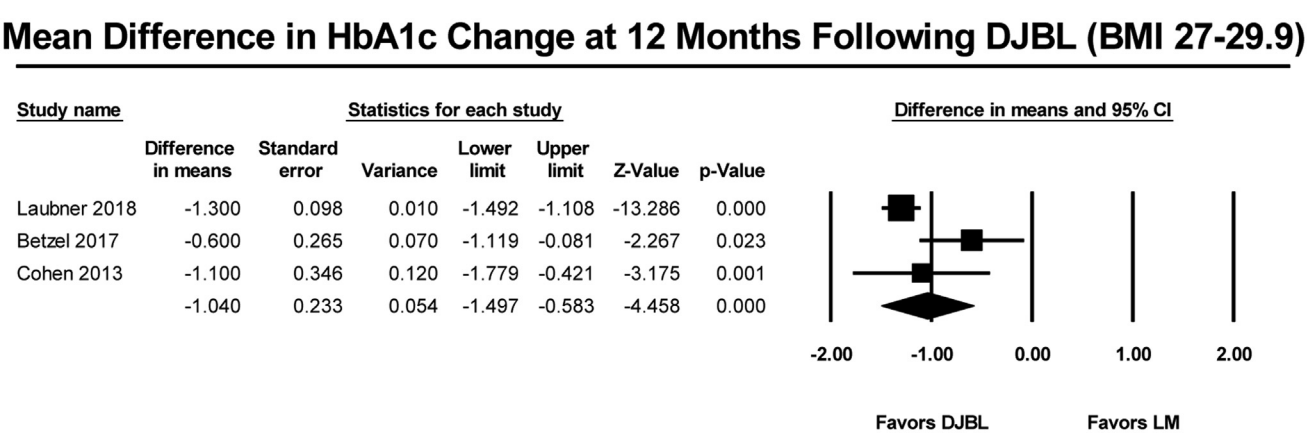
The SAE rate that occurred with the initial placement and during device implant were low at 3.3%. However, because of the low number of events and the low number of patients in the trials, the level of certainty was rated as low. The panel was also concerned about events related to eating behaviors that could occur after device removal. Both RCTs in the United States evaluated for eating disorders before and during the trial.[48,52] Patients with evidence of eating disorders were excluded from the trial, and evaluations to detect eating disorders were conducted throughout the trials. No evidence of new eating disorders was found in the groups treated with AT, but patients were not followed after the device was removed so it is unknown if eating disorders developed after device removal.

The panel found no impact on equity with this device currently, because it is not available. Unavailability of the device and continued lack of coverage by national health systems or insurance companies would have a significant impact on equity. The panel also noted that acceptability of this device was low. Although the device was the first choice of select patients, the panel noted that in practice very few patients seeking EBMTs who did not already know about AT before their initial consultation chose to proceed with AT after learning about it. This is in contrast to both IGBs and EGR, which anecdotally have higher patient acceptability.

Supplementary material

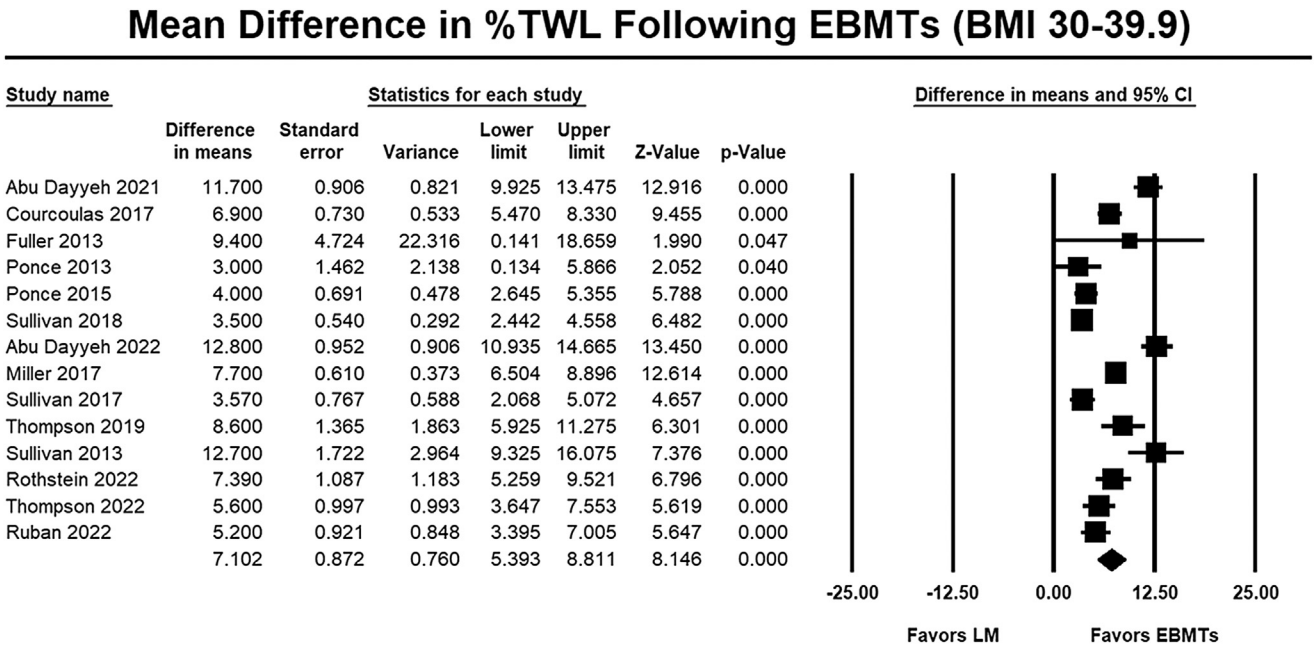


Supplementary Figure 1. Forest plot of %TWL at 6 to 12 months after EBMTs (BMI 27-29.9 kg/m^2). $I^2 = 99.5$; $P < .0001$. *BMI*, Body mass index; *%TWL*, percentage of total weight loss; *EBMT*, endoscopic bariatric and metabolic therapy; *CI*, confidence interval; *IGB*, intragastric balloon; *ESG*, endoscopic sleeve gastroplasty; *DJBL*, duodenal–jejunal bypass liner; *LM*, lifestyle modification.

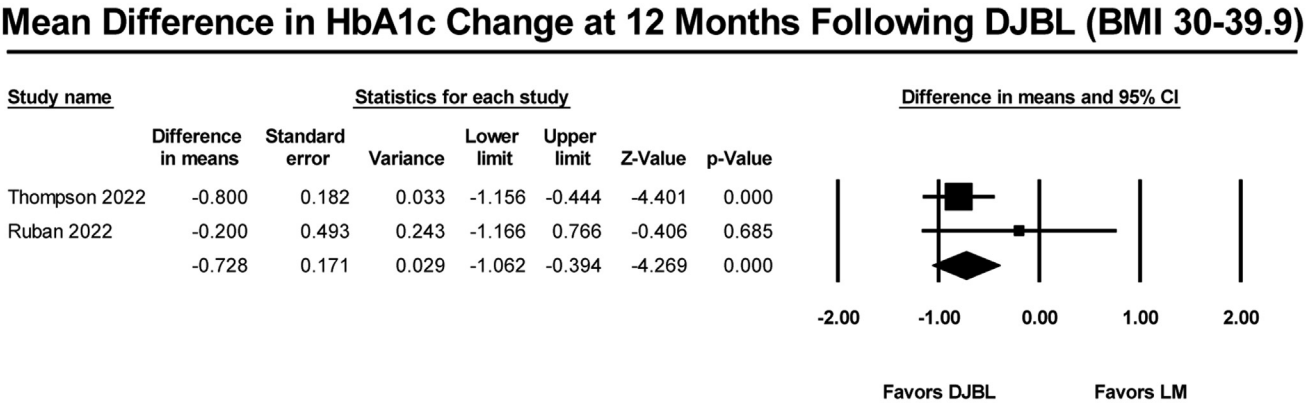


Supplementary Figure 2. Forest plot of the mean difference, representing the difference in pooled change in HbA1c of the DJBL group minus that of the control group, at 12 months (BMI 27-29.9 kg/m^2). Data derived from randomized controlled trials of DJBL use. $I^2 = 68.0$; $P = .04$. *BMI*, Body mass index; *DJBL*, duodenal–jejunal bypass liner; *CI*, confidence interval; *LM*, lifestyle modification.

Supplementary material

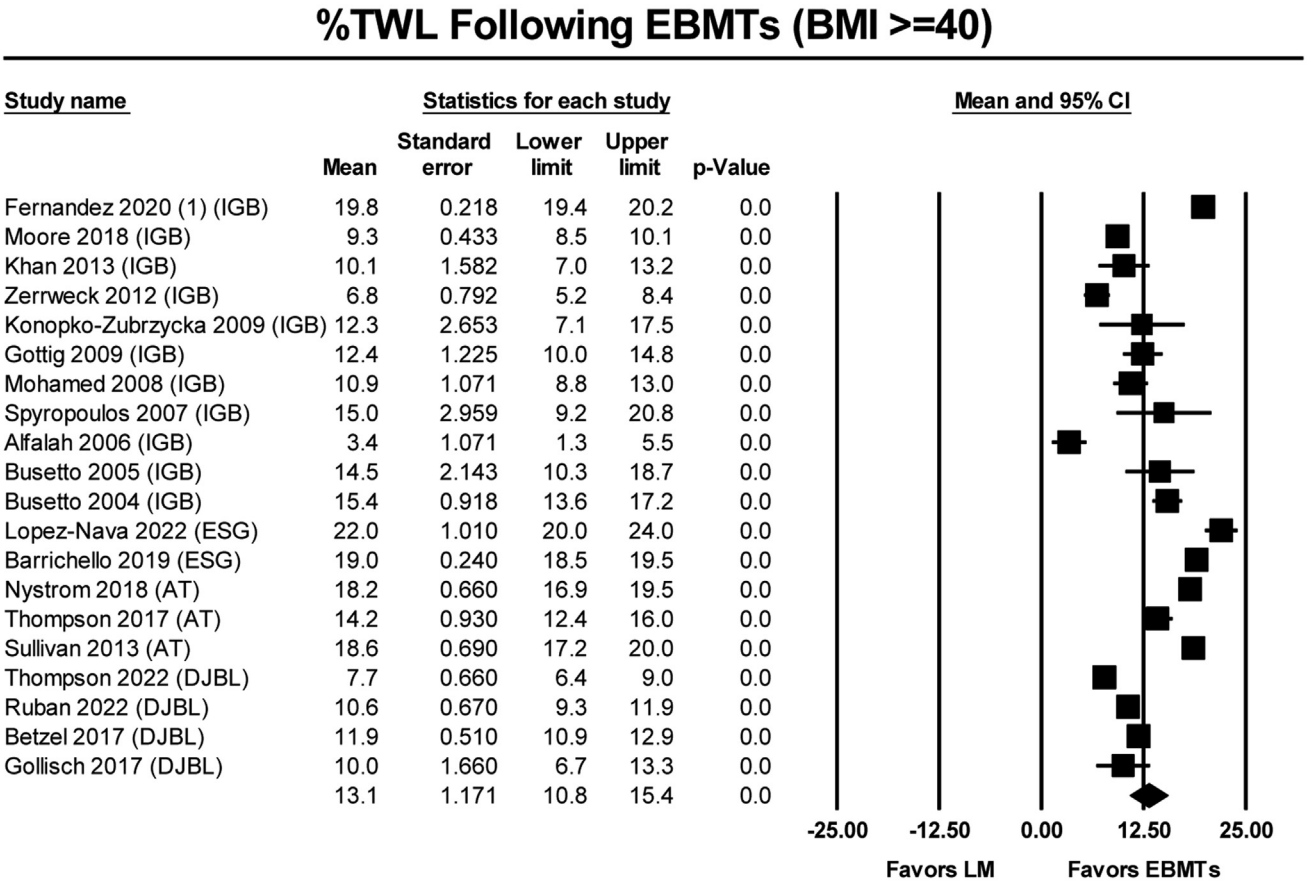


Supplementary Figure 3. Forest plot of the mean difference, representing the difference in mean %TWL of the EBMT group minus that of the control group, at 6 to 8 months (for intragastric balloon studies only) or 12 months after other EBMTs (BMI 30-39.9 kg/m^2). Data derived from randomized controlled trials of EBMTs. $I^2 = 92.1$; $P < .0001$. *BMI*, Body mass index; *%TWL*, percentage of total weight loss; *EBMT*, endoscopic bariatric and metabolic therapy; *CI*, confidence interval; *LM*, lifestyle modification.

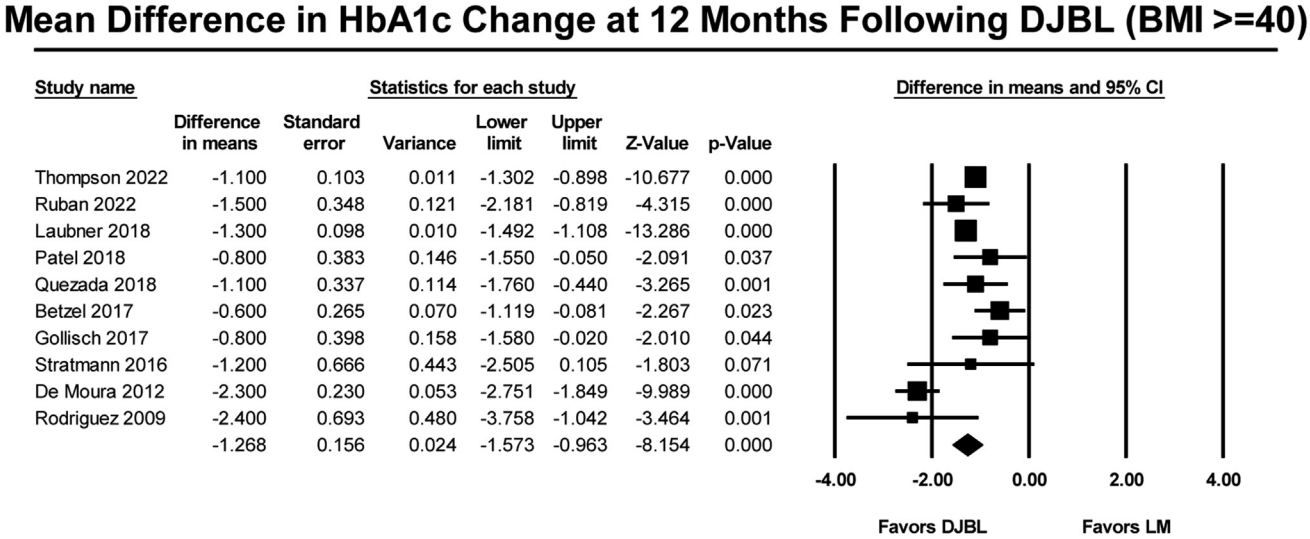


Supplementary Figure 4. Forest plot of the mean difference, representing the difference in pooled change in HbA1c of the DJBL group minus that of the control group, at 12 months (BMI 30-39.9 kg/m^2). Data derived from randomized controlled trials of DJBL. $I^2 = 23.4$; $P = .25$. *BMI*, Body mass index; *DJBL*, duodenal–jejunal bypass liner; *CI*, confidence interval; *LM*, lifestyle modification.

Supplementary material

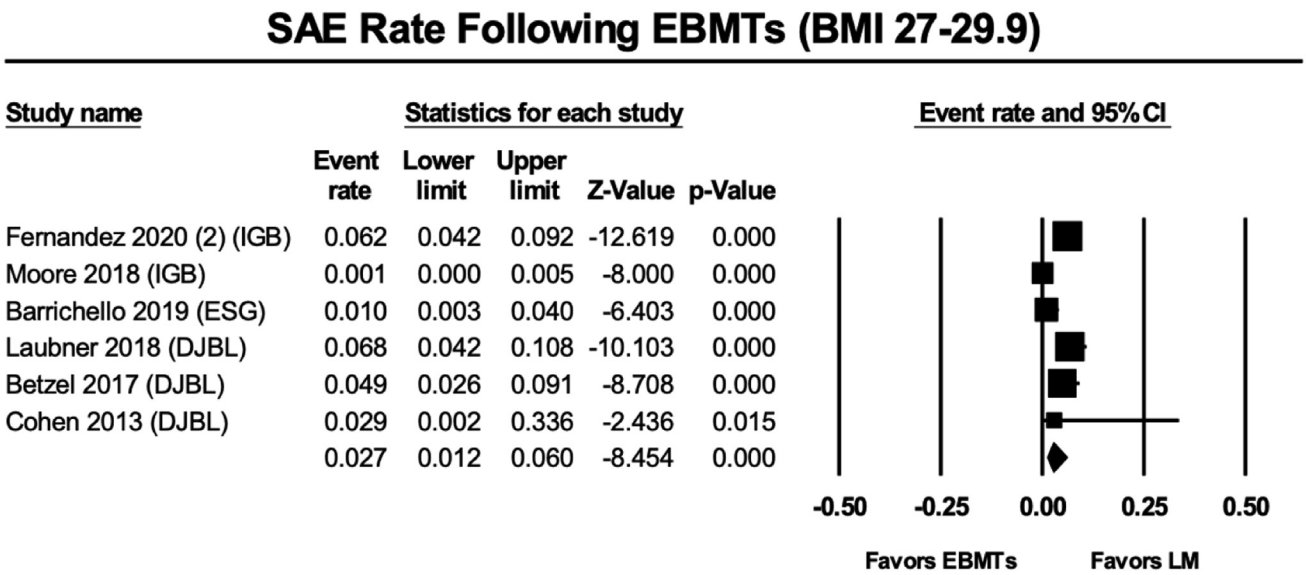


Supplementary Figure 5. Forest plot of %TWL at 6 to 12 months after EBMTs (BMI ≥40 kg/m^2). $I^2 = 98.6$; $P < .0001$. *BMI*, Body mass index; *%TWL*, percentage of total weight loss; *EBMT*, endoscopic bariatric and metabolic therapy; *CI*, confidence interval; *LM*, lifestyle modification.

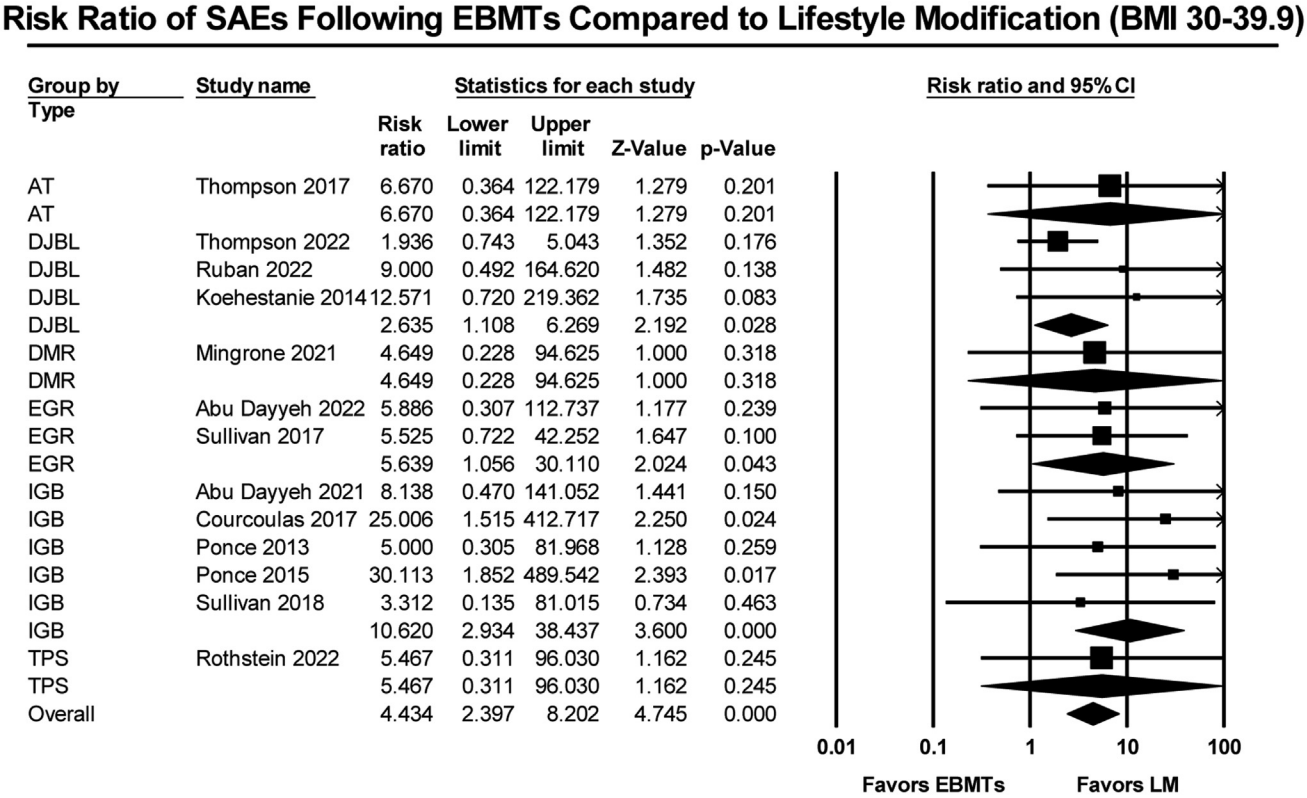


Supplementary Figure 6. Forest plot of the mean difference, representing the difference in pooled change in HbA1c of the DJBL group minus that of the control group, at 12 months (BMI ≥40 kg/m^2). Data derived from randomized controlled trials of DJBL use. $I^2 = 74.5$; $P < .0001$. *BMI*, Body mass index; *DJBL*, duodenal–jejunal bypass liner; *CI*, confidence interval; *LM*, lifestyle modification.

Supplementary material

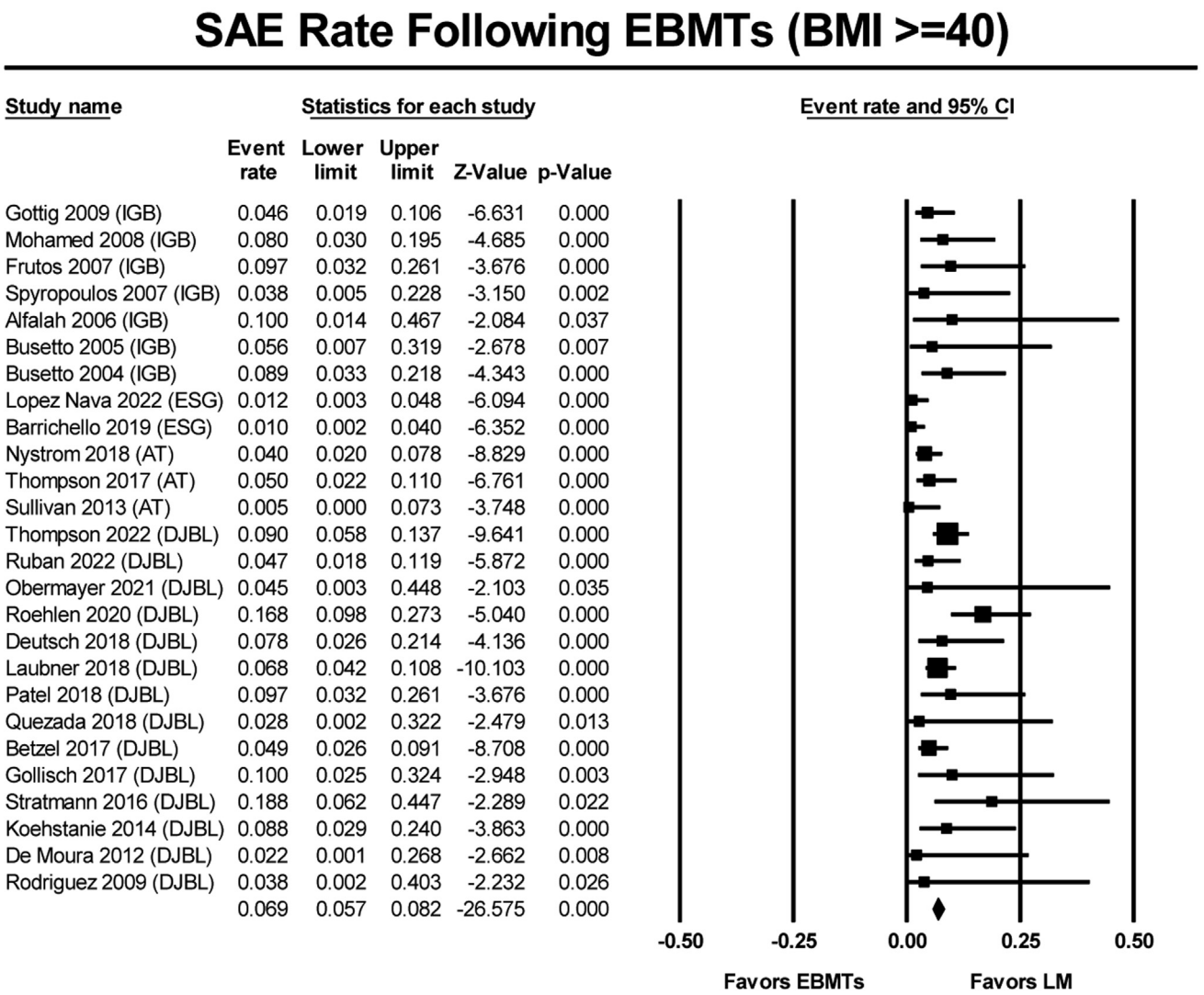


Supplementary Figure 7. Forest plot of SAE rate after EBMTs (BMI 27-29.9 kg/m^2). $I^2 = 82.8$; $P < .0001$. *BMI*, Body mass index; *SAE*, serious adverse event; *EBMT*, endoscopic bariatric and metabolic therapy; *CI*, confidence interval; *IGB*, intragastric balloon; *ESG*, endoscopic sleeve gastroplasty; *DJBL*, duodenal–jejunal bypass liner; *LM*, lifestyle modification.



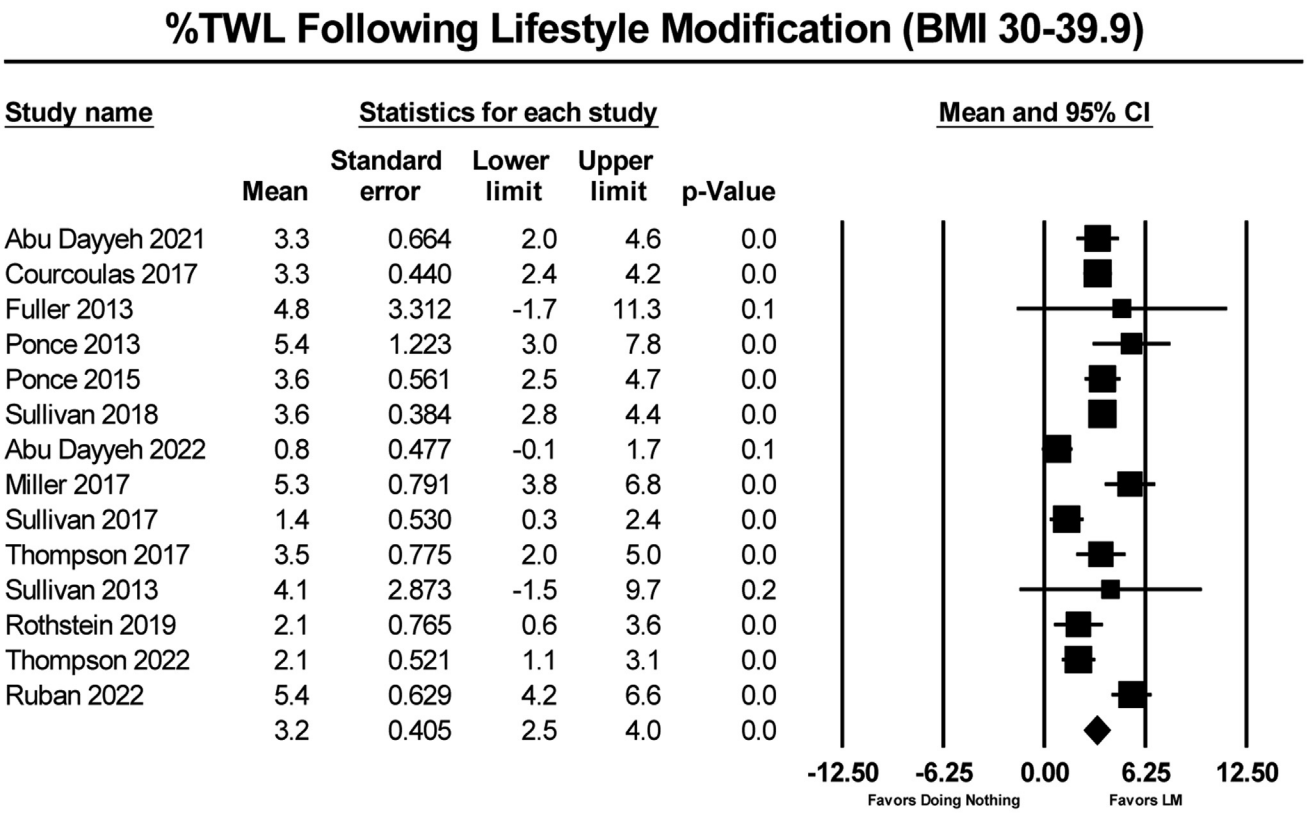
Supplementary Figure 8. Forest plot of SAE rate after EBMTs compared with control subjects (BMI 30-39.9 kg/m^2). Data derived from randomized controlled trials of EBMTs. $I^2 = 0$; $P = .84$. *BMI*, Body mass index; *SAE*, serious adverse event; *EBMT*, endoscopic bariatric and metabolic therapy; *AT*, aspiration therapy; *CI*, confidence interval; *IGB*, intragastric balloon; *ESG*, endoscopic sleeve gastroplasty; *DJBL*, duodenal–jejunal bypass liner; *DMR*, duodenal mucosal resurfacing; *TIPS*, transpyloric shuttle; *LM*, lifestyle modification.

Supplementary material

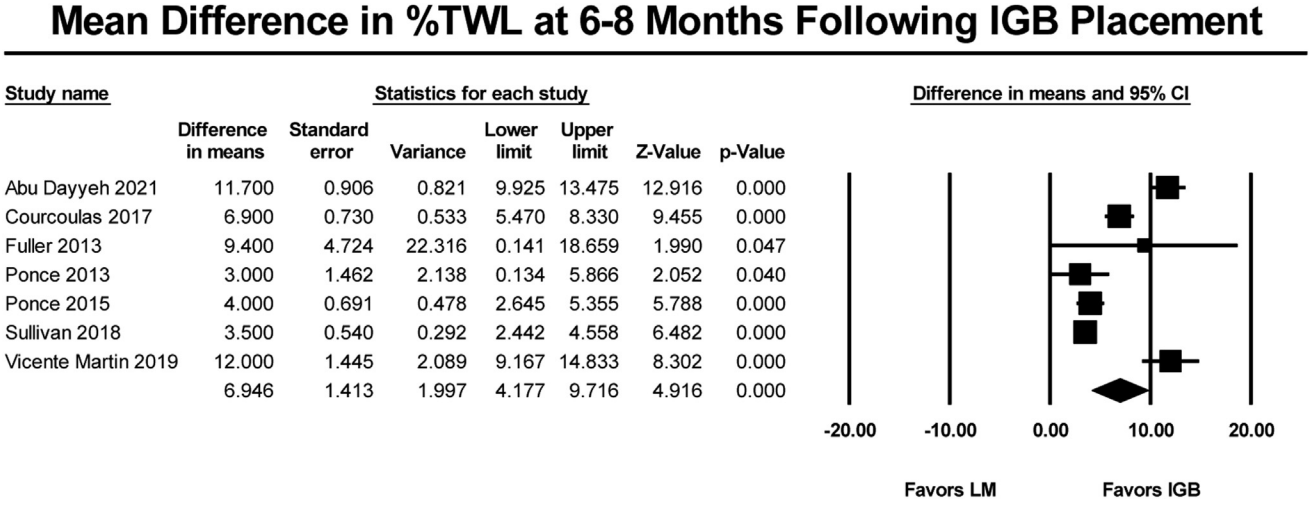


Supplementary Figure 9. Forest plot of SAE rate after EBMTs (BMI ≥40 kg/m^2). $I^2 = 39.8$; $P = .02$. *BMI*, Body mass index; *SAE*, serious adverse event; *EBMT*, endoscopic bariatric and metabolic therapy; *AT*, aspiration therapy; *CI*, confidence interval; *IGB*, intragastric balloon; *ESG*, endoscopic sleeve gastroplasty; *DJBL*, duodenal–jejunal bypass liner; *LM*, lifestyle modification.

Supplementary material

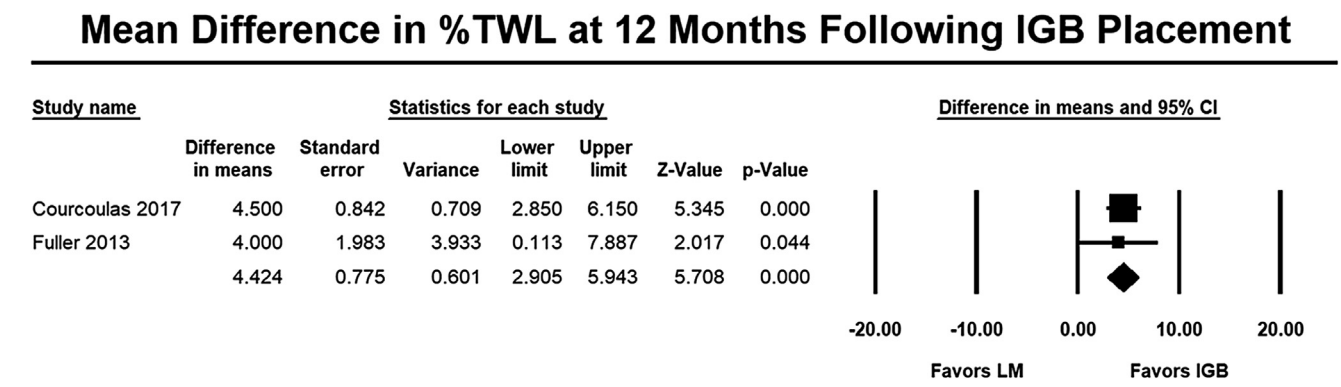


Supplementary Figure 10. %TWL of lifestyle modification alone. Data derived from the control arms of randomized controlled trials of endoscopic bariatric and metabolic therapies + lifestyle modification versus lifestyle modification alone. $I^2 = 80.6$; $P < .0001$. *BMI*, Body mass index; *%TWL*, percentage of total weight loss; *CI*, confidence interval; *LM*, lifestyle modification.

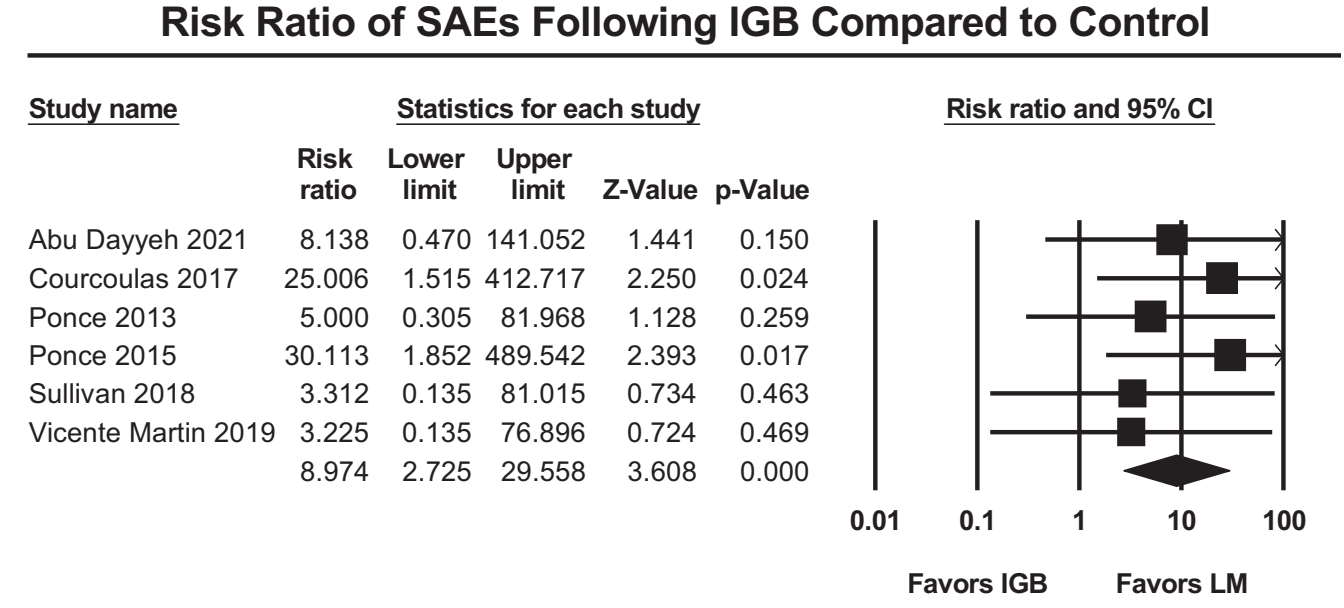


Supplementary Figure 11. Forest plot of the mean difference, representing the difference in mean %TWL of the IGB group minus that of the control group, at 6 to 8 months after IGB placement (ie, at time of IGB removal). Data derived from randomized controlled trials of IGB. $I^2 = 93.5$; $P < .0001$. *%TWL*, Percentage of total weight loss; *CI*, confidence interval; *IGB*, intragastric balloon; *LM*, lifestyle modification.

Supplementary material

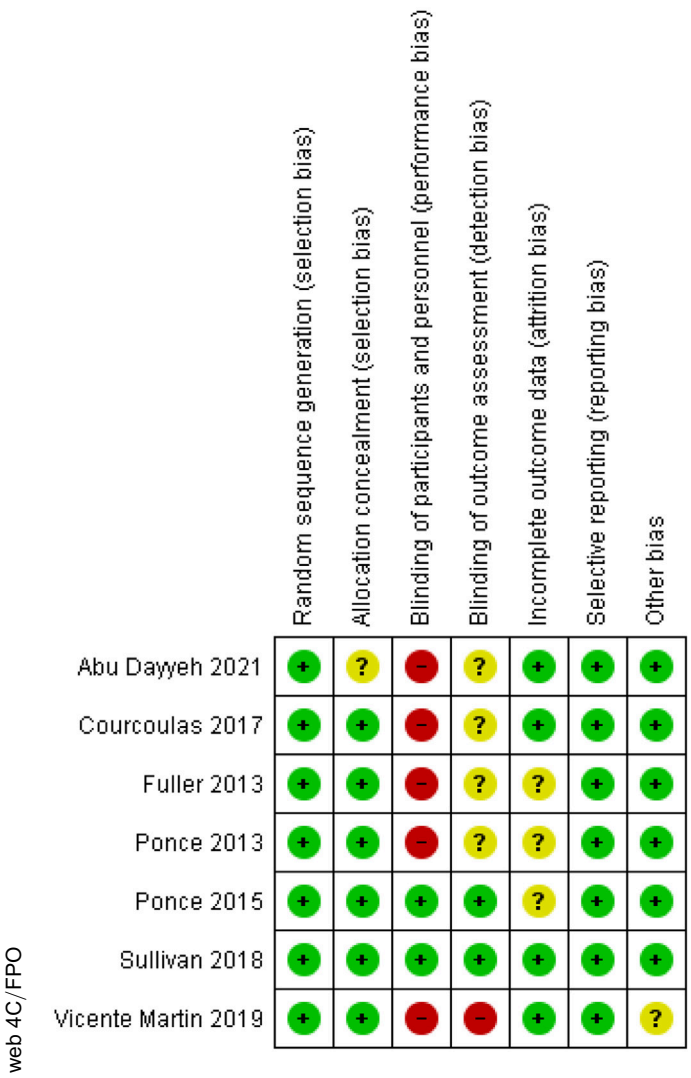


Supplementary Figure 12. Forest plot of SAEs after IGB placement compared with control. Data derived from randomized controlled trials of IGB. $I^2 = 0$; $P = .82$. *SAE*, Serious adverse event; *IGB*, intragastric balloon; *CI*, confidence interval; *LM*, lifestyle modification.

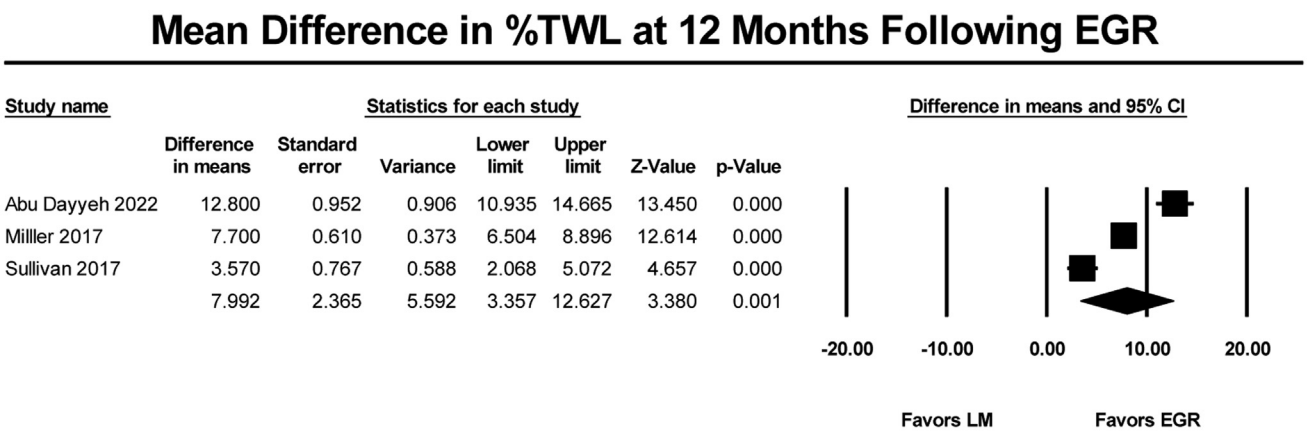


Supplementary Figure 13. Forest plot of SAEs following IGB compared to control. Data derived from RCTs of IGB. $I^2 = 0$; $P = .82$.

Supplementary material

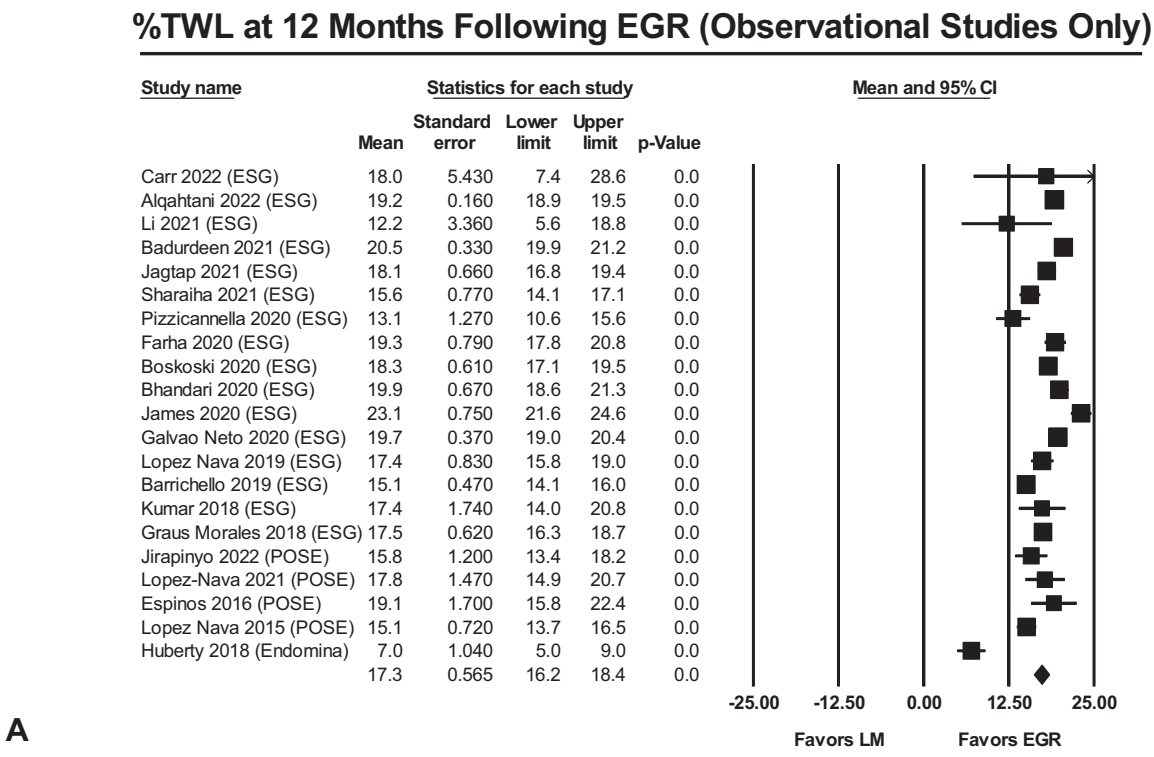


Supplementary Figure 14. Risk of bias of included studies on intragastric balloon placment.

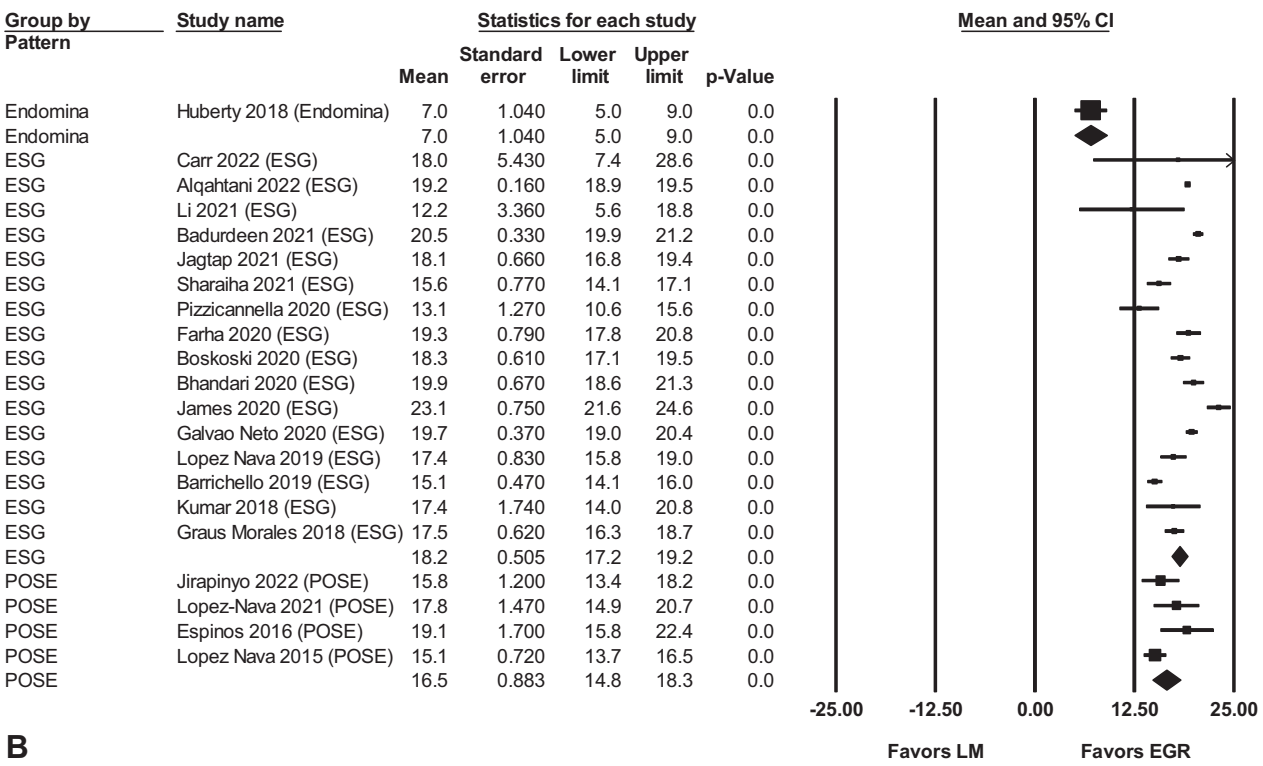


Supplementary Figure 15. Forest plot of the mean difference, representing the difference in mean %TWL of the EGR group minus that of the control group, at 12 months. Data derived from randomized controlled trials of EGR. $I^2 = 96.5$; $P < .0001$. *%TWL*, Percentage of total weight loss; *CI*, confidence interval; *EGR*, endoscopic gastric remodeling; *LM*, lifestyle modification.

Supplementary material



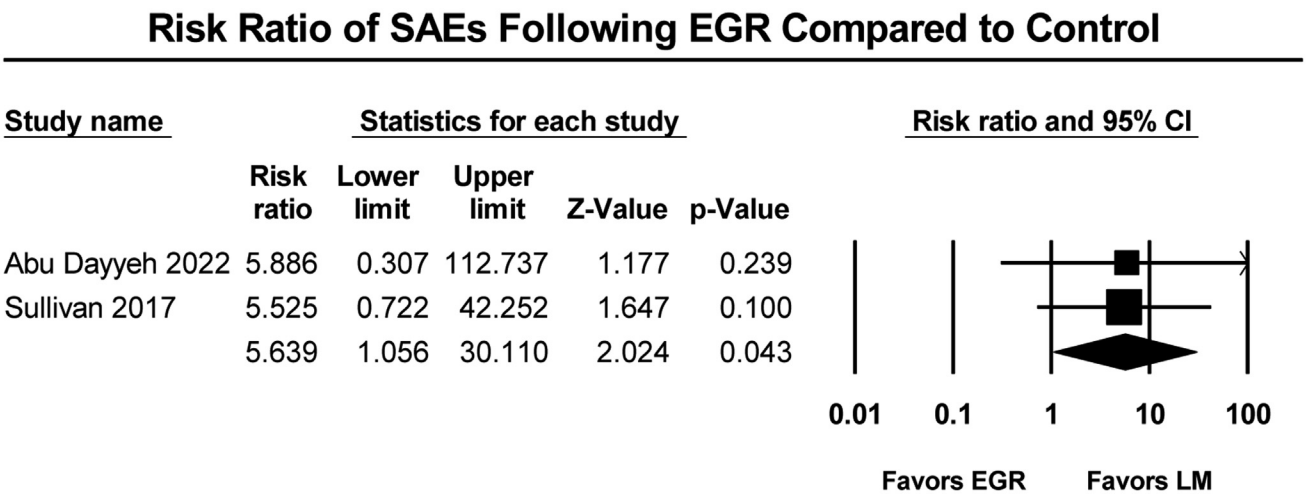
A



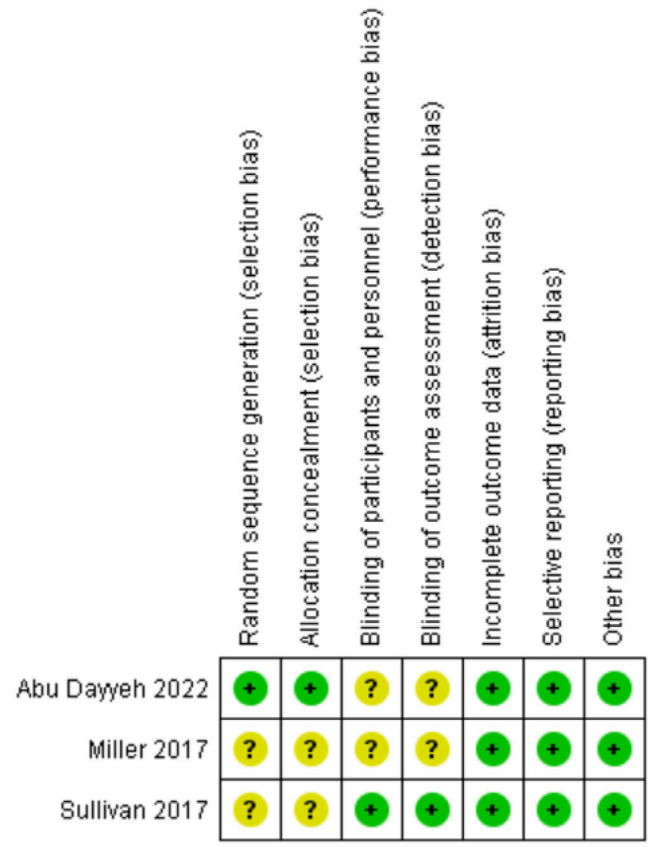
B

Supplementary Figure 16. Forest plot of %TWL at 12 months after EGR. Data derived from observational studies of EGR. $I^2 = 94.4$; $P < .0001$. *%TWL*, Percentage of total weight loss; *CI*, confidence interval; *EGR*, endoscopic gastric remodeling; *LM*, lifestyle modification; *ESG*, endoscopic sleeve gastroplasty; *POSE*, primary obesity surgical endoluminal.

Supplementary material



Supplementary Figure 17. Forest plot of SAEs after EGR compared with control. Data derived from randomized controlled trials of EGR. $I^2 = 0$; $P = .97$. *SAE*, Serious adverse event; *EGR,* endoscopic gastric remodeling; *CI*, confidence interval; *LM*, lifestyle modification.



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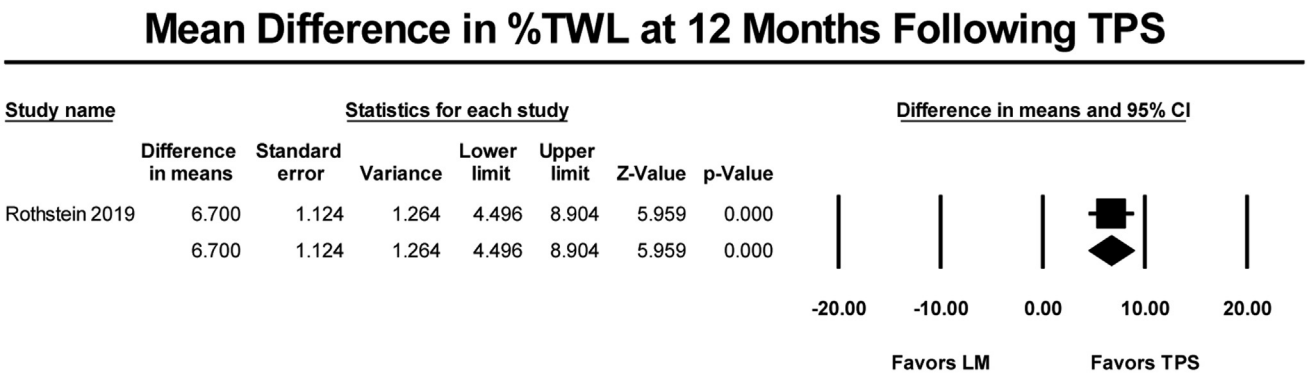
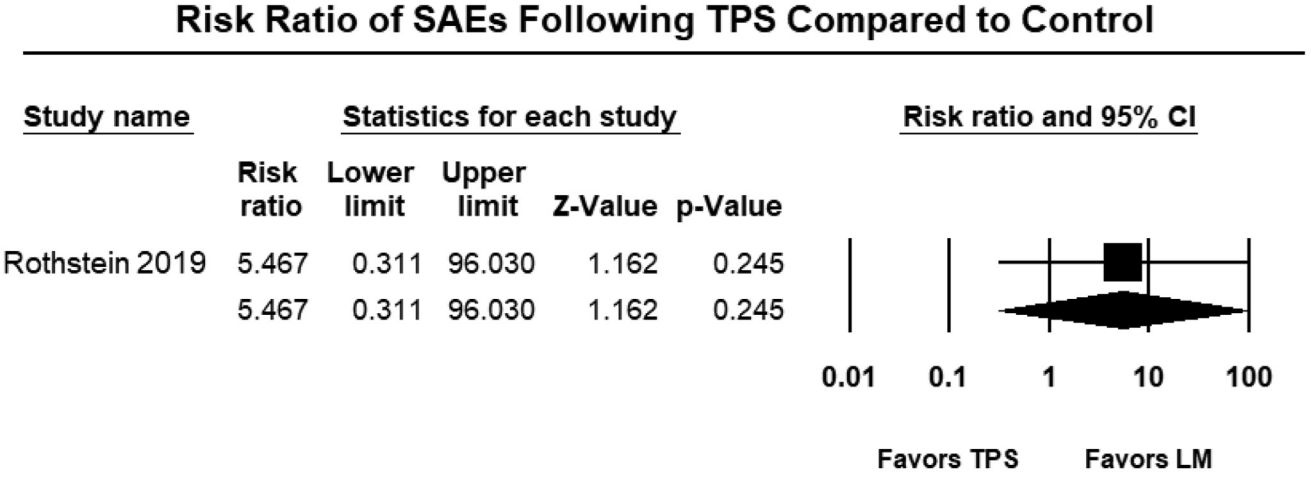
Supplementary Figure 18. Risk of bias of included studies on endoscopic gastric remodeling.

Supplementary material

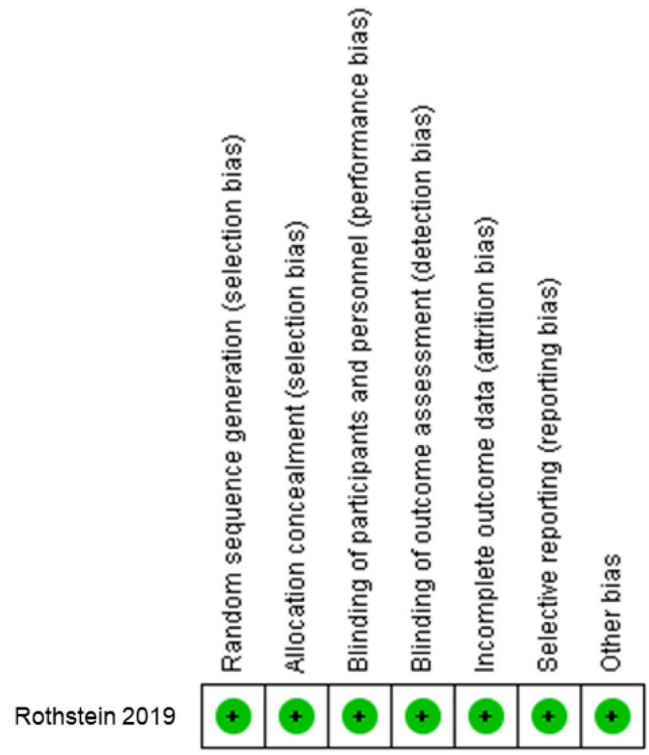


Supplementary Figure 19. Forest plot of the mean difference, representing the difference in mean %TWL of the TPS group minus that of the control group, at 12 months. Data derived from an RCT of TPS. $I^2 = 0$; $P = 1.00$. *%TWL*, Percentage of total weight loss; *CI*, confidence interval; *TPS*, transpyloric shuttle; *LM*, lifestyle modification.

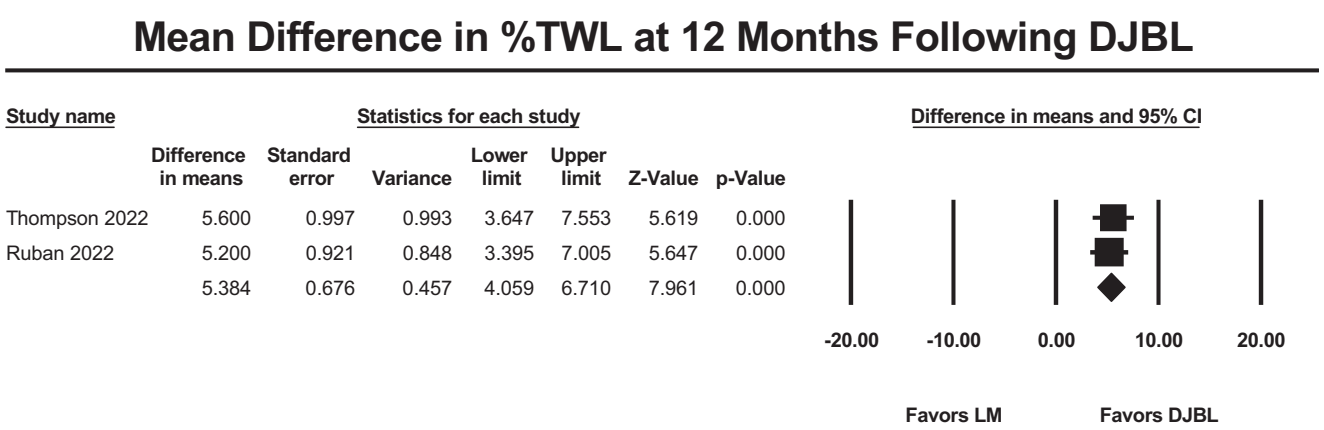


Supplementary Figure 20. Forest plot of SAEs after TPS compared with control. Data derived from a randomized controlled trial of TPS. $I^2 = 0$; $P = 1.00$. *SAE*, Serious adverse event; *TPS,* transpyloric shuttle; *CI*, confidence interval; *LM*, lifestyle modification.

Supplementary material

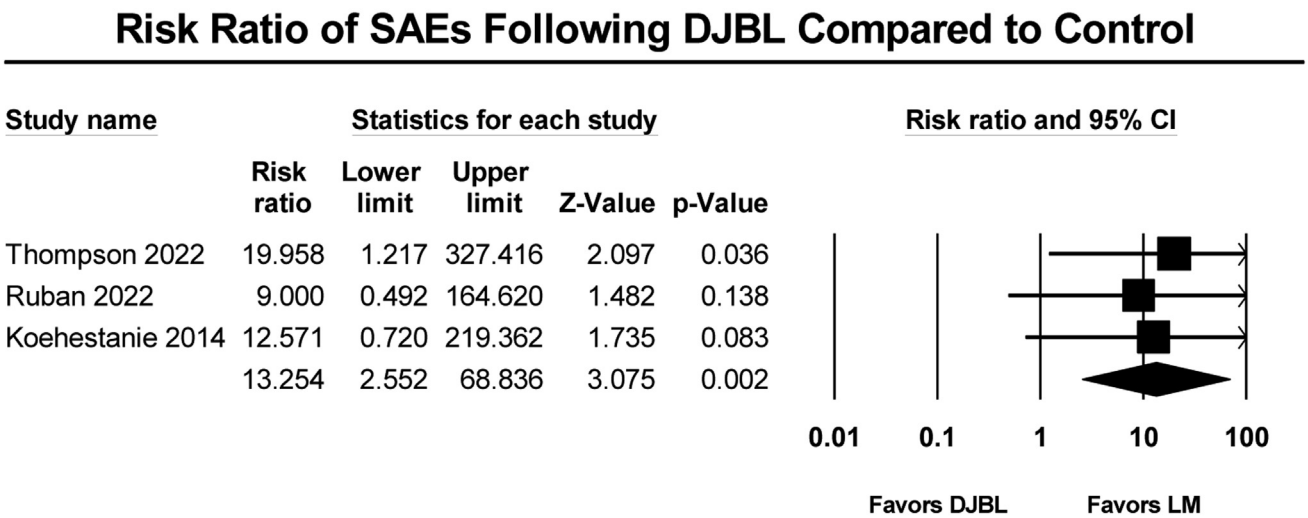


Supplementary Figure 21. Risk of bias of included studies on transpyloric shuttle use.

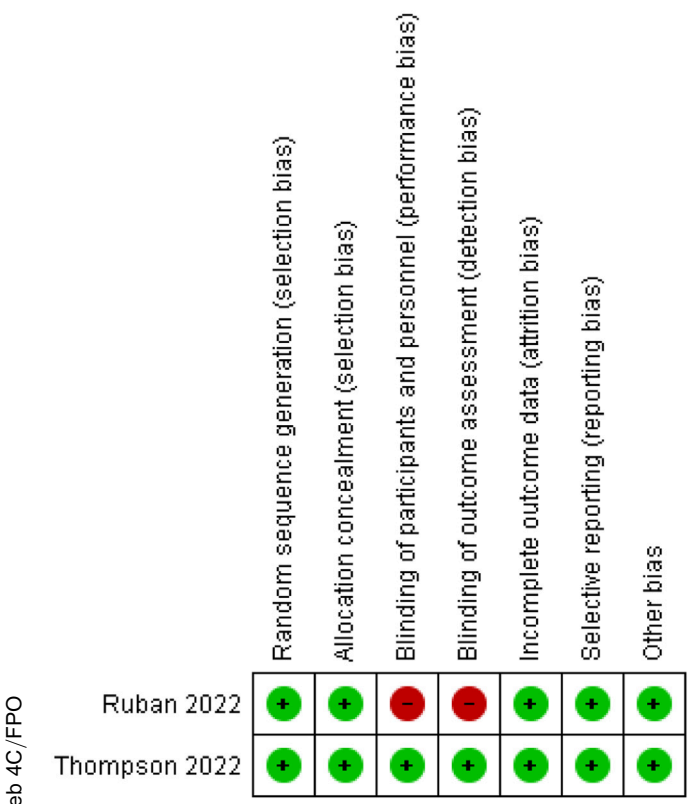


Supplementary Figure 22. Forest plot of the mean difference, representing the difference in mean change in HbA1c of the DJBL group minus that of the control group, at 12 months. Data derived from randomized controlled trials of DJBL use. $I^2 = 23.4$; $P = .25$. *DJBL*, Duodenal–jejunal bypass liner; *CI*, confidence interval; *LM*, lifestyle modification.

Supplementary material

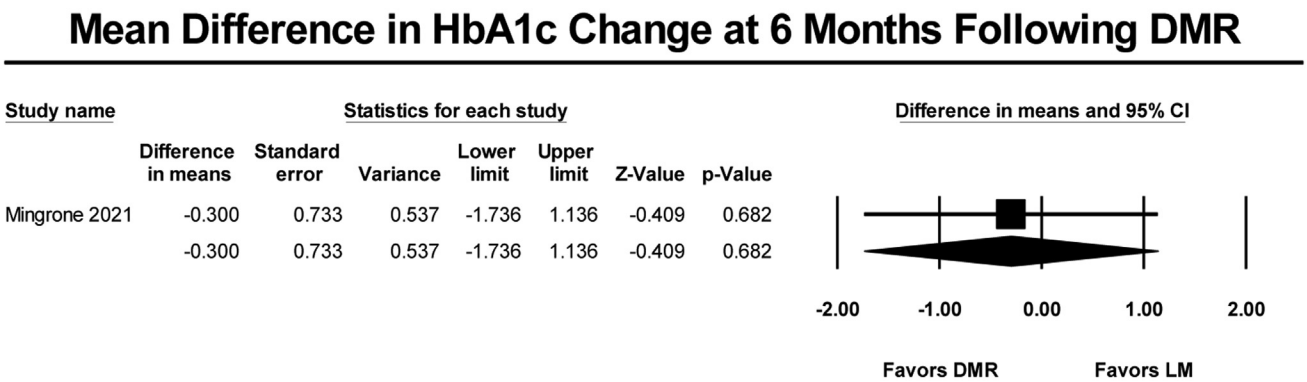


Supplementary Figure 23. Forest plot of SAEs after DJBL use compared with control. Data derived from randomized controlled trials of DJBL. $I^2 = 0$; $P = .93$. *SAE*, Serious adverse event; *DJBL*, duodenal–jejunal bypass liner; *CI*, confidence interval; *LM*, lifestyle modification.

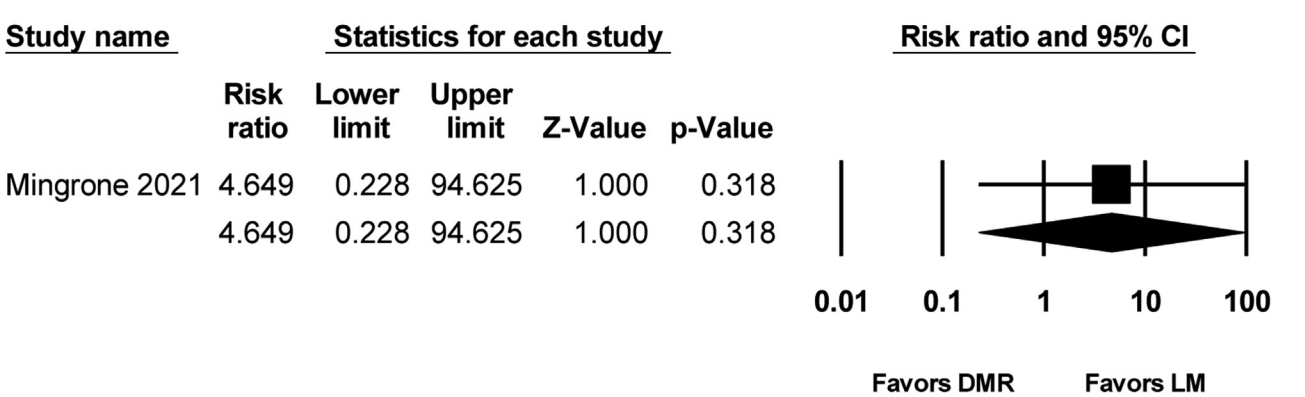


Supplementary Figure 24. Risk of bias of included studies on duodenal–jejunal bypass liner use.

Supplementary material

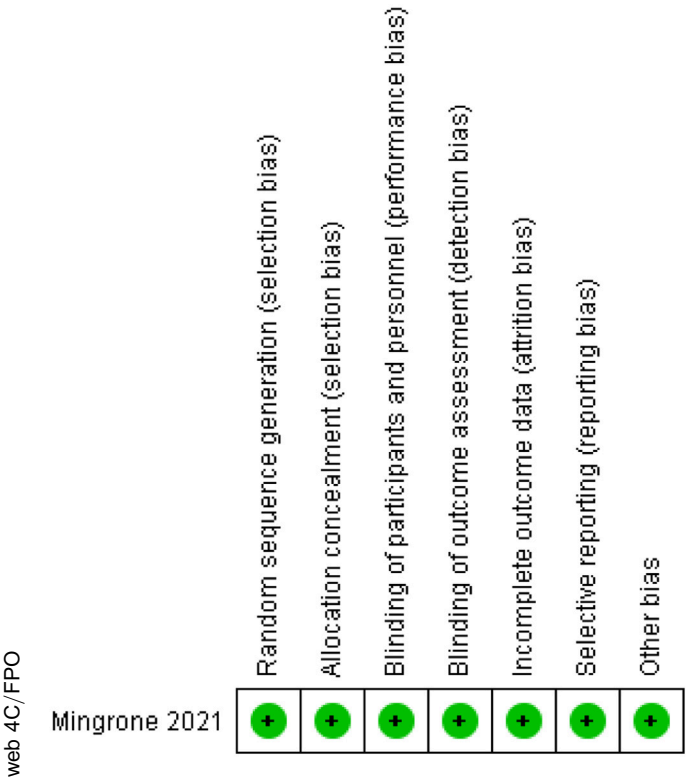


Supplementary Figure 25. Forest plot of the mean difference, representing the difference in mean change in HbA1c of the DMR group minus that of the control group, at 6 months. Data derived from a randomized controlled trial of DMR. $I^2 = 0$; $P = 1.00$. *DMR*, Duodenal mucosal resurfacing; *CI*, confidence interval; *LM*, lifestyle modification.



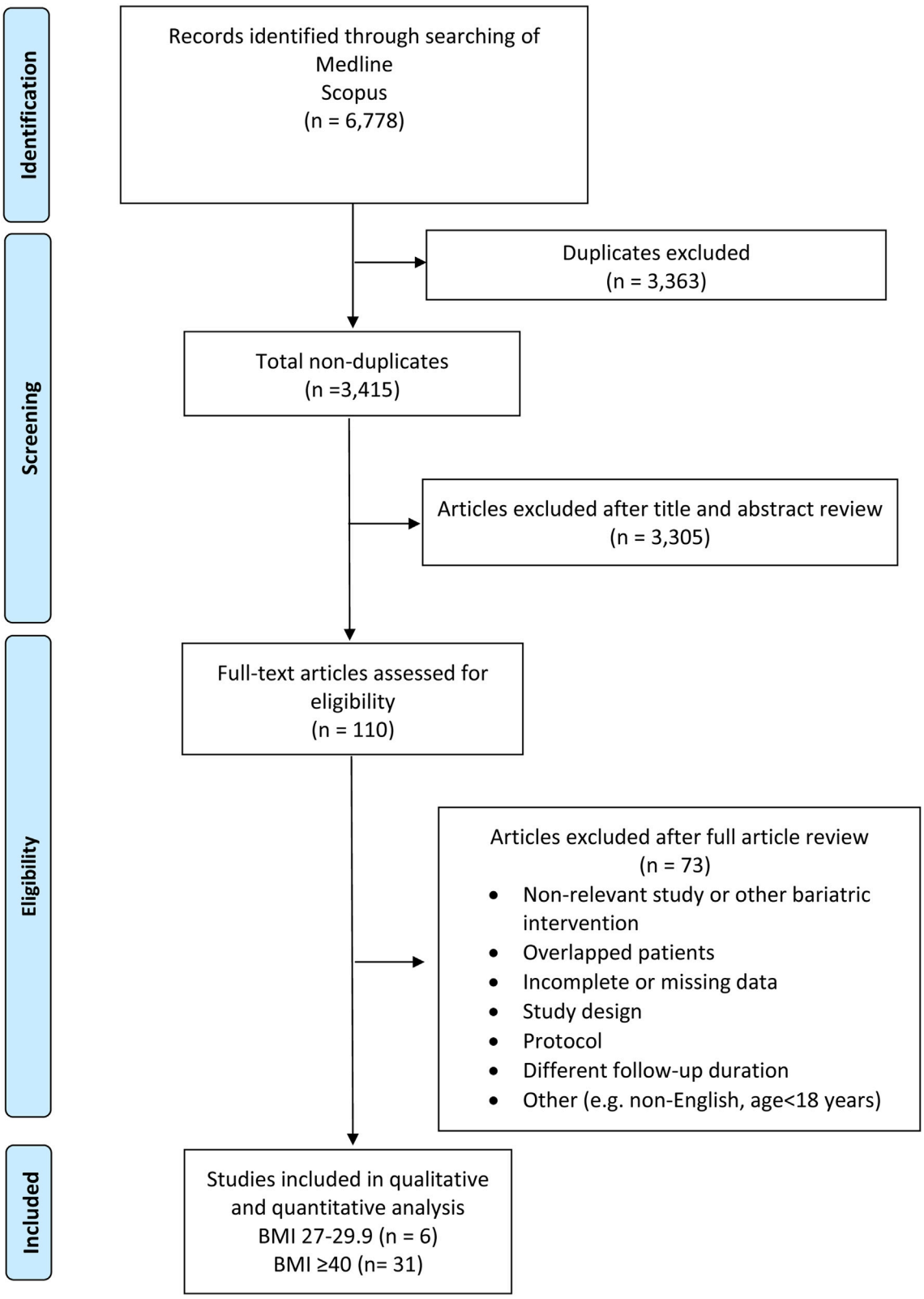
Supplementary Figure 26. Forest plot of SAEs after DMR compared with control. Data derived from a randomized controlled trial of DMR. $I^2 = 0$; $P = 1.00$. *SAE*, Serious adverse event; *DMR,* duodenal mucosal resurfacing; *CI*, confidence interval; *LM*, lifestyle modification.

Supplementary material



Supplementary Figure 27. Risk of bias of included studies on duodenal mucosal resurfacing.

Supplementary material



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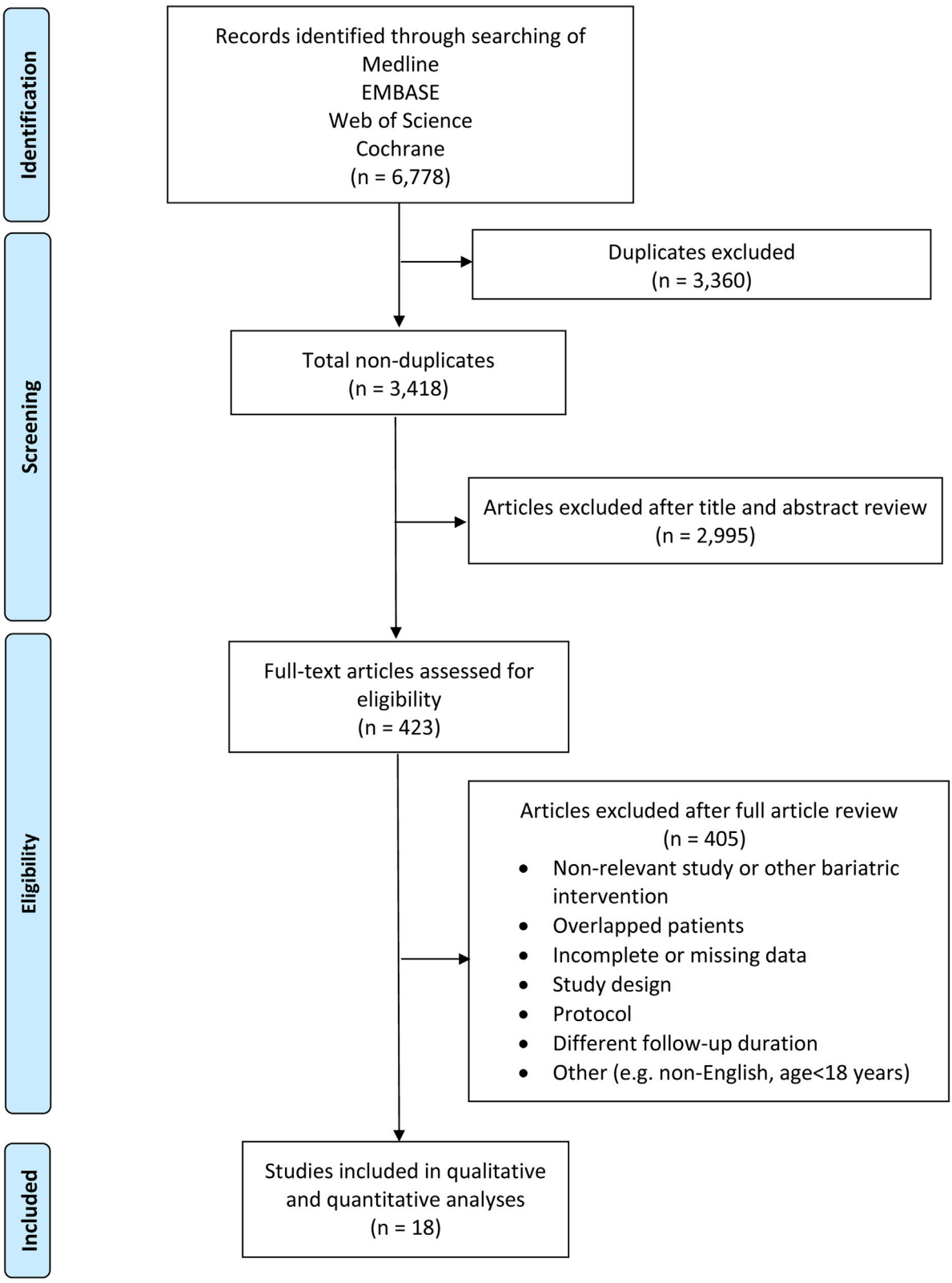
Supplementary Figure 28. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for the PICO question on benefits and harms of endoscopic bariatric and metabolic therapies.

Supplementary material



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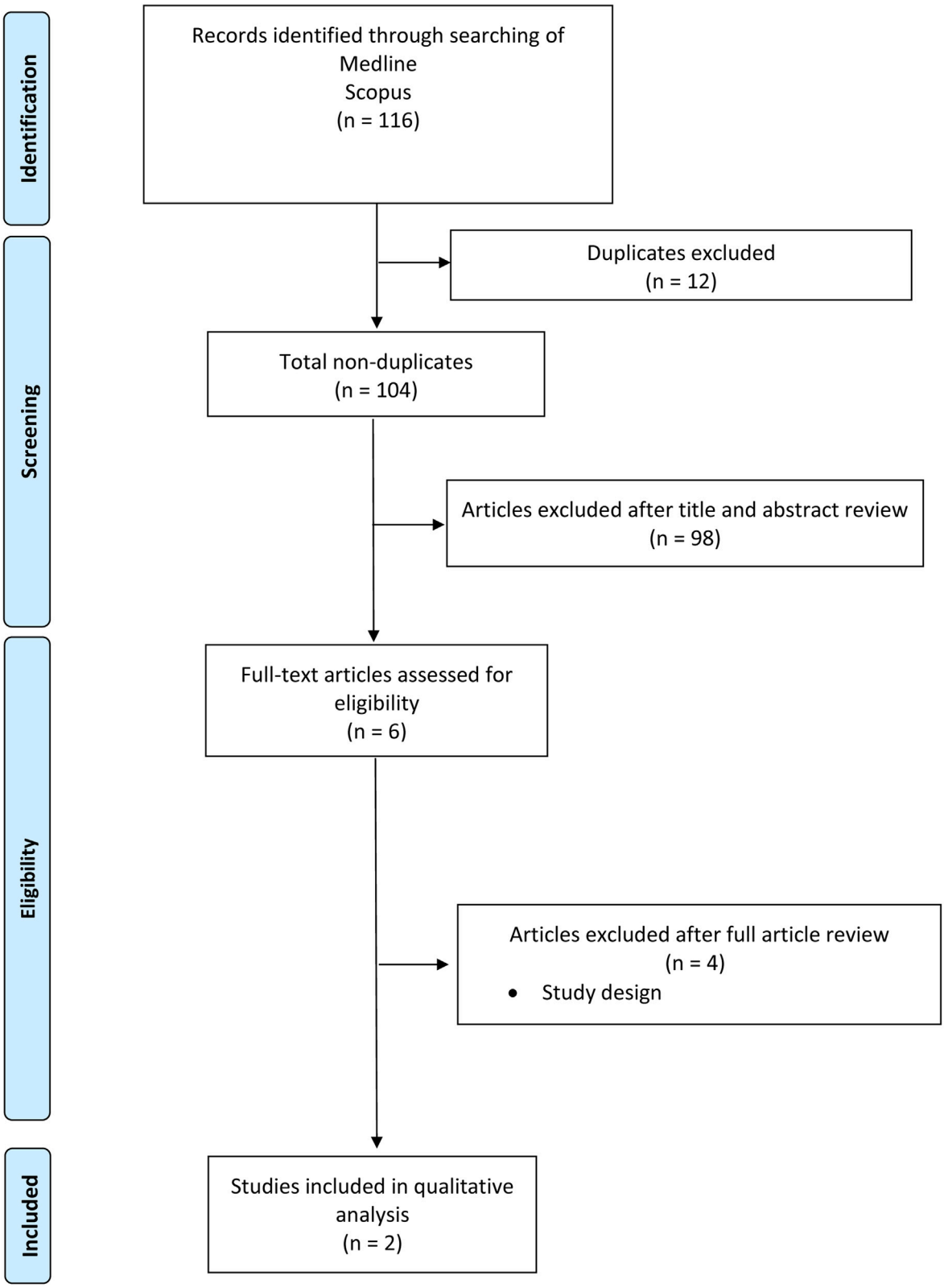
Supplementary Figure 29. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for the PICO question on the effect of endoscopic bariatric and metabolic therapies by BMI categories. *BMI*, Body mass index.

Supplementary material



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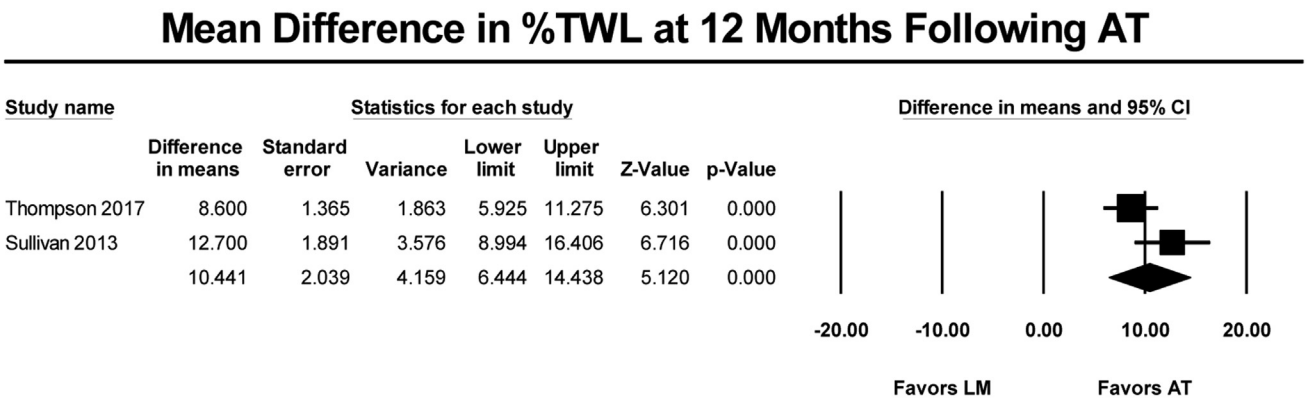
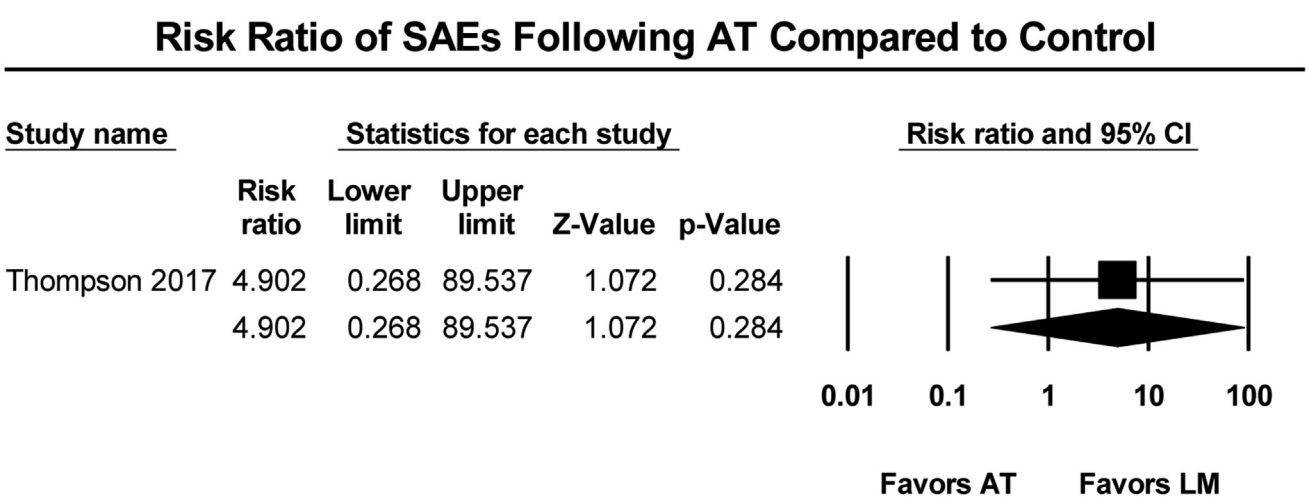
Supplementary Figure 30. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for the PICO question on periprocedural care.

Supplementary material

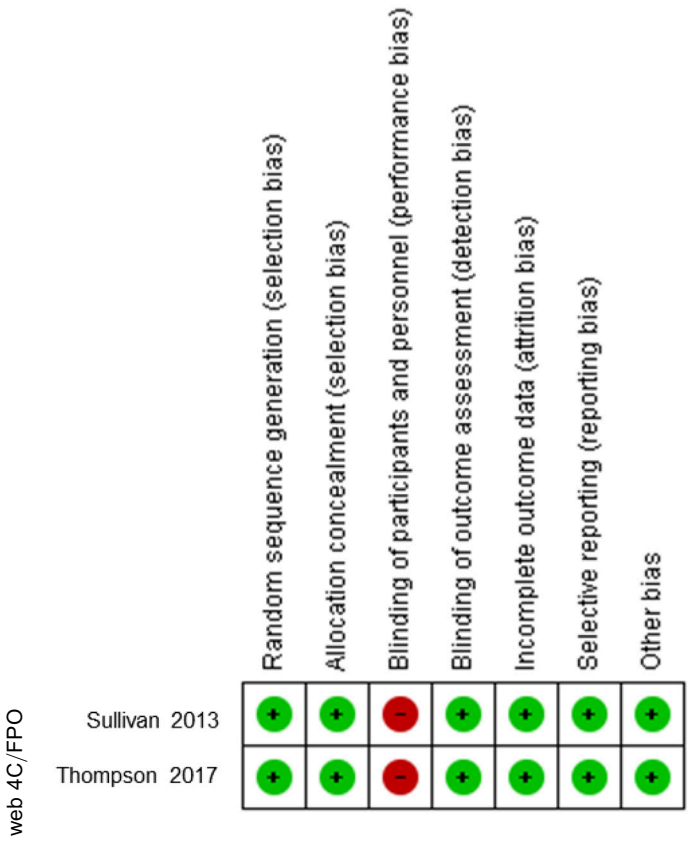


Supplementary Figure 31. Forest plot of the mean difference, representing the difference in mean %TWL of the AT group minus that of the control group, at 12 months. Data derived from randomized controlled trials of AT. $I^2 = 89.3$; $P = .002$. *%TWL*, Percentage of total weight loss; *CI*, confidence interval; *AT*, aspiration therapy; *LM*, lifestyle modification.



Supplementary Figure 32. Forest plot of SAEs after AT compared with control. Data derived from randomized controlled trials of AT. $I^2 = 0$; $P = 1.00$. *SAE*, Serious adverse event; *AT,* aspiration therapy; *CI*, confidence interval; *LM*, lifestyle modification.

Supplementary material



Supplementary Figure 33. Risk of bias of included studies on aspiration therapy.

Supplementary material

SUPPLEMENTARY TABLE 1. PICO questions (population, intervention, comparator, outcome)

PICO question no.	Population	Intervention	Comparator	Outcomes
1	Adults with body mass indices of 27-29.9 kg/m^2 with at least 1 obesity-related comorbidity or body mass indices $\geq$30 kg/m^2	Endoscopic bariatric and metabolic therapy + lifestyle modification	Lifestyle modification	• %TWL • HbA1c reduction • SAE rate
2	Adults with obesity	Intragastric balloon + lifestyle modification	Lifestyle modification	• %TWL • SAE rate
3	Adults with obesity undergoing intragastric balloon placement	Antiemetics	No antiemetics	• Incidence of PONV • Rate of ED visit within 30 days for PONV
4	Adults with obesity undergoing intragastric balloon placement	Pain medications	No pain medications	• Rate of ED visit within 30 days for pain management
5	Adults with obesity undergoing intragastric balloon placement	PPIs	No PPIs	• Rate of gastric ulcer • Rate of bleeding SAE
6	Adults with obesity	Endoscopic gastric remodeling + lifestyle modification	Lifestyle modification	• %TWL • SAE rate
7	Adults with obesity undergoing endoscopic gastric remodeling	Antiemetics	No antiemetics	• Incidence of PONV • Rate of ED visit within 30 days for PONV
8	Adults with obesity undergoing endoscopic gastric remodeling	Pain medications	No pain medications	• Rate of ED visit within 30 days for pain management
9	Adults with obesity undergoing endoscopic gastric remodeling	Prophylactic antibiotics	No prophylactic antibiotics	• Rate of gastric ulcer • Rate of bleeding SAE
10	Adults with obesity undergoing endoscopic gastric remodeling	PPIs	No PPIs	• Rate of postprocedure infection
11	Adults with obesity	Aspiration therapy + lifestyle modification	Lifestyle modification	• %TWL • SAE rate
12	Adults with obesity	Transpyloric shuttle + lifestyle modification	Lifestyle modification	• %TWL • SAE rate
13	Adults with obesity	Duodenal–jejunal bypass liner + lifestyle modification	Lifestyle modification	• HbA1c reduction • %TWL • SAE rate
14	Adults with obesity	Duodenal mucosal resurfacing + lifestyle modification	Lifestyle modification	• HbA1c reduction • SAE rate

%TWL, Percentage of total weight loss; *SAE*, serious adverse event; *PPI*, proton pump inhibitor; *PONV*, postoperative nausea and vomiting; *ED*, emergency department.

Supplementary material

SUPPLEMENTARY TABLE 2. Charactesristics of the included studies with patients who were overweight

Study	Country	Study design	No. of sites (no. of subjects for the entire study)	BMI indication (kg/m^2) (no. of subjects in this BMI subgroup)	Follow-up (mo)	Age (y)	Female sex (%)	BMI (kg/m^2)
Intragastric balloon								
Fittipaldi-Fernandez 2020[55]	Brazil	Observational	5 (5444)	27.0-29.9 (371)	6	38 ± 38*	75*	36.94 ± 5.67*
Moore 2018[56]	USA	Observational	108 (1343)	25.0-29.9 (124)	5-6	45.7 ± 10.8*	79*	35.4 ± 5.4*
Endoscopic gastric remodeling								
Barrichello 2019[57]	USA Brazil	Observational	7 (193)	25.0-29.9 (12)	12	42.3 ± 9.6*	100	29.7 ± .0
Duodenal–jejunal bypass liner								
Laubner 2018[58]	Germany	Observational	14 (235)	≥27 with T2DM	12†	52 ± 10	62	43.1 ± 6.9
Betzel 2017[59]	Netherlands	Observational	1 (185)	28.0-45.0 with T2DM	12	52 ± 8	49	35.1 ± 4.3
Cohen 2013[60]	Sweden	Observational	1 (16)	<36 with T2DM	12†	50 ± 7	35	30.0 ± 3.6

BMI, Body mass index; *T2DM*, type 2 diabetes mellitus.
For randomized controlled trials, only the data from the interventional arm were extracted to combine with those of the observational studies.
*Studies included patients in different overweight and obesity classes. Demographics reflected those of the entire cohort.
†Included for a pooled serious adverse event rate only.

SUPPLEMENTARY TABLE 3. Characteristics of the included studies with patients with classes I and II obesity

Study	Country	Study design	No. of sites (no. of subjects)	BMI indication (kg/m^2)	Intervention or device	Comparator	Age (y)	Female sex (%)	BMI (kg/m^2)
Intragastric balloon									
Konopko-Zubrzycka 2009[61]	Poland	RCT	1 (36) I:21, C:15		Orbera + Low intensity LM	Low intensity LM	I: 41 ± 12 C: 43 ± 9	I: 48 C: 60	I: 47.3 ± 5.7 C: 47.1 ± 6.9
Abu Dayyeh 2021[39]	USA	RCT	7 (288) I: 187, C: 101	30.0-39.9	Spatz + Moderate-intensity LM	Moderate-intensity LM	I: 44 ± 9 C: 44 ± 9	I: 87 C: 89	I: 35.8 ± 2.6 C: 35.8 ± 2.7
Sullivan 2018[44]	USA	RCT	15 (387) I: 198, C: 189	30.0-39.9	Obalon + moderate-intensity LM	Sham + moderate intensity LM	I: 43 ± 10 C: 43 ± 9	I: 86 C: 90	I: 35.2 ± 2.7 C: 35.5 ± 2.7
Courcoulas 2017[40]	USA	RCT	15 (255) I: 125, C: 130	30.0-39.9	Orbera + moderate-intensity LM	Moderate-intensity LM	I: 39 ± 9 C: 41 ± 10	I: 90 C: 90	35 for total population
Ponce 2015[43]	USA	RCT	15 (326) I: 187, C: 139	30.0-39.9	ReShape + moderate-intensity LM	Sham + moderate-intensity LM	I: 44 ± 10 C: 44 ± 10	I: 95 C: 95	I: 35.3 ± 2.8 C: 35.4 ± 2.6
Ponce 2013[42]	USA	RCT	3 (30) I: 21, C: 9	30.0-39.9	ReShape + moderate-intensity LM	Moderate-intensity LM	I: 39 ± 9 C: 45 ± 7	I: 81 C: 100	I: 34.7 ± 2.6 C: 35.6 ± 2.0
Fuller 2013[41]	Australia	RCT	1 (66) I: 31, C: 35	30.0-39.9	Orbera + moderate-intensity LM	Moderate-intensity LM	I: 43 ± 9 C: 48 ± 7	I: 68 C: 66	I: 36.0 ± 2.7 C: 36.7 ± 2.9
Endoscopic gastric remodeling									
Abu Dayyeh 2022[45]	USA	RCT	9 (209) I: 85, C: 124	30.0-39.9	Overstitch + moderate-intensity LM	Moderate-intensity LM	I: 47 ± 9 C: 46 ± 10	I: 88 C: 84	I: 35.5 ± 2.6 C: 35.7 ± 2.6

(*continued on the next page*)

Supplementary material

SUPPLEMENTARY TABLE 3. Continued

Study	Country	Study design	No. of sites (no. of subjects)	BMI indication (kg/m^2)	Intervention or device	Comparator	Age (y)	Female sex (%)	BMI (kg/m^2)
Huberty 2021[62,*]	Belgium Italy	RCT	2 (71) I: 49, C: 22	30.0-39.9	Endomina + Low-intensity LM	Low-intensity LM	I: 38 ± 10 C: 45 ± 12	I: 94 C: 91	I: 34.8 ± 2.7 C: 34.2 ± 2.5
Miller 2017[46]	Europe	RCT	3 (44) I: 34, C: 10	30.0-39.9	Incisionless Operating Platform + moderate-intensity LM	Moderate-intensity LM	I: 38 ± 10 C: 39 ± 13	I: 74 C: 90	I: 36.2 ± 3.3 C: 37.2 ± 3.7
Sullivan 2017[47]	USA	RCT	11 (332) I: 221, C: 111	30.0-39.9	Incisionless Operating Platform + Low-intensity LM	Sham + Low-intensity LM	I: 44 ± 9 C: 45 ± 9	I: 88 C: 91	I: 36.0 ± 2.4 C: 36.2 ± 2.2
Aspiration therapy									
Thompson 2017[52]	USA	RCT	10 (171) I: 111, C: 60	35.0-55.0	Aspiration therapy + moderate-intensity LM	Moderate-intensity LM	I: 42 ± 10 C: 47 ± 12	I: 87 C: 88	I: 42.0 ± 5.1 C: 40.9 ± 3.9
Sullivan 2013[48]	USA	RCT	1 (18) I: 11, C: 7	35.0-50.0	Aspiration therapy + moderate-intensity LM	Moderate-intensity LM	I: 38 ± 2 C: 45 ± 3	I: 100 C: 75	I: 42.0 ± 1.4 C: 39.3 ± 1.1
Transpyloric shuttle									
Rothstein 2022[49]	USA	RCT	9 (270) I: 181, C: 89	30.0-39.9	Transpyloric shuttle + moderate-intensity LM	Sham + moderate-intensity LM	I: 43 ± 9 C: 44 ± 9	I: 93 C: 93	I: 36.8 ± 2.2 C: 36.1 ± 2.4
Duodenal–jejunal bypass liner									
Thompson 2022[50]	USA	RCT	25 (320) I: 213, C: 107	30.0-55.0	DJBL + moderate-intensity LM	Sham + moderate-intensity LM	I: 53 ± 8 C: 52 ± 8	I: 60 C: 65	I: 38.4 ± 5.7 C: 38.3 ± 5.3
Ruban 2022[51]	UK	RCT	2 (170) I: 85, C: 85	30.0-50.0	DJBL + moderate-intensity LM	Moderate-intensity LM	I: 52 ± 8 C: 52 ± 9	I: 46 C: 46	I: 36.8 ± 5.0 C: 35.8 ± 4.2
Koehestanie 2014[63,*]	Netherlands	RCT	3 (77) I: 38, C: 39	30.0-50.0	DJBL + moderate-intensity LM	Moderate-intensity LM	I: 50 [42-58] C: 49 [44-55]	I: 38 C: 36	I: 34.6 [32.4-38.1] C: 36.8 [32.6-42.0]
Duodenal mucosal resurfacing									
Mingrone 2021[64]	Europe Brazil	RCT	11 (108) I: 56, C: 52	24.0-40.0	Duodenal mucosal resurfacing + moderate-intensity LM	Sham + moderate-intensity LM	I: 58 ± 14 C: 56 ± 14	I: 30 C: 31	I: 31.5 ± 4.7 C: 30.7 ± 5.7

Values are mean ± standard deviation, mean (standard deviation), or median [interquartile range].
BMI, Body mass index; *LM*, lifestyle modification; *RCT*, randomized-controlled trial; *I*, intervention; *C*, control; *DJBL*, duodenal–jejunal bypass liner.
*Included for a pooled serious adverse event rate only.

Supplementary material

SUPPLEMENTARY TABLE 4. Characteristics of the included studies with patients with class III obesity

Study	Country	Study design	No. of sites (no. of subjects for the entire study)	BMI indication (kg/m^2) (no. of subjects in this BMI subgroup)	Follow-up (mo)	Age (y)	Female sex (%)	BMI (kg/m^2)
Intragastric balloon								
Fittipaldi-Fernandez 2020[55]	Brazil	Observational	5 (5444)	≥40 (1264)	6	38 ± 38*	75*	36.94 ± 5.67*
Moore 2018[56]	USA	Observational	108 (1343)	>40 (192)	5-6	45.7 ± 10.8*	79*	35.4 ± 5.4*
Khan 2013[65]	UK	Observational	1 (40)	>60 (40)	6	45 ± 1.4	74	69.1 ± 1.0
Zerrweck 2012[66]	France	Observational	1 (23)	>60 (23)	6	44 ± 10.8	65	65 ± 3.8
Konopko-Zubrzycka 2009[61]	Poland	Observational	1 (21)	≥40 (21)	6	41 ± 11.9	48	47.3 ± 5.7
Gottig 2009[67]	Germany	Observational	1 (109)	>50 (109)	6	39.1 ± 8.4	41	68.8 ± 8.9
Mohamed 2008[69]	UK	Observational	1 (50)	≥40 (50)	6	41.4 ± 7.9	70	52.8 ± 8.2
Spyropoulos 2007[68]	Greece	Observational	1 (26)	≥50 (26)	6	40.8 ± 8.1	12	65.3 ± 9.8
Frutos 2007[70]	Spain	Observational	1 (31)	>40 (31)	6	40.08 ± 11.1	68	55.2 ± 6.9
Alfalah 2006[71]	France	Observational	1 (10)	≥50 (10)	6	33 ± 11	100	64.4 ± 7
Busetto 2005[72]	Italy	Observational	1 (17)	>40 (17)	6	26-62	0	55.8 ± 9.9
Busetto 2004[73]	Italy	Observational	1 (43)	>50 (43)	6	43.3 ± 10.5	40	58.4 ± 6.6
Endoscopic gastric remodeling								
Lopez-Nava 2019[110]	Spain	Observational	1 (435)	≥40 (161)	12	45 ± 11	61	44.5 ± 3.8
Barrichello 2019[57]	USA Brazil	Observational	7 (193)	≥40 (16)	12	42.3 ± 9.6*	44	42.2 ± .1
*Aspiration therapy**								
Nystrom 2018[75]	Sweden	Observational	5 (201)	35-70 (201)	12	46 ± 11	75	43.6 ± 7.4
Thompson 2017[52] (interventional arm only)	USA	RCT†	10 (111)	35-55 (111)	12	42 ± 10	87	42.0 ± 5.1
Sullivan 2013[48] (interventional arm only)	USA	RCT†	1 (10)	40-50 or 35.0-39.9 with comorbidities (10)	12	39 ± 2	100	42.0 ± 1.4
*Duodenal–jejunal bypass liner**								
Thompson 2022[50] (interventional arm only)	USA	RCT†	25 (212)	30-55 with T2DM	12	53 ± 8	60	38.4 ± 5.7
Ruban 2022[51] (interventional arm only)	UK	RCT†	2 (85)	30-50 with T2DM	12	52 ± 8	46	36.8 ± 5.0
Obermayer 2021[76]	Austria	Observational	1 (10)	30.0-49.9 with T2DM	9‡	48 ± 9	60	43.3 ± 5.0
Roehlen 2020[77]	Germany	Observational	1 (71)	≥30 with T2DM	9-12‡	47 (range, 21-66)	70	45.2 ± 8.0
Deutsch 2018[78]	Israel	Observational	1 (39)	≥30 with T2DM	9-12‡	58 ± 8	42	37.3 ± 4.9
Laubner 2018[58]	Germany	Observational	14 (235)	≥27 with T2DM	12	52 ± 10	62	43.1 ± 6.9
Patel 2018[79]	UK	Observational	3 (31)	30-50 with T2DM	12	50 ± 8	51	40.0 ± 5.8
Quezada 2018[80]	Chile	Observational	1 (17)	40-60 or ≥35 with a comorbidity + T2DM	12	35 ± 10*	69*	42.2 ± 5.0*
Betzel 2017[59]	Netherlands	Observational	1 (165)	28-45 with T2DM	12	52 ± 8	44	35.1 ± 4.2
Gollisch 2017[81]	Germany	Observational	1 (20)	≥35 with T2DM	12	53 [47-61]	70	41 [38-46]
Stratmann 2016[82]	Germany	Observational	1 (16)	≥ 35 with T2DM	12	50 ± 8	19	48.8 ± 8.5

(*continued on the next page*)

Supplementary material

SUPPLEMENTARY TABLE 4. Continued

Study	Country	Study design	No. of sites (no. of subjects for the entire study)	BMI indication (kg/m^2) (no. of subjects in this BMI subgroup)	Follow-up (mo)	Age (y)	Female sex (%)	BMI (kg/m^2)
Koehestanie 2014[63] (interventional arm only)	Netherlands	RCT†	1 (34)	30-50 with T2DM	6‡	50 [42-58]	38	34.6 [32.4–38.1]
De Moura 2012[83]	Brazil	Observational	1 (22)	40-60 with T2DM	12	46 ± 11	86	44.8 ± 7.4
Rodriguez 2009[84] (interventional arm only)	Chile	RCT	1 (12)	30-50 with T2DM	12	45 ± 7	67	38.9 ± 5.9

Values are mean ± standard deviation or median [interquartile range].
BMI, Body mass index; *RCT*, randomized controlled trial; *T2DM*, type 2 diabetes mellitus.
*Studies included patients in different overweight and obesity classes. Demographics reflected those of the entire cohort.
†For RCTs, only the data from the interventional arm were extracted to combine with those of the observational studies.
‡Included for a pooled serious adverse event rate only.

Supplementary material

SUPPLEMENTARY TABLE 5. Evidence profile for supporting the use of endoscopic bariatric and metabolic therapies in different BMI categories

Outcomes	No. of subjects (studies)	Certainty of the evidence (Grading of Recommendations Assessment, Development and Evaluation)	Benefits*	Harms†
BMI 27.0-29.9 kg/m^2 with ≥1 comorbidity				
%TWL at 6-12 mo	692 (4 observational)	Very low	11.9% TWL [7.7-16.0]	—
HbA1c reduction at 12 m	436 (3 observational)	Very low	1.0% [.6-1.5]	—
SAE rate	7416 (6 observational)	Very low	—	2.7% [1.2-6]
BMI 30.0-39.9 kg/m^2				
%TWL at 6-12 mo	2886 (14 RCTs)	Moderate	Mean difference of 6.3% TWL [5.3-7.3]	—
HbA1c reduction at 12 mo	490 (2 RCTs)	Moderate	Mean difference of .7% [.4-1.1]	—
SAE rate	3599 (16 RCTs)	Low	—	14 more per 1000 [6-30]
BMI ≥40 kg/m^2				
%TWL at 6-12 mo	2776 (20 observational)	Very low	13.1% TWL [10.8-15.4]	—
HbA1c reduction at 12 mo	815 (10 observational)	Very low	1.3% [1.0-1.6]	—
SAE rate	2042 (26 observational)	Very low	—	6.9% [5.7-8.2]

BMI, Body mass index; %*TWL*, percentage of total weight loss; *SAE*, serious adverse event; *RCT*, randomized controlled trial; —, not applicable.
*Pooled mean [95% confidence interval] for observational studies and mean difference [95% confidence interval] for RCTs.
†Pooled SAE rate [95% confidence interval] for observational studies and absolute risk [95% confidence interval] for RCTs.

Supplementary material

SUPPLEMENTARY TABLE 6. Evidence profile for supporting the use of endoscopic bariatric and metabolic therapies in BMI 27-29.9 kg/m^2 with at least 1 obesity-related comorbidity

Question: Endoscopic bariatric and metabolic therapies with lifestyle modification compared with lifestyle modification alone in patients with BMIs of 27-29.9 kg/m^2

Certainty assessment									
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Impact**	**Certainty**	**Importance**
%TWL at 6 mo (for IGB) or 12 mo (for EGR, DJBL)									
4	Observational studies	Serious*	Serious†	Serious‡	Not serious	None	Patients experienced a pooled weight loss of 11.9% TWL [95% CI, 7.7-16.0].	⨁◯◯◯ Very low	CRITICAL
Reduction in HbA1c at 12 mo (patients with concomitant diabetes mellitus) (for DJBL)									
3	Observational studies	Not serious	Serious§	Serious‖	Serious¶	All plausible residual confounding would reduce the demonstrated effect	Patients experienced a pooled reduction in HbA1c by 1.0% [95% CI, .6-1.5] at 12 mo.	⨁◯◯◯ Very low	CRITICAL
Serious adverse event rate (for IGB, EGR, DJBL)									
6	Observational studies	Not serious	Serious**	Serious‖	Serious†	None	The pooled serious adverse event rate was 2.7% [95% CI, 1.2-6].	⨁◯◯◯ Very low	CRITICAL

BMI, Body mass index; *%TWL*, percentage of total weight loss; *IGB*, intragastric balloon; *EGR*, endoscopic gastric remodeling; *DJBL*, duodenal–jejunal bypass liner; *CI*, confidence interval.

*Possible bias because of no clear exclusion of patients on antiobesity medications or thyroid medications.

†Fernandez 2020 had greater weight loss compared with other studies.

‡Betzel 2017 included patients with obesity in addition to overweight patients.

§Laubner 2018 had greater HbA1c reduction compared with the pooled reduction in HbA1c.

‖Some studies for DJBL included both overweight patients and patients with obesity.

¶Total sample size <400.

**Inconsistency in the serious adverse event rates among different studies.

††Low event rate (<300).

Supplementary material

SUPPLEMENTARY TABLE 7. Evidence profile for supporting the use of EBMTs in BMI 30-39.9 kg/m^2
Question: EBMTs with lifestyle modification compared with lifestyle modification alone in patients with BMIs of 30-39.9 kg/m^2

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
%TWL at 12 mo						
14	Randomized trials	Not serious	Serious*	Not serious†	Not serious	None
Reduction in HbA1c at 12 mo (patients with concomitant diabetes mellitus) (for DJBL)						
2	Randomized trials	Not serious	Not serious	Not serious	Serious‡	None
Serious adverse event rate						
16	Randomized trials	Not serious	Not serious	Not serious	Very serious§,‖	None

EBMT, Endoscopic bariatric and metabolic therapy; *BMI*, body mass index; *CI*, confidence interval; *DJBL*, duodenal-jejunal bypass liner; *%TWL*, percentage of total weight loss.
*There appeared to be inconsistency in the amount of weight loss. This was likely explained by the heterogeneity of the EBMT devices/procedures included in the analysis.
†Studies on aspiration therapy included patients with classes II and III obesity. Studies on duodenal–jejunal bypass liners included patients with class I to III obesity. Studies on duodenal mucosal resurfacing included overweight and classes I and II obesity. Nevertheless, all studies included patients with class I and/or class II obesity. We downgraded for indirectness once with inconsistency.
‡The pooled estimate crosses the minimally important difference (MID) line (.5% reduction in HbA1c).
§Low event rate (<300).
‖Wide CI.

Supplementary material

SUPPLEMENTARY TABLE 7. Continued

No. of patients		Effect			
EBMTs with lifestyle modification	**Lifestyle modification alone**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
%TWL at 12 mo					
The mean difference for percentage of total weight loss at 12 mo was 6.3% [5.3-7.3] in favor of EBMTs.				⨁⨁⨁◯ Moderate	CRITICAL
Reduction in HbA1c at 12 mo (patients with concomitant diabetes mellitus) (for DJBL)					
The mean difference for HbA1c reduction at 12 mo was .73% [.39-1.06] in favor of EBMTs.				⨁⨁⨁◯ Moderate	CRITICAL
Serious adverse event rate					
111/2135 (5.2%)	6/1464 (.4%)	Risk ratio, 4.43 (2.40-8.20)	14 more per 1000 (from 6 more to 30 more)	⨁⨁◯◯ Low	CRITICAL

Supplementary material

SUPPLEMENTARY TABLE 8. Evidence profile for supporting the use of endoscopic bariatric and metabolic therapies in BMI ≥40 kg/m^2
Question: Endoscopic bariatric and metabolic therapies with lifestyle modification compared with lifestyle modification alone in patients with BMIs of at least 40 kg/m^2

Certainty assessment									
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Impact**	**Certainty**	**Importance**
%TWL at 6 mo (for IGB) or 12 mo (for EGR, AT, DJBL)									
20	Observational studies	Serious*	Serious†	Serious‡	Not serious	None	Patients experienced a pooled weight loss of 13.1% TWL [95% CI, 10.8-15.4].	⨁◯◯◯ Very low	CRITICAL
Reduction in HbA1c at 12 mo (patients with concomitant diabetes mellitus) (for DJBL)									
10	Observational studies	Not serious	Serious§	Serious‖	Not serious	All plausible residual confounding would reduce the demonstrated effect	Patients experienced a pooled reduction in HbA1c by 1.3% [95% CI, 1.0-1.6] at 12 mo.	⨁◯◯◯ Very low	CRITICAL
Serious adverse event rate (for IGB, EGR, AT, DJBL)									
26	Observational studies	Not serious	Serious¶	Serious**	Serious††	None	The pooled serious adverse event rate was 6.9% [95% CI, 5.7-8.2].	⨁◯◯◯ Very low	CRITICAL

BMI, Body mass index; *%TWL*, percentage of total weight loss; *IGB*, intragastric balloon; *AT*, aspiration therapy; *ESG*, endoscopic sleeve gastroplasty; *DJBL*, duodenal–jejunal bypass liner; *CI*, confidence interval.
*Possible bias because of unclear exclusion of patients on antiobesity medications or thyroid medications.
†Inconsistency in the amount of weight loss among studies.
‡Some studies for AT and DJBL included patients with classes I or II obesity in addition to class III obesity.
§De Moura 2012 had greater HbA1c reduction, whereas Betzel 2017 had less HbA1c reduction compared with the pooled HbA1c reduction.
‖All studies except De Moura 2012 included patients with class II and/or class I obesity in addition to class III obesity.
¶Inconsistency in the SAE rates among different studies.
**Some studies for AT and DJBL included patients with class II and/or class I obesity in addition to class III obesity.
††Low event rate (<300).

Supplementary material

SUPPLEMENTARY TABLE 9. Characteristics of included studies

Study	Country	Study design	No. of sites (no. of subjects)	Follow-up* (mo)	Intervention or device	Comparator	Age (y)	Female sex (%)	Body mass index (kg/m^2)
Intragastric balloon									
Abu Dayyeh 2021[39]	USA	RCT	7 (288) I: 187, C: 101	8	Spatz + moderate-intensity LM	Moderate-intensity LM	I: 44 ± 9 C: 44 ± 9	I: 87 C: 89	I: 35.8 ± 2.6 C: 35.8 ± 2.7
Vicente Martin 2019[91]	Spain	RCT	1 (66) I: 39, C: 42	6	Orbera + moderate-intensity LM	Moderate-intensity LM	I: 43 ± 10 C: 43 ± 9	I: 66 C: 71	I: 46.4 [41.5-49] C: 46 [43-49.7]
Sullivan 2018[44]	USA	RCT	15 (387) I: 198, C: 189	6	Obalon + moderate-intensity LM	Sham + moderate-intensity LM	I: 43 ± 10 C: 43 ± 9	I: 86 C: 90	I: 35.2 ± 2.7 C: 35.5 ± 2.7
Courcoulas 2017[40]	USA	RCT	15 (255) I: 125, C: 130	6, 12	Orbera + moderate-intensity LM	Moderate-intensity LM	I: 39 ± 9 C: 41 ± 10	I: 90 C: 90	35 for total population
Ponce 2015[43]	USA	RCT	15 (326) I: 187, C: 139	6	ReShape + moderate-intensity LM	Sham + moderate-intensity LM	I: 44 ± 10 C: 44 ± 10	I: 95 C: 95	I: 35.3 ± 2.8 C: 35.4 ± 2.6
Ponce 2013[42]	USA	RCT	3 (30) I: 21, C: 9	6	ReShape + moderate-intensity LM	Moderate-intensity LM	I: 39 ± 9 C: 45 ± 7	I: 81 C: 100	I: 34.7 ± 2.6 C: 35.6 ± 2.0
Fuller 2013[41]	Australia	RCT	1 (66) I: 31, C: 35	6, 12	Orbera + moderate-intensity LM	Moderate-intensity LM	I: 43 ± 9 C: 48 ± 7	I: 68 C: 66	I: 36.0 ± 2.7 C: 36.7 ± 2.9
Endoscopic gastric remodeling									
Abu Dayyeh 2022[45]	USA	RCT	9 (209) I: 85, C: 124	12	Overstitch + moderate-intensity LM	Moderate-intensity LM	I: 47 ± 9 C: 46 ± 10	I: 88 C: 84	I: 35.5 ± 2.6 C: 35.7 ± 2.6
Huberty 2021[62]	Belgium Italy	RCT	2 (71) I: 49, C: 22	6*	Endomina + low-intensity LM	Low-intensity LM	I: 38 ± 10 C: 45 ± 12	I: 94 C: 91	I: 34.8 ± 2.7 C: 34.2 ± 2.5
Miller 2017[46]	Europe	RCT	3 (44) I: 34, C: 10	12	Incisionless Operating Platform + moderate-intensity LM	Moderate-intensity LM	I: 38 ± 10 C: 39 ± 13	I: 74 C: 90	I: 36.2 ± 3.3 C: 37.2 ± 3.7
Sullivan 2017[47]	USA	RCT	11 (332) I: 221, C: 111	12	Incisionless Operating Platform + low-intensity LM	Sham + low-intensity LM	I: 44 ± 9 C: 45 ± 9	I: 88 C: 91	I: 36.0 ± 2.4 C: 36.2 ± 2.2
Aspiration therapy									
Thompson 2017[52]	USA	RCT	10 (171) I: 111, C: 60	12	Aspiration therapy + moderate-intensity LM	Moderate-intensity LM	I: 42 ± 10 C: 47 ± 12	I: 87 C: 88	I: 42.0 ± 5.1 C: 40.9 ± 3.9
Sullivan 2013[48]	USA	RCT	1 (18) I: 11, C: 7	12	Aspiration therapy + moderate-intensity LM	Moderate-intensity LM	I: 38 ± 2 C: 45 ± 3	I: 100 C: 75	I: 42.0 ± 1.4 C: 39.3 ± 1.1
Transpyloric shuttle									
Rothstein 2022[49]	USA	RCT	9 (270) I: 181, C: 89	12	Transpyloric shuttle + moderate-intensity LM	Sham + moderate-intensity LM	I: 43 ± 9 C: 44 ± 9	I: 93 C: 93	I: 36.8 ± 2.2 C: 36.1 ± 2.4
Duodenal-jejunal bypass liner									
Thompson 2022[50]	USA	RCT	25 (320) I: 213, C: 107	12	DJBL + low-intensity LM	Sham + low-intensity LM	I: 53 ± 8 C: 52 ± 8	I: 60 C: 65	I: 38.4 ± 5.7 C: 38.3 ± 5.3
Ruban 2022[51]	UK	RCT	2 (170) I: 85, C: 85	12	DJBL + moderate-intensity LM	Moderate-intensity LM	I: 52 ± 8 C: 52 ± 9	I: 46 C: 46	I: 36.8 ± 5.0 C: 35.8 ± 4.2
Koehestanie 2014[63]	Netherlands	RCT	3 (77) I: 38, C: 39	6*	DJBL + moderate-intensity LM	Moderate-intensity LM	I: 50 [42-58] C: 49 [44-55]	I: 38 C: 36	I: 34.6 [32.4-38.1] C: 36.8 [32.6-42.0]
Duodenal mucosal resurfacing									
Mingrone 2021[64]	Europe Brazil	RCT	11 (108) I: 56, C: 52	6	Duodenal mucosal resurfacing + low-intensity LM	Sham + low-intensity LM	I: 58 ± 14 C: 56 ± 14	I: 30 C: 31	I: 31.5 ± 4.7 C: 30.7 ± 5.7

Values are mean ± standard deviation or median [interquartile range].
RCT, Randomized-controlled trial; *LM*, lifestyle modification; *I*, intervention, *C*, control; *DJBL*, duodenal-jejunal bypass liner.
*Included for pooled serious adverse event rate only.

Supplementary material

SUPPLEMENTARY TABLE 10. Serious adverse events reported in intragastric balloon randomized controlled trials

Study	Active arm	Control arm
Abu Dayyeh 2021[39]	7/187 • Nausea, vomiting, abdominal pain, abdominal discomfort • Diarrhea • GERD • Metabolism and nutrition disorders • Dehydration • Failure to thrive • Hypokalemia	0/101
Courcoulas 2017[40]	16/160 • Device intolerance resulting in early removal (8) • Severe dehydration (2) • Gastric outlet obstruction • Gastric perforation with sepsis • Aspiration pneumonia • Severe abdominal cramping • Laryngospasm • Esophageal mucosal injuries	0/121
Konopko 2009[61]	0/21	0/15
Ponce 2013[42]	5/21 • Nausea requiring readmission (4) • Brief hypoxia during device removal requiring endotracheal intubation for a few minutes	0/9
Ponce 2015[43]	28/264 • 28 events occurred in 20 patients • Accommodative symptoms requiring emergency room visit (21) • Esophageal mucosal tear during removal • Gastroesophageal junction ulcer-associated bleeding • Contained cervical esophageal perforation during removal • Postremoval pneumonitis	0/139
Sullivan 2018[44]	1/336 • Bleeding gastric ulcer after taking protocol-inhibited nonsteroidal anti-inflammatory drugs	0/371
Vicente Martin 2019[91]	1/39 • GI bleeding	0/42

Supplementary material

SUPPLEMENTARY TABLE 11. Evidence profile for supporting the use of endoscopic bariatric and metabolic therapies for the treatment of obesity

Outcomes	No. of subjects (studies)	Certainty of the evidence (Grading of Recommendations Assessment, Development and Evaluation)	Benefits Mean difference [95% CI]	Harms Absolute risk [95% CI]
Intragastric balloon				
%TWL at 6-8 mo	1341 (7 RCTs)	Moderate	6.9% TWL [4.1-9.7]	—
%TWL at 12 mo	300 (2 RCTs)	Moderate	4.4% TWL [2.9-6.0]	—
SAE rate	1826 (7 RCTs)	Moderate	—	32 more per 1000 [7-114]
Endoscopic gastric remodeling				
%TWL at 12 mo	585 (3 RCTs)	Moderate	8.0% TWL [3.4- 12.6]	—
SAE rate	688 (4 RCTs)	Moderate	—	5.6 more per 1000 [1.1-30.1]
Aspiration therapy				
%TWL at 12 mo	189 (2 RCTs)	Moderate	9.0% TWL [6.7-11.2]	—
SAE rate	189 (RCTs)	Low	—	16 more per 1000 [3-354]
Transpyloric shuttle				
%TWL at 12 mo	270 (1 RCT)	Moderate	7.4% TWL [5.4-9.4]	—
SAE rate	302 (1 RCT)	Low	—	18 more per 1000 [3-380]
Duodenal–jejunal bypass liner				
HbA1c reduction at 12 mo	492 (2 RCTs)	Moderate	.7% [.4-1.1]	—
%TWL at 12 mo	492 (2 RCTs)	High	5.4% TWL [4.1-6.7]	—
SAE rate	563 (3 RCTs)	Moderate	—	24 more per 1000 [8-59]
Duodenal mucosal resurfacing				
HbA1c reduction at 12 mo	108 (1 RCT)	Low	1.0% [.1-1.9]	—
SAE rate	108 (1 RCT)	Low	—	15 more per 1000 [3-375]

CI, Confidence interval; *%TWL*, percentage of total weight loss; *SAE*, serious adverse event; *RCT*, randomized controlled trial.

Supplementary material

SUPPLEMENTARY TABLE 12. Evidence profile for supporting the use of IGBs

Question: IGB placement with lifestyle modification compared with lifestyle modification alone in patients seeking endoscopic bariatric and metabolic therapies

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
%TWL at 6 mo						
7	Randomized trials	Not serious	Not serious	Not serious	Serious*	None
%TWL at 12 mo (6 mo after IGB removal)						
2	Randomized trials	Not serious	Not serious	Not serious	Serious†	None
Serious adverse events						
7	Randomized trials	Not serious	Not serious	Not serious	Serious‡	None

IGB, Intragastric balloon; *CI*, confidence interval; *%TWL*, percentage of total weight loss; *MD*, mean difference.

*Wide CI and some inconsistency

†Small total sample size (<400) and pooled effect crosses MID line.

‡Wide CI and low event rate (<300).

Supplementary material

SUPPLEMENTARY TABLE 12. Continued

No.of patients		Effect			
IGB placement with lifestyle modification	Lifestyle modification alone	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
%TWL at 6 mo					
735	606	—	MD 6.89% TWL higher (4.09 higher to 9.7 higher)	⨁⨁⨁◯ Moderate	CRITICAL
%TWL at 12 mo (6 mo after IGB removal)					
148	152	—	MD 4.42% TWL higher (2.9 higher to 5.95 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Serious adverse events					
58/1028 (5.6%)	0/798 (.0%)	Risk ratio 8.97 (2.72-29.56)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
	.4%		32 more per 1000 (from 7 more to 114 more)		

Supplementary material

SUPPLEMENTARY TABLE 13. Serious adverse events reported in endoscopic gastric remodeling randomized controlled trials

Study	Active arm	Control arm
Abu Dayyeh 2022[45]	3/131 • Abdominal abscess treated with endoscopy • Upper GI bleeding managed conservatively, without transfusion • Malnutrition treated with endoscopic sleeve gastroplasty reversal	0/110
Huberty 2021[62]	0/49	0/22
Miller 2017[46]	0/34	0/10
Sullivan 2017[47]	11/221 • Extraluminal bleeding treated with laparoscopy • Hepatic abscess treated with percutaneous drainage and antibiotics • Abdominal pain, nausea, or vomiting resulting in prolonged hospitalization (n = 9)	1/111 • Vomiting resulting in prolonged hospitalization

Supplementary material

SUPPLEMENTARY TABLE 14. Evidence profile for supporting the use of EGR

Question: EGR with lifestyle modification compared with lifestyle modification alone with or without sham in patients with obesity seeking endoscopic bariatric and metabolic therapies

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
%TWL at 12 mo						
3	Randomized trials	Not serious	Not serious*	Serious†	Not serious‡	None
Serious adverse event rate						
4	Randomized trials	Not serious	Not serious	Not serious	Serious§	None

EGR, Endoscopic gastric remodeling *CI*, confidence interval; *%TWL*, percentage of total weight loss.

*Inconsistency between Abu Dayyeh vs Miller/Sullivan could be explained by techniques (gastric body vs fundus). Inconsistency between Miller vs Sullivan could be explained by nonsham vs sham control arm.

†Miller 2017 and Sullivan 2017 used an older primary obesity surgical endoluminal technique involving fundic plications. Data from these 2 studies were used as a surrogate of the current technique, which involves gastric body plications sparing the fundus.

‡We noted a wide CI that was driven by explainable inconsistency and indirectness, the latter of which was already downgraded.

§Low event rate (<300) and wide CI.

Supplementary material

SUPPLEMENTARY TABLE 14. Continued

No. of patients		Effect			
EGR with lifestyle modificaiton	**Lifestyle modification alone with or without sham**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
%TWL at 12 mo					
340	245	—	Mean difference 7.99% TWL higher (3.36 higher to 12.63 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Serious adverse event rate					
14/435 (3.2%)	1/253 (.4%)	Risk ratio 5.63 (1.05-30.13)	18 more per 1000 (from 0 fewer to 115 more)	⨁⨁⨁◯ Moderate	CRITICAL

Supplementary material

SUPPLEMENTARY TABLE 15. Serious adverse events reported in transpyloric shuttle randomized controlled trials

Study	Active arm	Control arm
Rothstein 2022[49]	6/213 • Esophageal rupture with bilateral pneumothoraces • Upper abdominal pain • Vomiting and device impaction • Device intolerance and device impaction • Gastric ulcer and device impaction • Device impaction	0/89

Supplementary material

SUPPLEMENTARY TABLE 16. Evidence profile for supporting the use of TPS

Question: TPS with lifestyle modification compared with lifestyle modification alone with or without sham in patients seeking endoscopic bariatric and metabolic therapies

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
%TWL at 12 mo						
1	Randomized trials	Not serious	Not serious	Not serious	Very serious*	None
Serious adverse event rate						
1	Randomized trials	Not serious	Not serious	Not serious	Very serious†,‡	None

TPS, Transpyloric shuttle; *CI*, confidence interval; *%TWL*, percentage of total weight loss.
*Total sample size <400.
†Low event rate (<300).
‡Wide CI and poled effect show both increased and decreased harm.

Supplementary material

SUPPLEMENTARY TABLE 16. Continued

No. of patients		Effect			
TPS with lifestyle modification	**Lifestyle modification alone with or without sham**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
%TWL at 12 mo					
181	89	—	Mean difference 6.7% TWL higher (4.5 higher to 8.9 higher)	⨁⨁◯◯ Low	CRITICAL
Serious adverse event rate					
6/213 (2.8%)	0/89 (.0%) .4%	Risk ratio 5.47 (.31-96.03)	0 fewer per 1000 (from 0 fewer to 0 fewer) 18 more per 1000 (from 3 fewer to 380 more)	⨁⨁◯◯ Low	CRITICAL

Supplementary material

SUPPLEMENTARY TABLE 17. Serious adverse events reported in duodenal-jejunal bypass liner randomized controlled trials

Study	Active arm	Control arm
Thompson 2012[50]	19/212 • Atrial fibrillation • Abdominal pain • Dehydration • GI hemorrhage • Intestinal perforation • Liver abscess • Obstruction • Pancreatitis • Increase in transminases	0/108
Ruban 2022[51]	4/85 • GI bleeding requiring early removal • Cholecystitis requiring early removal • Liver abscess	0/85
Koehestanie 2014[63]	5/34 • Melena, nothing on endoscopy • Dehydration, treated with conservative management • Sleeve blockage • Cholelithiasis treated with cholecystectomy • Esophageal perforation during explantation	0/39

Supplementary material

SUPPLEMENTARY TABLE 18. Evidence profile for supporting the use of the DJBL

Question: DJBL with lifestyle modification compared with lifestyle modification alone with or without sham for patients seeking primary endoscopic bariatric and metabolic therapies

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
Reduction in HbA1c at 12 mo (patients with obesity + diabetes mellitus)						
2	Randomized trials	Not serious	Not serious	Not serious	Serious*	None
%TWL at 12 mo (patients with obesity + diabetes mellitus)						
2	Randomized trials	Not serious	Not serious	Not serious	Not serious	None
Serious adverse event rate (patients with obesity + diabetes mellitus)						
3	Randomized trials	Not serious	Not serious	Not serious	Serious†	None

DJBL, Duodenal-jejunal bypass liner; *CI*, confidence interval; *MD*, mean difference; *%TWL*, Percentage of total weight loss.
*The pooled estimate crosses the MID line (.5% reduction in HbA1c).
†Wide CI and low event rate (<300).

Supplementary material

SUPPLEMENTARY TABLE 18. Continued

No. of patients		Effect			
DJBL with lifestyle modification	**Lifestyle modification alone with or without sham**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
Reduction in HbA1c at 12 mo (patients with obesity + diabetes mellitus)					
298	192	—	MD .73 more (.39 more to 1.06 more)	⨁⨁⨁◯ Moderate	CRITICAL
%TWL at 12 mo (patients with obesity + diabetes mellitus)					
298	192	—	MD 5.38 higher (4.06 higher to 6.71 higher)	⨁⨁⨁⨁ High	CRITICAL
Serious adverse event rate (patients with obesity + diabetes mellitus)					
26/331 (7.9%)	0/232 (.0%) .4%	Risk ratio 7.0 (3.1-15.8)	0 fewer per 1000 (from 0 fewer to 0 fewer) 24 more per 1000 (from 8 more to 59 more)	⨁⨁⨁◯ Moderate	CRITICAL

Supplementary material

SUPPLEMENTARY TABLE 19. Serious adverse events reported in duodenal mucosal resurfacing randomized controlled trials

Study	Active arm	Control arm
Mingrone 2021[64]	2/56 • Hematochezia because of external hemorrhoids • Jejunal perforation treated with surgical repair	0/52

Supplementary material

SUPPLEMENTARY TABLE 20. Evidence profile for supporting the use of DMR
Question: DMR with lifestyle modification compared with lifestyle modification alone for patients seeking primary endoscopic bariatric and metabolic therapies

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
Reduction in HbA1c at 6 mo (diabetes mellitus only)						
1	Randomized trials	Not serious	Not serious	Not serious	Very serious[*,†]	None
Serious adverse event rate (diabetes mellitus only)						
1	Randomized trials	Not serious	Serious[‡]	Not serious	Serious[§,‖]	None

DMR, Duodenal mucosal resurfacing; *CI*, confidence interval.
[*]Small total sample size (<400).
[†]Does not meet the minimally important threshold of .5% difference in change in HbA1c.
[‡]One randomized controlled trial only.
[§]Wide CI.
[‖]Low event rate (<300).

Supplementary material

SUPPLEMENTARY TABLE 20. Continued

No. of patients		Effect			
DMR with lifestyle modification	Lifestyle modification alone	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
Reduction in HbA1c at 6 mo (diabetes mellitus only)					
56	52	—	Mean difference .3% more (1.1 fewer to 1.7 more)	⨁⨁◯◯ Low	CRITICAL
Serious adverse event rate (diabetes mellitus only)					
2/56 (3.6%)	0/52 (.0%) .4%	Risk ratio 4.65 (.23-94.63)	0 fewer per 1000 (from 0 fewer to 0 fewer) 15 more per 1000 (from 3 fewer to 375 more)	⨁⨁◯◯ Low	CRITICAL

SUPPLEMENTARY TABLE 21. SEARCH STRATEGIES FOR PICO QUESTIONS ON PATIENT POPULATIONS THAT ENDOSCOPIC BARIATRIC AND METABOLIC THERAPIES SHOULD BE CONSIDERED AND ON BENEFITS AND HARMS OF ENDOSCOPIC BARIATRIC AND METABOLIC THERAPIES

MEDLINE (Ovid)

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R) 1946 to March 26, 2021

March 29, 2021; updated on August 1, 2022.

2329 Records

1. (((endoscopy/ or exp endoscopy, digestive system/) and exp gastroplasty/) or gastric balloon/)
2. ((bariatric* or sleev* or gastroplast* or plication* or metabolic or volume reduction or malabsorptive) adj3 (endoscop* or endobariatric or trans oral or transoral or endoluminal or endoluminal)).ab,ti,kf
3. (((gastric or intragastric) adj3 balloon*).ab,ti,kf)
4. (allurion* or aspiration therap* or aspireassist or aspire assist or endalis or endomina* or endosleev* or endozip* or medsil or obalon* OR orbera* or transpyloric shuttle* or pose procedure or primary obesity surgery endoluminal or primary obesity surgery endolumenal).ab,ti,kf or (pose adj2 procedure).ab,ti,kf
5. ((reshape OR elipse or heliosphere or spatz or end ball or esg or igb or tps or pose) adj3 (balloon* or gastroplast* or intragastric or gastric or bariatric or endobariatric or endoscop* or trans oral or transoral or endoluminal or endolumenal)).ab,ti,kf
6. or/1-5

Embase (Elsevier; 1974-)

March 29, 2021

2256 Records

1. 'gastric balloon'/exp OR ('gastroplasty'/exp AND ('endoscopy'/de OR 'gastroscopy'/exp))
2. ((bariatric* OR sleev* OR gastroplast* OR plication* OR metabolic OR 'volume reduction' OR malabsorptive) NEAR/3 (endoscop* OR endobariatric OR 'trans oral' OR transoral OR endoluminal OR endoluminal)):ab,ti,kw
3. ((gastric OR intragastric) NEAR/3 balloon*):ab,ti,kw
4. (allurion* OR 'aspiration therap*' OR aspireassist OR 'aspire assist' OR endalis OR endomina* OR endosleev* OR endozip* OR medsil OR obalon* OR orbera* OR 'transpyloric shuttle*' OR 'primary obesity surgery endoluminal' OR 'primary obesity surgery endolumenal'):ab,ti,kw OR (pose NEAR/2 procedure):ab,ti,kw
5. ((reshape OR elipse OR heliosphere OR spatz OR 'end ball' OR esg OR igb OR tps OR pose) NEAR/3 (balloon* OR gastroplast* OR intragastric OR gastric OR bariatric OR endobariatric OR endoscop* OR 'trans oral' OR transoral OR endoluminal OR endolumenal)):ab,ti,kw
6. (#1 OR #2 OR #3 OR #4 OR #5) NOT ('conference abstract'/it OR 'conference paper'/it OR 'conference review'/it)

Web of Science Core Collection (Clarivate)

March 29, 2021

1986 Records

1. TS=(("bariatric*" OR "sleev*" OR "gastroplast*" OR "plication*" OR "metabolic" OR "volume reduction" OR "malabsorptive") NEAR/3 ("endoscop*" OR "endobariatric" OR "trans oral" OR "transoral" OR "endoluminal" OR "endoluminal"))
2. TS=(("gastric" OR "intragastric") NEAR/3 "balloon*")
3. TS=("allurion*" OR "aspiration therap*" OR "aspireassist" OR "aspire assist" OR "endalis" OR "endomina*" OR "endosleev*" OR "endozip*" OR "medsil" OR "obalon*" OR "orbera*" OR "transpyloric shuttle*" OR "primary obesity surgery endoluminal" OR "primary obesity surgery endolumenal" OR ("pose" NEAR/2 "procedure"))
4. TS=(("reshape" OR "elipse" OR "heliosphere" OR "spatz" OR "end ball" OR "esg" OR "igb" OR "tps" OR "pose") NEAR/3 ("balloon*" OR "gastroplast*" OR "intragastric" OR "gastric" OR "bariatric" OR "endobariatric" OR "endoscop*" OR "trans oral" OR "transoral" OR "endoluminal" OR "endolumenal"))
5. (#1 OR #2 OR #3 OR #4) NOT (Meeting Abstracts OR Proceedings Papers)

****

Supplementary material

Cochrane Central Register of Controlled Trials (Wiley)

March 29, 2021

207 Records

((bariatric* OR sleev* OR gastroplast* OR plication* OR metabolic OR "volume reduction" OR malabsorptive) NEAR/3 (endoscop* OR endobariatric OR trans oral OR transoral OR endoluminal OR endoluminal))

OR

((gastric OR intragastric) NEAR/3 balloon*)

OR

(allurion* OR aspiration therap* OR aspireassist OR "aspire assist" OR endalis OR endomina* OR endosleev* OR endozip* OR medsil OR obalon* OR orbera* OR "transpyloric shuttle" OR "primary obesity surgery endoluminal" OR "primary obesity surgery endolumenal" OR (pose NEAR/2 procedure))

OR

((reshape OR elipse OR heliosphere OR spatz OR "end ball" OR esg OR igb OR tps OR pose) NEAR/3 (balloon* OR gastroplast* OR intragastric OR gastric OR bariatric OR endobariatric OR endoscop* OR "trans oral" OR transoral OR endoluminal OR endolumenal))

****

SUPPLEMENTARY TABLE 22. SEARCH STRATEGIES FOR THE PICO QUESTIONS ON PERIPROCEDURAL CARE

MEDLINE (OvidSP)

December 15, 2022

12 records

(adult/ OR adult.ti,ab,kw OR adults.ti,ab,kw OR middle aged.ti,ab,kw) AND (obesity/ OR obesity hypoventilation syndrome/ OR obesity, abdominal/ OR obesity, metabolically benign/ OR obesity, morbid/ OR obese.ti,ab,kw OR obesity.ti,ab,kw OR overweight.ti,ab,kw) AND (Endoscopic Bariatric.ti,ab,kw OR Intra-gastric balloon*.ti,ab,kw OR Intragastric balloon*.ti,ab,kw OR orbera*.ti,ab,kw OR Obalon Reshape.ti,ab,kw OR Spatz.ti,ab,kw OR Endoscopic sleeve.ti,ab,kw OR endoscopic sleeve gastroplasty.ti,ab,kw OR primary obesity surgical endoluminal.ti,ab,kw OR endoscopic gastric plication.ti,ab,kw OR aspiration therap*.ti,ab,kw OR Duodeno-Jejunal Bypass Liner.ti,ab,kw OR duodenal-jejunal bypass liner.ti,ab,kw OR duodenal mucosal resurfacing.ti,ab,kw) AND

(Proton Pump Inhibitors/ OR Proton Pump Inhibitor*.ti,ab,kw OR exp omeprazole/ OR omeprazole.ti,ab,kw,nm OR Prilosec.ti,ab,kw,nm OR Esomeprazole.ti,ab,kw,nm OR Nexium.ti,ab,kw,nm OR Nexiam.ti,ab,kw,nm OR pantoprazole/ OR pantoprazole.ti,ab,kw,nm OR Protonix.ti,ab,kw,nm OR lansoprazole/ OR lansoprazole*.ti,ab,kw,nm OR pantomed.ti,ab,kw,nm

OR Aprepitant/ OR Aprepitant.ti,ab,kw,nm OR Ondansetronn.ti,ab,kw,nm OR Dexamethasonne.ti,ab,kw,nm OR Scopolamine patch*.ti,ab,kw,nm OR Metoclopramide/ OR Metoclopramide.ti,ab,kw,nm OR Maxolon.ti,ab,kw,nm OR Rimetin.ti,ab,kw,nm OR Primperan.ti,ab,kw,nm OR Reglan.ti,ab,kw,nm OR Cerucal.ti,ab,kw,nm OR Palonsetronn.ti,ab,kw,nm OR Promethazine/ OR Promethazine.ti,ab,kw,nm OR Proazamine.ti,ab,kw,nm OR

Rumergan.ti,ab,kw,nm OR Diprazin.ti,ab,kw,nm OR Isopromethazine.ti,ab,kw,nm OR Phenergan.ti,ab,kw,nm OR Phenargan.ti,ab,kw,nm OR Phensedyl.ti,ab,kw,nm OR Pipolfen.ti,ab,kw,nm OR Pipolphen.ti,ab,kw,nm OR Prothazin.ti,ab,kw,nm OR Pyrethia.ti,ab,kw,nm OR Remsed.ti,ab,kw,nm OR Atosil.ti,ab,kw,nm OR Diphergan.ti,ab,kw,nm

OR Prochlorperazine/ OR Prochlorperazine.ti,ab,kw,nm OR Compazine.ti,ab,kw,nm OR Lorazepam/ OR Lorazepam.ti,ab,kw,nm OR Haloperidol/ OR Haloperidol.ti,ab,kw,nm OR Haldol.ti,ab,kw,nm OR Droperidol/ OR Droperidol.ti,ab,kw,nm OR Inapsine.ti,ab,kw,nm OR Dehidrobenzperidol.ti,ab,kw,nm OR Dehydrobenzperidol.ti,ab,kw,nm OR Droleptan.ti,ab,kw,nm

OR Acetaminophen/ OR Acetaminophen.ti,ab,kw,nm OR Hydroxyacetanilide.ti,ab,kw,nm OR Acetamidophenol.ti,ab,kw,nm OR Acephen.ti,ab,kw,nm OR Acetaco.ti,ab,kw,nm OR Tylenol.ti,ab,kw,nm OR Datril.ti,ab,kw,nm OR Panadol.ti,ab,kw,nm OR Acamol.ti,ab,kw,nm OR Algotropyl.ti,ab,kw,nm OR Anti-Inflammatory Agents, Non-Steroidal/ OR Nonsteroidal Anti-Inflammatory Agent*.ti,ab,kw,nm OR NSAIDS.ti,ab,kw,nm OR Analgesics, Opioid/ OR Opioid*.ti,ab,kw,nm OR Tramadol/ OR Tramadol.ti,ab,kw,nm OR Tramundin.ti,ab,kw,nm OR Biodalgic.ti,ab,kw,nm OR Jutadol.ti,ab,kw,nm OR Nobligan.ti,ab,kw,nm OR Prontofort.ti,ab,kw,nm OR Zytram.ti,ab,kw,nm OR Takadol.ti,ab,kw,nm OR Theradol.ti,ab,kw,nm OR Topalgic.ti,ab,kw,nm OR Tradol.ti,ab,kw,nm OR Tradonal.ti,ab,kw,nm OR Tralgiol.ti,ab,kw,nm OR Trama Dorsch.ti,ab,kw,nm OR Trama-Dorsch.ti,ab,kw,nm OR Biokanol.ti,ab,kw,nm OR Tramabeta.ti,ab,kw,nm OR Tramadin.ti,ab,kw,nm OR Tramadoc.ti,ab,kw,nm OR Trasedal.ti,ab,kw,nm OR Ultram.ti,ab,kw,nm OR Zamudol.ti,ab,kw,nm OR Zumalgic.ti,ab,kw,nm OR Zydol.ti,ab,kw,nm OR Tramadolor.ti,ab,kw,nm OR Tramadura.ti,ab,kw,nm OR Tramagetic.ti,ab,kw,nm OR Tramagit.ti,ab,kw,nm OR Tramake.ti,ab,kw,nm OR Tramal.ti,ab,kw,nm OR Tramex.ti,ab,kw,nm OR Adolonta.ti,ab,kw,nm OR Contramal.ti,ab,kw,nm OR Amadol.ti,ab,kw,nm OR Hyosciamine.ti,ab,kw,nm OR Dicyclominne.ti,ab,kw,nm OR Gabapentin/ OR Gabapentin.ti,ab,kw,nm OR Neurontin.ti,ab,kw,nm OR

Convalis.ti,ab,kw,nm OR Pregabalin/ or Pregabalin.ti,ab,kw,nm OR Lyrica.ti,ab,kw,nm OR Antidepressive Agents, Tricyclic/ OR Tricyclic Antidepressant.ti,ab,kw,nm OR Tricyclic Antidepressive Agent*.ti,ab,kw,nm

OR exp Anti-Bacterial Agents/ OR Anti-Bacterial Agent*.ti,ab,kw,nm OR Antibacterial Agent*.ti,ab,kw,nm OR Antibiotic*.ti,ab,kw,nm OR Bacteriocid*.ti,ab,kw,nm OR Antibiotic Prophylaxis/ OR prophylaxis.ti,ab,kw)

Supplementary material

Scopus

December 15, 2022

104 records

(adult OR adults OR "middle aged") AND (obese OR obesity OR overweight) AND ("Endoscopic Bariatric" OR "Intra-gastric balloon*" OR "Intragastric balloon*" OR orbera* OR "Obalon Reshape" OR Spatz OR "Endoscopic sleeve" OR "endoscopic sleeve gastroplasty" OR "primary obesity surgical endoluminal" OR "endoscopic gastric plication" OR "aspiration therap*" OR "Duodeno-Jejunal Bypass Liner" OR "duodenal-jejunal bypass liner" OR "duodenal mucosal resurfacing") AND

("Proton Pump Inhibitor*" OR omeprazole OR Prilosec OR Esomeprazole OR Nexium OR Nexiam OR pantoprazole OR Protonix OR lansoprazole* OR pantomed OR Aprepitant OR Ondansetronn OR Dexamethasonne OR "Scopolamine patch*" OR Metoclopramide OR Maxolon OR Rimetin OR Primperan OR Reglan OR Cerucal OR Palonsetronn OR Promethazine OR Proazamine OR Rumergan OR Diprazin OR Isopromethazine OR Phenergan OR Phenargan OR Phensedyl OR Pipolfen OR Pipolphen OR Prothazin OR Pyrethia OR Remsed OR Atosil OR Diphergan OR Prochlorperazine OR Compazine OR Lorazepam OR Haloperidol OR Haldol OR Droperidol OR Inapsine OR Dehidrobenzperidol OR Dehydrobenzperidol OR Droleptan OR Acetaminophen OR Hydroxyacetanilide OR Acetamidophenol OR Acephen OR Acetaco OR Tylenol OR Datril OR Panadol OR Acamol OR Algotropyl OR "Nonsteroidal Anti-Inflammatory Agent*" OR NSAIDS OR Opioid* OR Tramadol OR Tramundin OR Biodalgic OR Jutadol OR Nobligan OR Prontofort OR Zytram OR Takadol OR Theradol OR Topalgic OR Tradol OR Tradonal OR Tralgiol OR "Trama Dorsch" OR TramaDorsch OR Biokanol OR Tramabeta OR Tramadin OR Tramadoc OR Trasedal OR Ultram OR Zamudol OR Zumalgic OR Zydol OR Tramadolor OR Tramadura OR Tramagetic OR Tramagit OR Tramake OR Tramal OR Tramex OR Adolonta OR Contramal OR Amadol OR Hyosciamine OR Dicyclominne OR Gabapentin OR Neurontin OR Convalis OR Pregabalin OR Lyrica OR "Tricyclic Antidepressant" OR "Tricyclic Antidepressive Agent*" OR "Anti-Bacterial Agent*" OR "Antibacterial Agent*" OR Antibiotic* OR Bacteriocid* OR prophylaxis)

Supplementary material

SUPPLEMENTARY TABLE 23. Periprocedural care for fluid-filled intragastric balloons

Periprocedural care	Values
No. of experts placing ≥10 fluid-filled intragastric balloons	15/17 (88)
Total number of fluid-filled intragastric balloons cases performed (min-max)	2587 (10-1000)
Antiemetics	
No. of experts prescribing antiemetic medications periprocedurally	15 (100)
Favored antiemetic regimen prescribed*	Ondansetron (93), aprepitant (73), scopolamine patch (60), dexamethasone (60)
Patients with PONV (within 72 hours) under the above antiemetic regimen, %	31.6
Patients requiring hospital care for PONV (within 72 h) under the above regimen, %	7.7
No. of experts prescribing antiemetic medications routinely on discharge	14 (93)
No. of experts prescribing antiemetic medications on discharge as needed	1 (7)
Favored antiemetic regimen prescribed*	Ondansetron (86), scopolamine patch (64), aprepitant (36), lorazepam (36)
Patients with PONV (within 30 days) under the above antiemetic regimen, %	25.5
Patients requiring hospital care for PONV (within 30 days) under the above antiemetic regimen, %	9.2
Patients experiencing adverse events on under the above regimen, %	12.1
Pain management	
No. of experts prescribing pain medications periprocedurally	12/15 (80)
Favored pain medications prescribed*	Acetaminophen (67), hyoscyamine (58), opioid (42)
Patients having pain (within 30 days) under the above regimen, %	27.5
Patients requiring hospital care for pain management (within 30 days) under the above regimen, %	3.1
Patients experiencing adverse events or intolerance under the above regimen, %	2.7
Proton pump inhibitor	
No. of experts prescribing proton pump inhibitor periprocedurally	15/15 (100)

Values are n or n/N (%) unless otherwise defined.
PONV, Postoperative nausea and vomiting.
*Values in parentheses are percents.

Supplementary material

SUPPLEMENTARY TABLE 24. Evidence profile for antiemetic use in patients undergoing intragastric balloon placement
Question: Antiemetics compared with no antiemetics for patients undergoing intragastric balloon placement

Certainty assessment					
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**
Incidence of postoperative nausea and vomiting (midazolam + ondansetron [intervention] vs ondansetron [control]) (follow-up: 1 day)					
1	Randomized trials	Serious*	Not serious	Serious†	Serious‡
Incidence of vomiting (alizapride vs tropisetron vs tropisetron + droperidol) (follow-up: 1 day)					
1	Randomized trials	Serious§	Not serious	Serious†	Serious‡

CI, Confidence interval.
*Abdelhamid 2014: Unclear randomization and blinding. Allocation concealment was done using odd and even file numbers.
†The control group is different from that of our PICO question (eg, no antiemetics).
‡Low event rate or total sample size <400.
§Van Hee 2003: Unclear random sequence generation, allocation concealment, and blinding.

Supplementary material

SUPPLEMENTARY TABLE 24. Continued

Certainty assessment	No. of patients		Effect			
Other considerations	Antiemetics	No antiemetics	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
Incidence of postoperative nausea and vomiting (midazolam + ondansetron [intervention] vs ondansetron [control]) (follow-up: 1 day)						
None	10/29 (34.5%)	14/25 (56.0%)	Risk ratio .62 (.33-1.13)	213 fewer per 1000 (from 375 fewer to 73 more)	⨁◯◯◯ Very low	CRITICAL
Incidence of vomiting (alizapride vs tropisetron vs tropisetron + droperidol) (follow-up: 1 day)						
None	Group 1 (alizapride; n = 15): rate = .31 Group 2 (tropisetron; n = 19): rate = .17 Group 3 (tropisetron + droperidol; n = 17): rate = .20				⨁◯◯◯ Very low	CRITICAL

Supplementary material

SUPPLEMENTARY TABLE 25. Periprocedural care for EGR

Periprocedural care	Values
No. of experts performing ≥10 EGR procedures	16/17 (94)
Total no. of EGR cases performed (min-max)	2700 (20-700)
Antiemetics	
No. of experts prescribing antiemetic medications periprocedurally	14/16 (88)
Favored antiemetic regimen prescribed*	Ondansetron (79), dexamethasone (64), aprepitant (57), scopolamine patch (50)
Patients with PONV (within 72 h) under the above antiemetic regimen, %	19.5
Patients requiring hospital care for PONV (within 72 h) under the above antiemetic regimen, %	2.5
No. of experts prescribing antiemetic medications on discharge	14 (88)
Favored antiemetic regimen prescribed*	Ondansetron (64), scopolamine patch (57), aprepitant (36), metoclopramide (29)
Patients with PONV (within 30 days) under the above antiemetic regimen, %	13.3
Patients requiring hospital care for PONV (within 30 days) under the above antiemetic regimen, %	2.9
Patients experiencing adverse events on the above antiemetic regimen, %	5.3
Pain management	
No. of experts prescribing pain medications periprocedurally	14/16 (88)
Favored pain medications prescribed*	Acetaminophen (57), opioids (36), nonsteroidal anti-inflammatory drugs (14)
Patients having pain (within 30 days) under the above regimen, %	15.1
Patients requiring hospital care for pain management (within 30 days) under the above regimen, %	2.0
Patients experiencing adverse events or intolerance under the above regimen, %	4.1
Antibiotics	
No. of experts using periprocedural antibiotics	10 (63)
Average no. of EGR cases performed for	
Endoscopists prescribing antibiotics (range)	230 (20-70)
Endoscopists not prescribing antibiotics (range)	67 (20-200)
Favored antibiotics prescribed*	Cirpofloxacin ± metronidazole (50), amoxicillin-clavulanate acid or ampicillin-sulbactam (30), cephalosporin (20)
No. of experts prescribing intravenous antibiotics	
Periprocedurally only	6 (60)
Periprocedurally plus a 3-day course of oral antibiotics	4 (40)
Patients having an infection under the above antibiotic regimen, %	.2
Patients experiencing adverse events or intolerance to antibiotics under the above antibiotic regimen, %	.8

Values are n or n/N (%) unless otherwise defined.
EGR, Endoscopic gastric remodeling; *PONV*, postoperative nausea and vomiting.
*Values in parentheses are percents.

Supplementary material

SUPPLEMENTARY TABLE 26. Serious adverse events reported in aspiration therapy randomized controlled trials

Study	Active arm	Control arm
Thompson 2017[52]	4/111 • Peritonitis treated with antibiotics • Severe abdominal pain resulting in hospitalization, treated with intravenous pain medications • Prepyloric ulcer • Skin port malfunction requiring A-tube replacement	0/60
Sullivan 2013[48]	0/11	0/7

Supplementary material

SUPPLEMENTARY TABLE 27. Evidence profile for supporting the use of aspiration therapy

Question: Aspiration therapy with lifestyle modification compared with lifestyle modification alone with or without sham in patients with obesity seeking endoscopic bariatric and metabolic therapies

Certainty assessment						
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
%TWL at 12 mo						
2	Randomized trials	Not serious	Not serious	Not serious	Serious*	None
Serious adverse event rate						
2	Randomized trials	Not serious†	Not serious	Not serious	Very serious‡,§	None

CI, Confidence interval; *%TWL*, percentage of total weight loss.
*Total sample size <400.
†Given the nature of the procedure with the presence of the A-tube, a blinded study is not possible to conduct.
‡Low event rate (<300).
§Wide CI and pooled effect show both increased and decreased harm.

Supplementary material

SUPPLEMENTARY TABLE 27. Continued

No. of patients		Effect			
Aspiration therapy with lifestyle modification	**Lifestyle modification alone with or without sham**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
%TWL at 12 mo					
122	67	—	Mean difference 10.44% TWL higher (6.44 higher to 14.44 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Serious adverse event rate					
4/122 (3.3%)	0/67 (.0%)	Risk ratio 4.90 (.27-89.54)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⨁⨁◯◯ Low	CRITICAL
	.4%		16 more per 1000 (from 3 fewer to 354 more)		

