Comparative effectiveness of balloons, adjustable balloons, and endoscopic sleeve gastroplasty: a network meta-analysis of randomized trials

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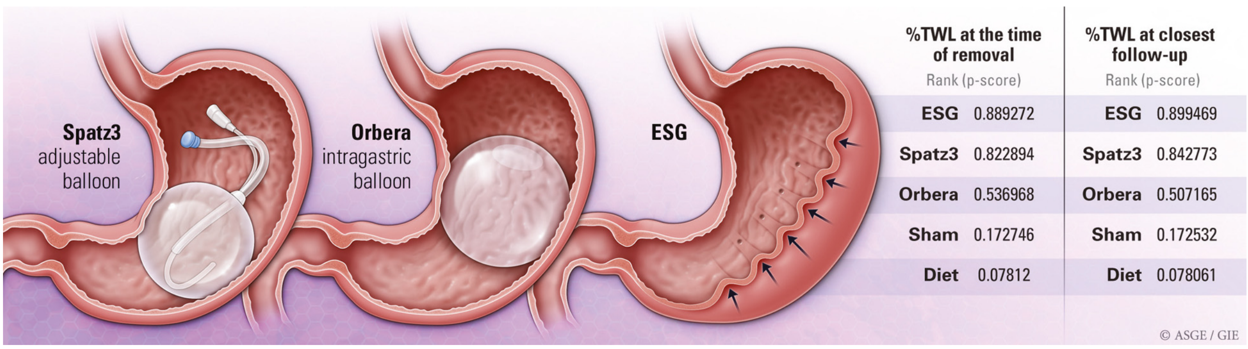
GRAPHICAL ABSTRACT



Background and Aims: Individual randomized controlled trials (RCTs) and pairwise meta-analyses do not compare all commercially available endoscopic bariatric therapies (EBTs) head-to-head. Therefore, the choice among them is currently made by inference or indirect data. We therefore assessed the comparative efficacy and safety of EBTs through a network meta-analysis.

Methods: We searched MEDLINE, EMBASE, and Cochrane CENTRAL from inception for intragastric balloons (IGBs) and from 2013 for endoscopic sleeve gastroplasty (ESG) until May 2023. Only RCTs comparing any of the currently commercially available EBTs with controls were considered eligible. Outcomes included percentage of total weight loss (%TWL), serious adverse events (SAEs), and intolerability.

Results: We identified 821 citations, of which 10 and 8 were eligible for the qualitative and quantitative analysis, respectively. Considering %TWL at the time of IGB removal, all EBTs were associated with statistically higher %TWL than controls. There were no significant differences among EBTs. However, considering the %TWL at the follow-up closest to 12 months, both ESG and the Spatz3 gastric balloon (Spatz Medical, Fort Lauderdale, Fla, USA) were more effective than the Orbera gastric balloon (Apollo Endosurgery, Austin, Tex, USA), with no statistical difference between ESG and Spatz3. For both outcomes, *P* score and ranking score suggested that ESG was probably associated with a greater weight loss (.889272 and .899469, respectively), followed by Spatz3 (.822894 and .842773, respectively), and Orbera (.536968 and .507165, respectively).

Conclusions: All currently available EBTs approved by the U.S. Food and Drug Administration are more effective than both diet plus lifestyle intervention and sham procedures with an acceptable safety profile. ESG seems the most effective and may be prioritized for patients fit for both ESG and IGBs. Direct controlled trials between EBTs are warranted to confirm these findings. (Gastrointest Endosc 2025;101:527-36.)

(footnotes appear on last page of article)

Obesity is a chronic and multifactorial disease developing from the interaction of genetic, metabolic, social, behavioral, and cultural factors. It has been associated with an increase in cardiovascular diseases and type 2 diabetes.[1] The prevalence of obesity has been steadily increasing over the last decades, often described as being of epidemic proportions.[2]

Metabolic and bariatric surgery is the most effective therapy for weight loss and improving related comorbidities for moderate and severe obesity.[3] However, less than 2% of patients who are otherwise eligible receive these interventions.[4] This huge gap is multifactorial and may be because of costs, lack of appeal, morbidity, and mortality associated with bariatric surgery.[4,5] On the other hand, the use of glucagon-like peptide-1 receptor agonists for weight loss purposes is on the rise, but the lack of current available data on their long-term benefits and risks discourages both physician and patient alike. Therefore, other minimally invasive approaches could potentially bridge the gap between medical and surgical management and have been recommended in this context.[6,7]

In this context, endoscopic bariatric therapies (EBTs) have been developed to offer effective weight loss options by targeting gastric and small intestinal pathways. EBTs have the advantage of a better safety profile because of their anatomy-preserving and incisionless nature.[4,8]

Currently, 3 commercially available EBTs approved by the U.S. Food and Drug Administration (FDA) for weight loss, namely, adjustable fluid-filled intragastric balloons (IGBs), nonadjustable fluid-filled IGBs, and endoscopic sleeve gastroplasty (ESG). IGBs are space-occupying devices inserted in the stomach through endoscopy to promote delayed gastric emptying and early satiety.[9] The Spatz3 (Spatz Medical, Fort Lauderdale, Fla, USA) is a 12-month indwelling, liquid-filled IGB that allows for upward or downward adjustments. The Orbera (Apollo Endosurgery, Austin, Tex, USA) is a 6-month indwelling, liquid-filled, nonadjustable IGB. Finally, ESG is an endoluminal, gastric-remodeling, organ-sparing procedure that uses a full-thickness suturing device to reduce the size and length of the stomach.[10] It has gained popularity over the past decade and was recently granted FDA approval.[11]

Considering that the indications for these therapies overlap, it is difficult to determine the best approach in terms of weight loss, intolerability, and safety profile. Individual randomized controlled trials (RCTs) or even pairwise meta-analyses do not compare head-to-head all these modalities, and the choice among them is currently made by inference or indirect data. Therefore, we conducted a network meta-analysis (NMA) of RCTs to assess the comparative efficacy and safety of EBTs.

METHODS

We followed the recommendations from the Preferred Reporting Items for Systematic reviews and Meta-Analyses[12] and Cochrane Handbook for Systematic Reviews of Interventions guidelines.[13]

Eligibility criteria

We considered eligible randomized studies comparing any of the currently commercially available EBT with controls, either sham procedures or diet plus lifestyle interventions for patients with obesity or overweight. The eligible EBTs included IGBs (BioEnterics Intragastric Balloon (Orbera and BIB are part of the same system) and Spatz3) and ESG. Outcomes of interest were weight loss (percentage of total weight loss [%TWL] and percentage of excess weight loss), adverse events (as reported in the studies), severe adverse events (SAEs; defined as leading to death, life-threatening, requiring hospitalization, and/or intervention to prevent permanent impairment), intolerability (early removal or reversal rates), impact on quality of life (to be assessed in qualitative analysis and per study definitions), and improvement in metabolic parameters and nonalcoholic steatohepatitis.

Search strategy

We conducted 2 different search strategies to increase the sensitivity of each of them. The first search strategy focused on ESG studies and the second on IGB studies. We constructed comprehensive search strategies using the PubMed search engine and adapted them for other databases (EMBASE and Central Cochrane) (Appendix 1, available online at www.giejournal.org).

We retrieved records from inception for IGBs and from 2013 for ESG (date the procedure was first described) until May 2023. A cross-referencing search was carried out by screening references of relevant studies and previous meta-analyses.

Data extraction

Two reviewers independently screened records for eligibility using separate spreadsheets. Next, their results were compared, and disagreements were resolved by consensus including a third senior researcher. Then, 1 researcher extracted data using a shared standardized spreadsheet, and 2 others validated the data extraction.

Risk of bias and critical appraisal

Only randomized studies were considered eligible for this systematic review. Therefore, we used a standardized critical appraisal tool, the Risk of Bias in Randomized trials,[13] to assess risk of bias and quality of the included studies. This tool analyzes 5 domains for the risk of bias and ultimately classifies the study as low risk, some concerns, and high risk.

Statistical analyses

The Review Manager computer program (version 5.4, 2020; Cochrane Collaboration, London, England) was used to carry out the pairwise meta-analysis. When the

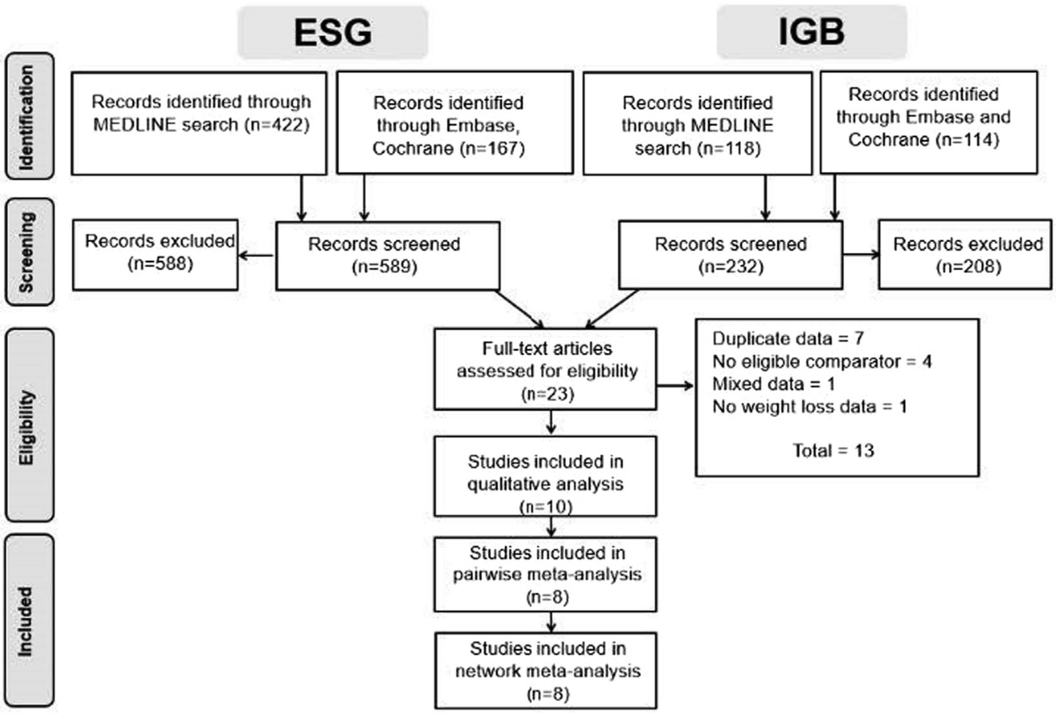


Figure 1. Inclusion flowchart. *ESG*, Endoscopic sleeve gastroplasty; *IGB*, intragastric balloon.

study did not provide means and standard deviations, we estimated medians and ranges using appropriate imputation methods.[14,15] For estimating standard deviation based on interquartile ranges or 95% confidence intervals (CIs), we followed the instructions in the Cochrane Handbook (chapter 6, section 6-5-2).[13] If the article did not provide any measure for dispersion or sample size, we attempted to obtain them by contacting the authors by email. If unsuccessful, we proceeded with data input based on the graphs provided.[13]

Continuous variables are expressed as means and standard deviations and categorical variables as rates or frequencies. A $P < .05$ was considered statistically significant. We presented the results using the mean difference (MD) as a measure of effect and pooled across studies using the random-effects model because of anticipated heterogeneity in study populations and settings. Heterogeneity among studies was assessed using the Higgins test (I^2) and *P* value based on the Cochrane Q statistic.

The Grading of Recommendations Assessment, Development, and Evaluation approach was used to rate certainty in the estimates derived from direct and indirect comparisons of efficacy outcomes. In this approach, direct evidence from RCTs starts at high certainty and is rated down by risk of bias, indirectness, imprecision, inconsistency, or publication bias to moderate, low, or very low.[16] Indirect evidence starts at the lowest rating of the 2 pairwise estimates that contribute as first-order loops to the indirect estimate but can be further down-rated for imprecision, intransitivity, or inconsistency between direct and indirect comparisons.[17]

For the NMA, we fitted a mixed-treatment comparison model following a frequentist approach as implemented in the statistical package.[18] We also used a random-effects model because of anticipated heterogeneity in trial populations and settings. We estimated the MD and 95% CI for each pairwise comparison combining direct and indirect estimates when available and estimating the *P* scores, which express the extent of certainty that a treatment is better than another treatment, averaged over all competing treatments.[19] Because the current NMA does not have closed loops, evaluation of the consistency between direct and indirect estimates was not possible. The NMA was conducted using R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

The 2 searches provided 821 identified citations, of which 8 were included for pairwise meta-analysis and NMA after screening and assessment for eligibility (Fig. 1).

Qualitative analysis

The eligible RCTs originated from multiple countries and backgrounds, including America, Europe, Asia, and Australia, and were published between 2006 and 2022. Four articles[20,21,24,26] compared BIB/Orbera with sham procedures, 4 compared[23,25,34,35] BIB/Orbera with dietary and lifestyle changes, and 2 compared ESG[11] and Spatz3,[22] respectively, with diet changes. Older studies included subjects with severe obesity[20,21] and body mass indices in the range of 40 to 50 kg/m^2, whereas more recent studies[22,23]

TABLE 1. Risk of bias of the studies included in the qualitative analysis

Study reference	Period and randomization (D1a)	carryover effect (D-S)	Effect of assignment to intervention (D2)	Risk of Bias in Randomized trials 2 tool Effect of adhering to intervention (D2)	Missing outcome data (D3)	Measurement of the outcome (D4)	Selection of the reported result (D5)	Overall risk of bias
Spatz vs diet + lifestyle interventions								
Abu Dayyeh et al[22]	Low		Low	Low	Low	Low	Low	Low
Orbera vs diet + lifestyle interventions								
Fuller et al[34]	Low		Low	Low	Low	Low	Low	Low
Courcoula et al[25]	Low		Low	Low	Low	Low	Low	Low
Ahmed et al[23]	Some concerns		High	High	Low	Low	Low	High
Kashani et al[35]	Some concerns		Some concerns	Low	Low	Low	Low	Some concerns
Orbera vs sham procedure								
Genco et al[20]	Low	Low	Low	Low	Low	Low	Low	Low
Lee et al[24]	Low		High	High	High	Low	Low	High
Martinez-Brocca et al[21]	Low	Low	Low	Some concerns	Low	Low	Low	Some concerns
Mathus-Vliegen et al[26]	Low		High	Some concerns	High	Low	Low	High
Endoscopic sleeve gastroplasty vs diet + lifestyle interventions								
Abu Dayyeh et al[11]	Low	Low	Some concerns	Some concerns	Low	Low	Some concerns	

included only patients with mild or moderate obesity (body mass index < 40 kg/m^2). In Orbera studies, the indwelling time ranged from 3 to 6 months and for Spatz, 8 months. These data, however, are not applicable for ESG.

All studies were conducted on adult patients, with no pediatric patients included in any of the RCTs. Diabetes, hypertension, and dyslipidemia were noted in patients in 5 studies.[11,21,22,24,25]

Only 4 studies followed up %TWL for a full year or more than 6 to 8 months. Martinez-Brocca et al[21] and Mathus-Vliegen et al[26] reported ghrelin results after the interventions, showing no significant changes in fasting or postprandial ghrelin. Improvement in liver function tests were noted with the Spatz balloon in Abu Dayyeh et al,[22] just as improvement in the nonalcoholic fatty liver disease activity score was noted with BIB use in Lee et al.[24]

As for improvements in comorbidities, Abu Dayyeh et al[22] reported improvements in fasting glucose levels, HB_{A1c}, blood pressure, and total cholesterol with use of the Spatz3. Studies that compared Orbera with diet or sham procedures concluded that there were improvements in metabolic syndrome, diabetes mellitus, fasting insulin, blood pressure, and quality of life. With ESG, amelioration of most comorbidities was seen, such as metabolic syndrome; fasting glucose; diabetes mellitus; HB_{A1c}; fasting insulin; homeostasis model assessment for insulin resistance; blood pressure; triglycerides; high-density-lipoprotein, low-density-lipoprotein, and total cholesterol; and quality of life. Supplementary Table 1 (available online at www.giejournal.org) summarizes demographic and qualitative data of the included studies, Supplementary Table 2 (available online at www.giejournal.org) summarizes weight loss outcomes, and Supplementary Table 3 (available online at www.giejournal.org) summarizes comorbidity-related outcomes.

Risk of bias

Study quality was assessed using the Risk of Bias in Randomized trials 2 critical appraisal tool. Four studies were at low overall risk of bias, 2 had some concerns, and 3 were at high risk. Results are summarized in Table 1, and detailed explanations are presented in the supplementary file.

Quantitative analysis (pairwise meta-analysis)

Considering %TWL at the time of IGB removal and at the follow-up visit closest to 12 months, all analyses favored EBTs over sham procedures and over diet plus lifestyle only (Spatz3 vs diet +lifestyle: MD, –11.70; Orbera vs diet + lifestyle: MD, –7.37; Orbera vs sham: MD, –5.40; ESG vs diet + lifestyle: MD, –12.80). The comparison between Orbera and sham procedures had a high heterogeneity (MD, –5.40; 95% CI, –11.68 to .87), but the remaining comparisons were homogeneous. Figure 2 and

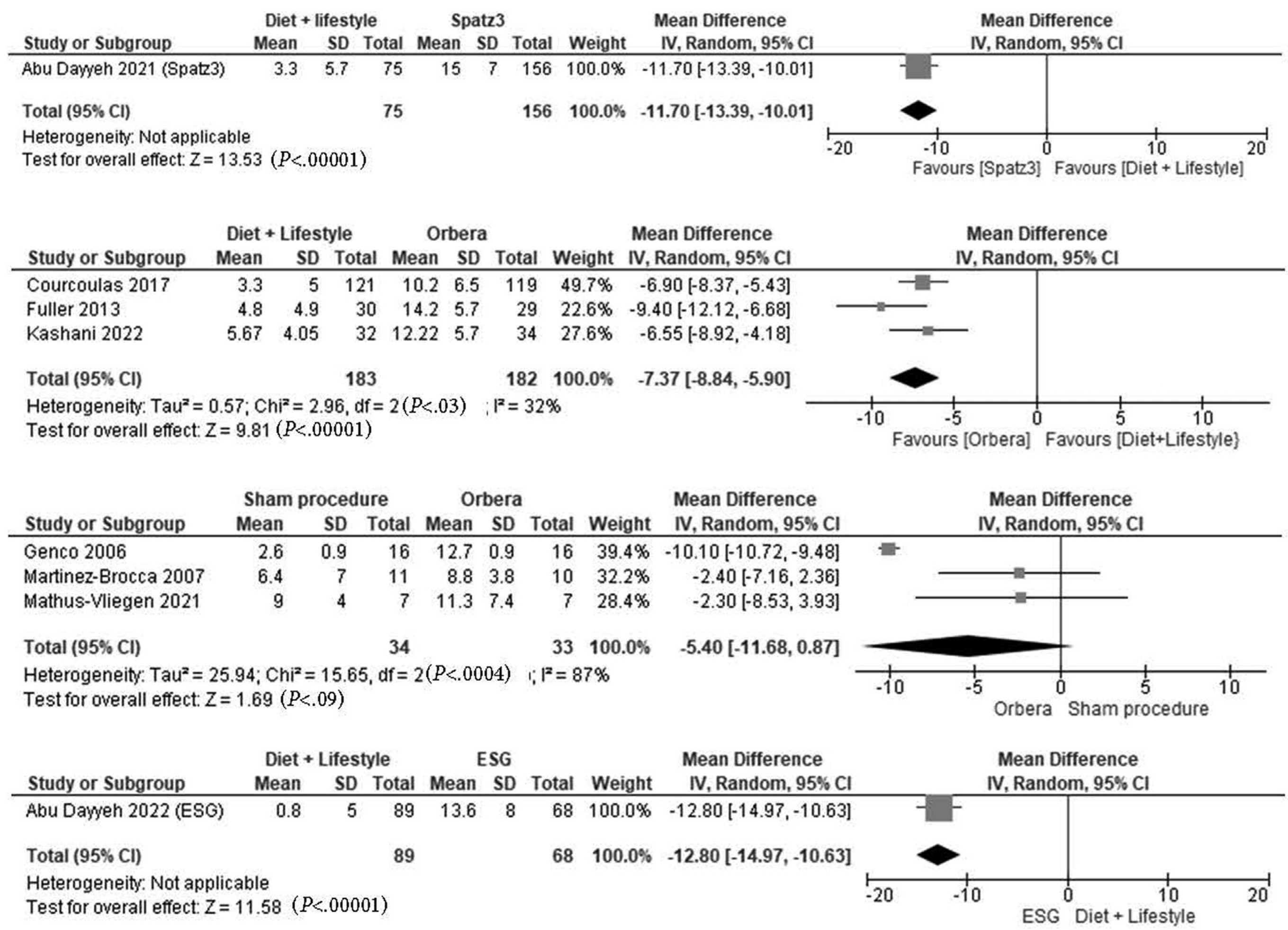


Figure 2. Forest plots for percentage of total weight loss at the time of device removal. *SD*, Standard deviation; *CI*, confidence interval; *ESG*, endoscopic sleeve gastroplasty.

Supplementary Figure 1 (available online at www.giejournal.org) depict the forest plots for the meta-analyses concerning %TWL at removal and at the follow-up closest to 12 months, respectively.

For intolerability (early removal or reversal rates), there was no difference between ESG and lifestyle interventions (MD, –.01; 95% CI, –.03 to .1) and between Orbera and sham interventions (MD, –.04; 95% CI, –.13 to .04). However, intolerability rates were significantly higher with the use of Spatz3 (MD, –.17; 95% CI, –.22 to –.11) and Orbera when compared with lifestyle plus dietary interventions (MD, –.12; 95% CI, –.28 to .03). Intolerability for diet and lifestyle was defined for the purpose of this analysis as a lack of compliance or dropout. Figure 3 shows the forest plots for intolerability.

Serious adverse events

The rates of SAEs were low, and some studies had small samples, leading to some comparisons showing no differences between active and control groups. Orbera had similar SAE rates to sham interventions (MD, .00; 95% CI, –.11 to .11) and diet plus lifestyle interventions (MD, –.07; 95% CI, –.14 to .01). ESG (MD, –.04; 95% CI, –.07 to –.01) and Spatz3 (MD, –.04; 95% CI, –.07 to –.01) had significantly higher rates of SAEs compared with diet plus lifestyle interventions (Supplementary Fig. 2, available online at www.giejournal.org).

Network meta-analysis

Eight studies provided data for NMA for the outcome of %TWL (Supplementary Fig. 3, available online at www.giejournal.org). Data for intolerability and SAEs were insufficient for NMA.

Considering %TWL at the time of IGB removal, all EBTs were significantly more effective than sham procedures and diet plus lifestyle interventions (Supplementary Fig. 3). There were no significant differences among EBTs. However, considering the %TWL at the follow-up closest to 12 months, both ESG and Spatz3 were more effective than Orbera. There was no statistical difference between ESG and Spatz3 (Fig. 4B). For both outcomes, ESG and Spatz3 had the highest *P* scores (.899469 and

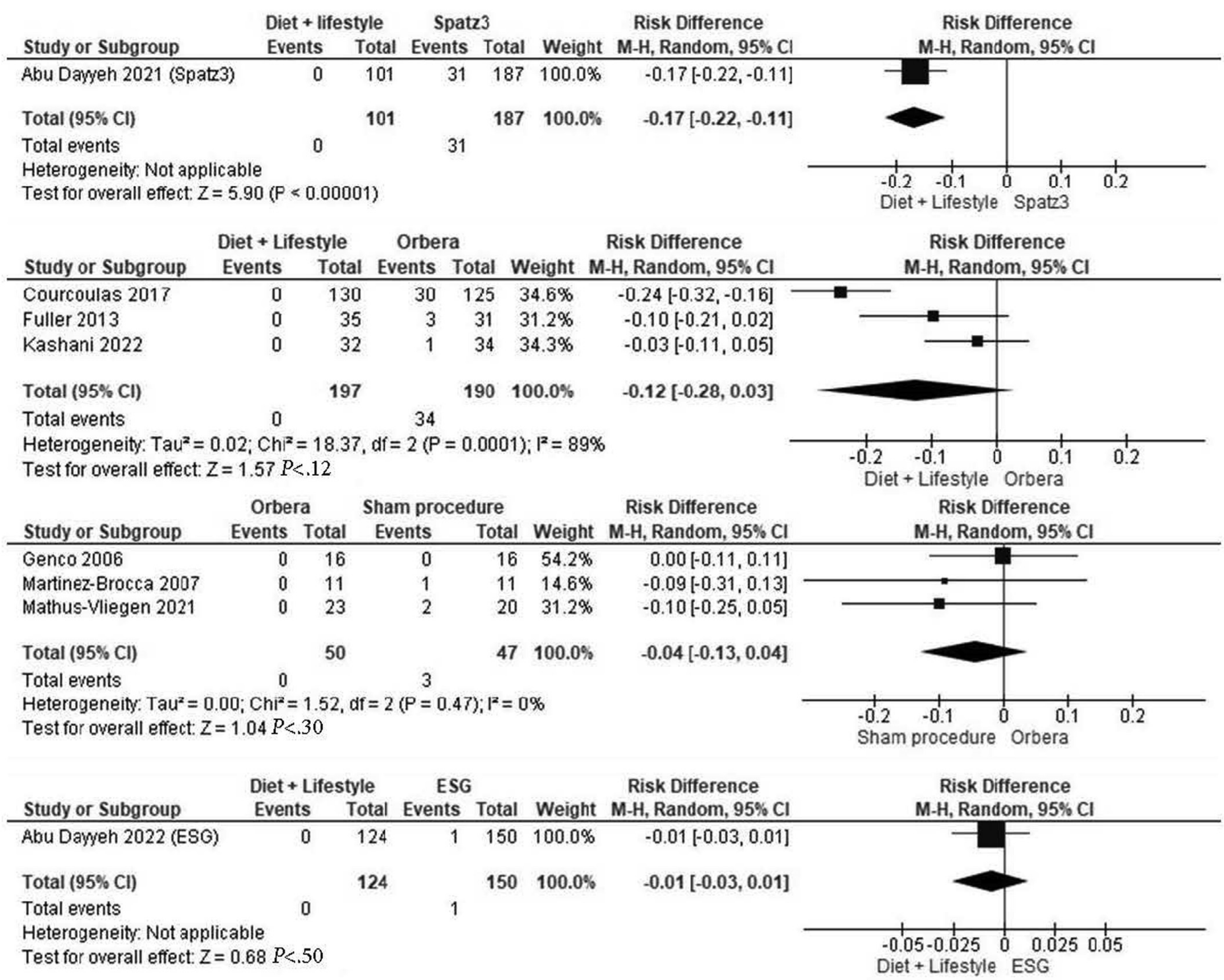


Figure 3. Forest plots assessing intolerability to the endoscopic bariatric therapies compared with controls. *ESG*, Endoscopic sleeve gastroplasty; *CI*, confidence interval.

.842773, respectively), followed by Orbera (.507165), then sham (.172532), and finally diet plus lifestyle interventions (.078061). Ranking score showed ESG as probably most effective considering %TWL at removal and %TWL at follow-up closest to 12 months, followed by Spatz3 and Orbera. The assessment of certainty of evidence with the Grading of Recommendations Assessment, Development, and Evaluation approach showed moderate certainty on the %TWL analysis and low certainty in the intolerability analysis (Fig. 5).

DISCUSSION

To the best of our knowledge, this is the first NMA comparing all 3 currently available, FDA-approved EBTs. The NMA approach provides indirect comparisons of multiple interventions without the need for head-to-head trials. This allowed us to rank EBTs at the time of removal and closest follow-up, providing valuable information to both patients and physicians when deciding which procedure to use. Of note, Bazerbachi et al[27] compared different EBTs in an NMA, but it was limited to IGBs and included air-filled balloons that are no longer available.

Our findings indicate all 3 endoscopic procedures lead to greater weight loss compared with interventions involving diet and lifestyle adjustments and sham procedures. This trend was observed both on removal of the EBT device and on the closest follow-up period. Among the EBTs, ESG demonstrated the most significant overall impact on %TWL, followed by IGB therapies, with the Spatz balloon outperforming the Orbera balloon. This latter finding could probably be explained by the upward adjustment allowed by the Spatz3 balloon. Abu Dayyeh et al[11] reported an

%TWL at the time of removal

					Rank (p-score)	
Diet + lifestyle	**-12.80(-14.97 to −10.63)**	**-7.37(-8.84 to −5.90)**	·	**-11.70(-13.39 to −10.01)**	ESG	0.889272
-12.80 (-14.97 to −10.63)	ESG	·	·	·	Spatz3	0.822894
-7.37(-8.84 to -5.90)	5.24 (-1.11 to 11.60)	Orbera	**-5.40 (-11.68 to 0.87)**	·	Orbera	0.536968
-1.21 (-6.06 to 3.64)	**11.59 (4.26 to 18.92)**	**-5.40(-11.68 to 0.87)**	Sham	·	Sham	0.172746
-11.70(-13.39 to −10.01)	1.10 (-6.55 to 8.75)	-4.14 (-10.35 to 2.06)	**-10.49 (-17.69 to -3.29)**	Spatz	Diet	0.07812

A

%TWL at the closest follow-up

					Rank (p-score)	
Diet + lifestyle	**-12.80(-14.97 to −10.63)**	**-5.03 (-8.34 to -1.73)**	·	**-11.70(-13.39 to −10.01)**	ESG	0.899469
-12.80(-14.97 to −10.63)	ESG	·	·	·	Spatz3	0.842773
-5.03 (-8.34 to -1.73)	**7.77 (1.23 to 14.31)**	Orbera	**6.29 (2.55 to 10.03)**	·	Orbera	0.507165
1.25 (-3.74 to 6.24)	14.05 (6.52 to 21.59)	**6.29 (2.55 to 10.03)**	Sham	·	Sham	0.172532
-11.70(-13.39 to −10.01)	1.10 (-6.77 to 8.97)	**-6.67 (-13.07 to -0.27)**	**-12.95 (-20.37 to -5.54)**	Spatz	Diet	0.078061

B

Figure 4. A, League table and ranking for percentage of total weight loss (%TWL) at the time of removal of the intragastric balloon (values in bold indicate statistical significance). Cells above the *diagonal line* represent direct comparisons, whereas those under it are indirect estimates obtained through the network meta-analysis. *Blank cells* mean no direct comparisons. **B,** League table and ranking for %TWL at the follow-up closest to 12 months (values in bold indicate statistical significance). Cells above the *diagonal line* represent direct comparisons, whereas those under it are indirect estimates obtained through the network meta-analysis. *ESG*, Endoscopic sleeve gastroplasty.

additional 5.2% TWL in the subgroup of patients undergoing upward adjustment throughout follow-up.[22] Sham procedures and diet and lifestyle modifications ranked lower in terms of their effect on %TWL, with ESG exhibiting the most substantial mean %TWL difference when compared with diet alone, registering an MD of –12.8%.

A case-matched study comparing ESG with an intensive diet and lifestyle regimen consistently showcased higher %TWL for ESG recipients at 1, 3, 6, and 12 months.[28] Conversely, the outcomes of diet and lifestyle changes displayed variability in terms of weight loss. In comparison with diet and lifestyle approaches, IGB therapy exhibited superior results, aligning with another systematic review indicating that an IGB volume >400 mL led to greater weight loss compared with diet alone.[29] However, when juxtaposed with a rigorous multidisciplinary weight loss program like OPTIFAST (Nestle Health Science, Vevey, Switzerland), the IGB was overshadowed according to a propensity score–matched analysis.[30] In this study, although the IGB achieved the anticipated %TWL level (∼12%), OPTIFAST reached approximately 20% TWL, a notably higher value than the conventional results of our study's typical diet and lifestyle interventions. This reinforces the concept that these interventions yield widely

Outcome	Pairwise certainty domains	NMA certainty domains	Treatment Effect (95% CI)	No of participants (studies)	Certainty
Total Body Weight Loss % (TBWL%) at removal	Imprecision (small sample size) No serious concerns about other domains	Consistency not evaluated due to lack of closed loops. No serious concerns about intransitivity	**Mean difference (NMA)** -11.70 [-13.39,-10.01] (Spatz-control) -7.37 [-8.84, -5.90] (BIB-diet+lifestyle) -5.40 [-11.68, 0.87] (BIB-Sham) -12.80 [-14.97, -10.63] (ESG-control)	849 (8 RCTs)	Moderate
Tolerabilty (Events)	Severe imprecision (small sample size and wide confidence intervals that include substantial benefit and harm) No serious concerns about other domains	NA	Absolute effect (pairwise) -0.17 [-0.22, -0.11] RD (Spatz-control) -0.12 [-0.28, 0.03] RD (BIB-diet-lifestyle) -0.04 [-0.13, 0.04] RD (BIB-Sham) -0.01 [-0.03, 0.01] RD (ESG-control)	849 (8 RCTs)	Low

Figure 5. Certainty of evidence according to the Grading of Recommendations Assessment, Development, and Evaluation approach. Of note, when studying Orbera, the attenuation of effect when changing control group from diet to sham is probably because of the placebo effect. *NMA*, Network meta-analysis; *CI*, confidence interval; *RCT*, randomized controlled trial; *NA*, not available.

varying outcomes and that they should be considered complementary rather than exclusionary.

Considering ESG versus IGBs, our study's results mirror a prior meta-analysis evaluating both procedures and suggest that ESG is probably the most effective EBT in terms of weight loss.[29] Of note, we could not detect statistically significant differences other than %TWL at the closest follow-up between ESG and Orbera, favoring the former. Still, no RCT has directly compared the 2 balloon types, rendering our results the most reliable data on the comparative efficacy of Orbera and Spatz3.

Interestingly, in our NMA, the sham procedure outranked diet and lifestyle modifications. One plausible explanation is that patients believe they have undergone an actual procedure and the placebo effect contributes to some degree of weight loss. This might be attributed to a perceived reduction in appetite among patients who experience this placebo effect. Moreover, it could have improved compliance with diet and implementation of a healthier lifestyle, thereby increasing weight loss in the control subjects. This could point to sham procedures being a superior control than diet and lifestyle for EBTs given that it better replicates the patient's experience and is then more comparable.

Our hierarchical ranking prioritized ESG as the most likely effective option based on its impact on weight loss outcomes. Nevertheless, our systematic review also revealed that ESG may offer additional benefits when compared with IGBs. In the qualitative assessment of the included studies, ESG yielded more substantial improvements in obesity-related comorbidities, as shown by laboratory parameters measuring diabetes, hypertension, and dyslipidemia and quality of life. These findings come from the MERIT trial, where up to 78% of patients receiving ESG experienced improvements in at least 1 comorbid condition.[11] The MERIT trial also demonstrated the long-lasting effects of ESG, with sustained weight loss observed 2 years after the procedure.[11] One should also note that ESG is a 1-time procedure, whereas IGBs typically require separate implantation and removal procedures. This presents an additional practical advantage for physicians and, more importantly, for patients.

Studies also indicate that adverse event rates between the 2 procedures are comparable but slightly higher in the IGB groups. Unfortunately, we could not conduct an NMA for intolerance or SAE rates among different EBTs; still, this reinforces the extremely low rates of both intolerability and SAEs of all EBTs, which is characteristic of such minimally invasive procedures. In a cohort study, however, Fayad et al[31] reported a statistically significant higher rates of adverse events in the IGB group compared with the ESG group (17% vs 5.2%, $P = .048$). Singh et al[32] also elaborated on these outcomes between both EBTs, showing that .15% of ESG patients required reversal compared with 5.92% of IGB patients requiring early removal. In addition, there was an adverse event rate of 1.52% versus 3.97% in ESG and IGB patients, respectively.[32] Considering all these findings, we hypothesize that an eventual future NMA for intolerability and SAEs might reflect the same rankings as that of %TWL.

With the recent rise of weight loss medications, it should be noted that even though these therapies may appeal to the general public for their accessibility and seemingly ease of use, it should be noted that %TWL is around 5.9% at 3 months and 10.9% at 6 months of follow-up, with adverse events occurring in 85% of patients taking these medications.[33] EBTs have demonstrated better outcomes for now with very minimal rates of adverse events and still have of high relevance and importance in the fight against obesity.

The most relevant limitation of this study is the small number of included studies. Also, when comparing different therapeutic modalities, we had to group results for weight loss at different time points to properly compare them. That could have led to unadjusted comparisons. We tried to minimize the impact on our results by running 2 different analyses: %TWL at removal and %TWL at follow-up closest to 12 months. The results of these analyses are similar, suggesting little to no impact of such unequal comparison on the final results.

In conclusion, this NMA shows that all currently available, FDA-approved EBTs are more effective than both diet and lifestyle intervention and sham procedures with an acceptable safety profile. ESG seems to be more effective than other EBTs and should be prioritized for patients fit for both ESG and IGBs. Direct controlled trials between EBTs are warranted to confirm our data.

DISCLOSURE

B. Abu Dayyeh serves as a consultant and has received research support from Boston Scientific and Medtronic. He is also a consultant for Olympus and receives research funding from EndoGastric Solutions (now MERIT Medical) and USGI Medical. Additionally, he is a co inventor of Endogenex, a technology licensed by the Mayo Clinic. V. Brunaldi is speaker, proctor, preceptor, and consultant for Boston Scientific LATAM, and consultant for GI Windows USA. All other authors disclosed no financial relationships.

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Abbreviations: CI, confidence interval; EBT, endoscopic bariatric therapy; ESG, endoscopic sleeve gastroplasty; FDA, U.S. Food and Drug Administration; IGB, intragastric balloon; MD, main difference; NMA, network meta-analysis; RCT, randomized controlled trial; SAE, serious adverse event; %TWL, percentage of total weight loss.

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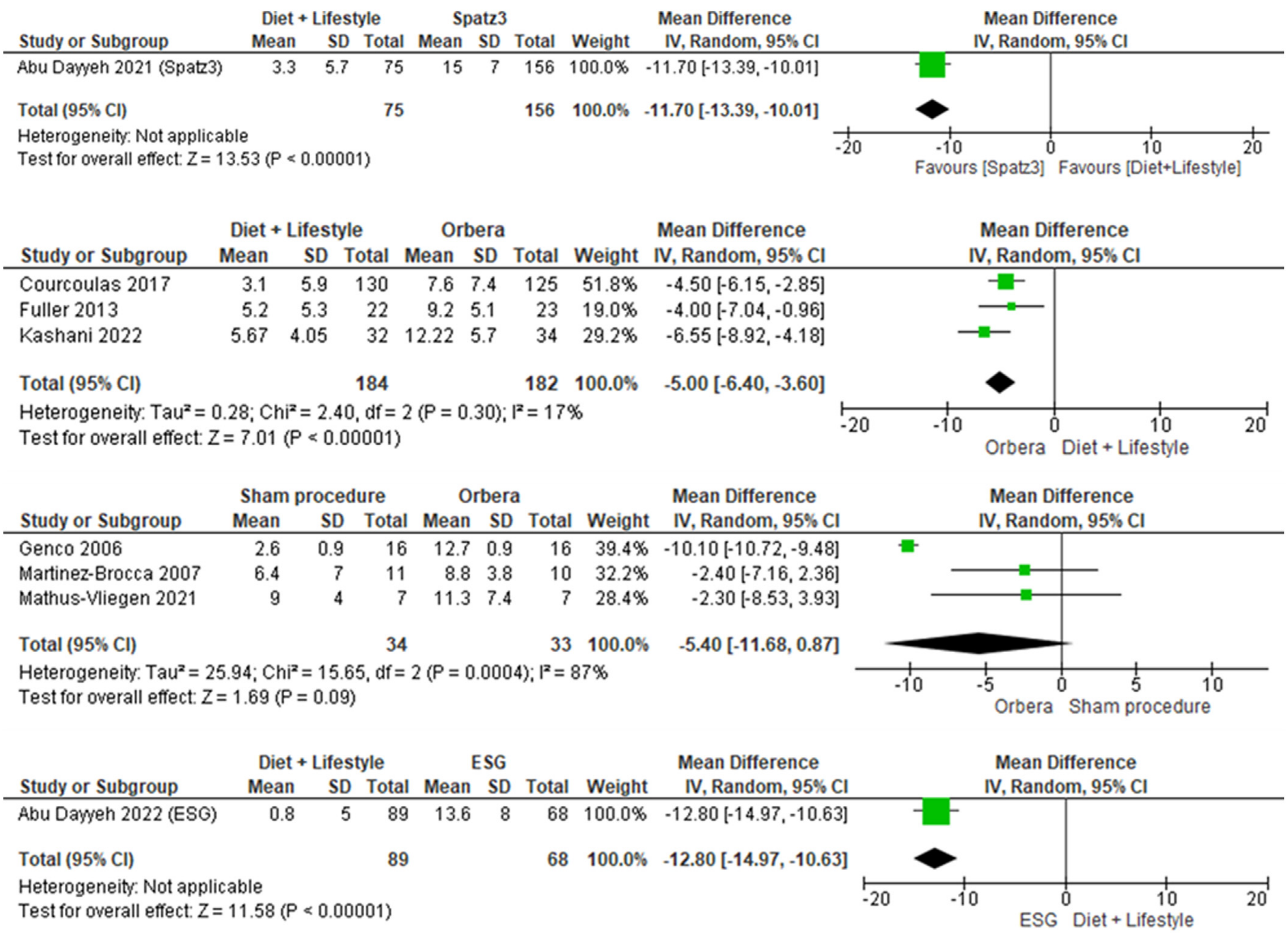
APPENDIX 1. SEARCH STRATEGY FOR MEDLINE AND PUBMED

Intragastric balloon

("weight loss"[MeSH Terms] OR ("weight"[All Fields] AND "loss"[All Fields]) OR "weight loss"[All Fields] OR ("overweight"[MeSH Terms] OR "overweight"[All Fields] OR "overweighted"[All Fields] OR "overweightness"[All Fields] OR "overweights"[All Fields]) OR ("obeses"[All Fields] OR "obesity"[MeSH Terms] OR "obesity"[All Fields] OR "obese"[All Fields] OR "obesities"[All Fields] OR "obesity s"[All Fields])) AND ((("intragastral"[All Fields] OR "intragastrally"[All Fields] OR "intragastric"[All Fields] OR "intragastrical"[All Fields] OR "intragastrically"[All Fields]) AND ("balloon"[All Fields] OR "balloon s"[All Fields] OR "balloons"[All Fields])) OR ("gastric balloon"[MeSH Terms] OR ("gastric"[All Fields] AND "balloon"[All Fields]) OR "gastric balloon"[All Fields]) OR ("intra-gastric"[All Fields] AND ("balloon"[All Fields] OR "balloon s"[All Fields] OR "balloons"[All Fields])) OR ("bioenteric"[All Fields] OR "bioenterics"[All Fields]) OR "orbera"[All Fields] OR "elipse"[All Fields] OR ("spatz"[All Fields] OR "spatz s"[All Fields]) OR "spatz3"[All Fields]) AND "random*"[All Fields]

Endoscopic sleeve gastroplasty

((("excess"[All Fields] OR "excesses"[All Fields] OR "excessive"[All Fields] OR "excessively"[All Fields]) AND ("weight s"[All Fields] OR "weighted"[All Fields] OR "weighting"[All Fields] OR "weightings"[All Fields] OR "weights and measures"[MeSH Terms] OR ("weights"[All Fields] AND "measures"[All Fields]) OR "weights and measures"[All Fields] OR "weight"[All Fields] OR "body weight"[MeSH Terms] OR ("body"[All Fields] AND "weight"[All Fields]) OR "body weight"[All Fields] OR "weights"[All Fields])) OR ("overweight"[MeSH Terms] OR "overweight"[All Fields] OR "overweighted"[All Fields] OR "overweightness"[All Fields] OR "overweights"[All Fields]) OR ("obeses"[All Fields] OR "obesity"[MeSH Terms] OR "obesity"[All Fields] OR "obese"[All Fields] OR "obesities"[All Fields] OR "obesity s"[All Fields])) AND (("endoscopie"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopies"[All Fields] OR "endoscopy s"[All Fields] OR ("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) OR "transoral*"[All Fields] OR "peroral*"[All Fields] OR "incisionless"[All Fields]) AND ("sleeve"[All Fields] OR "sleeved"[All Fields] OR "sleeves"[All Fields] OR "sleeving"[All Fields] OR "overstitch"[All Fields] OR ("gastroplasty"[MeSH Terms] OR "gastroplasty"[All Fields] OR "gastroplasties"[All Fields]) OR (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("plicate"[All Fields] OR "plicated"[All Fields] OR "plicates"[All Fields] OR "plicating"[All Fields] OR "plication"[All Fields] OR "plications"[All Fields] OR "plicator"[All Fields])) OR (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("imbricate"[All Fields] OR "imbricated"[All Fields] OR "imbricating"[All Fields] OR "imbrication"[All Fields] OR "imbrications"[All Fields])))) AND ("life style"[MeSH Terms] OR ("life"[All Fields] AND "style"[All Fields]) OR "life style"[All Fields] OR "lifestyle"[All Fields] OR "lifestyles"[All Fields] OR ("diet"[MeSH Terms] OR "diet"[All Fields]) OR ("exercise"[MeSH Terms] OR "exercise"[All Fields] OR "exercises"[All Fields] OR "exercise therapy"[MeSH Terms] OR ("exercise"[All Fields] AND "therapy"[All Fields]) OR "exercise therapy"[All Fields] OR "exercise s"[All Fields] OR "exercised"[All Fields] OR "exerciser"[All Fields] OR "exercisers"[All Fields] OR "exercising"[All Fields]) OR ("counsel"[All Fields] OR "counseled"[All Fields] OR "counselings"[All Fields] OR "counselled"[All Fields] OR "counselling"[All Fields] OR "counseling"[MeSH Terms] OR "counseling"[All Fields] OR "counsellings"[All Fields] OR "counsels"[All Fields]) OR ("salicylhydroxamic acid"[Supplementary Concept] OR "salicylhydroxamic acid"[All Fields] OR "sham"[All Fields]) OR ("placeboes"[All Fields] OR "placebos"[MeSH Terms] OR "placebos"[All Fields] OR "placebo"[All Fields]).



Study or Subgroup	Diet + Lifestyle Mean	SD	Total	Spatz3 Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Abu Dayyeh 2021 (Spatz3)	3.3	5.7	75	15	7	156	100.0%	-11.70 [-13.39, -10.01]
Total (95% CI)			**75**			**156**	**100.0%**	**-11.70 [-13.39, -10.01]**

Heterogeneity: Not applicable
Test for overall effect: Z = 13.53 (P < 0.00001)

Study or Subgroup	Diet + Lifestyle Mean	SD	Total	Orbera Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Courcoulas 2017	3.1	5.9	130	7.6	7.4	125	51.8%	-4.50 [-6.15, -2.85]
Fuller 2013	5.2	5.3	22	9.2	5.1	23	19.0%	-4.00 [-7.04, -0.96]
Kashani 2022	5.67	4.05	32	12.22	5.7	34	29.2%	-6.55 [-8.92, -4.18]
Total (95% CI)			**184**			**182**	**100.0%**	**-5.00 [-6.40, -3.60]**

Heterogeneity: Tau² = 0.28; Chi² = 2.40, df = 2 (P = 0.30); I² = 17%
Test for overall effect: Z = 7.01 (P < 0.00001)

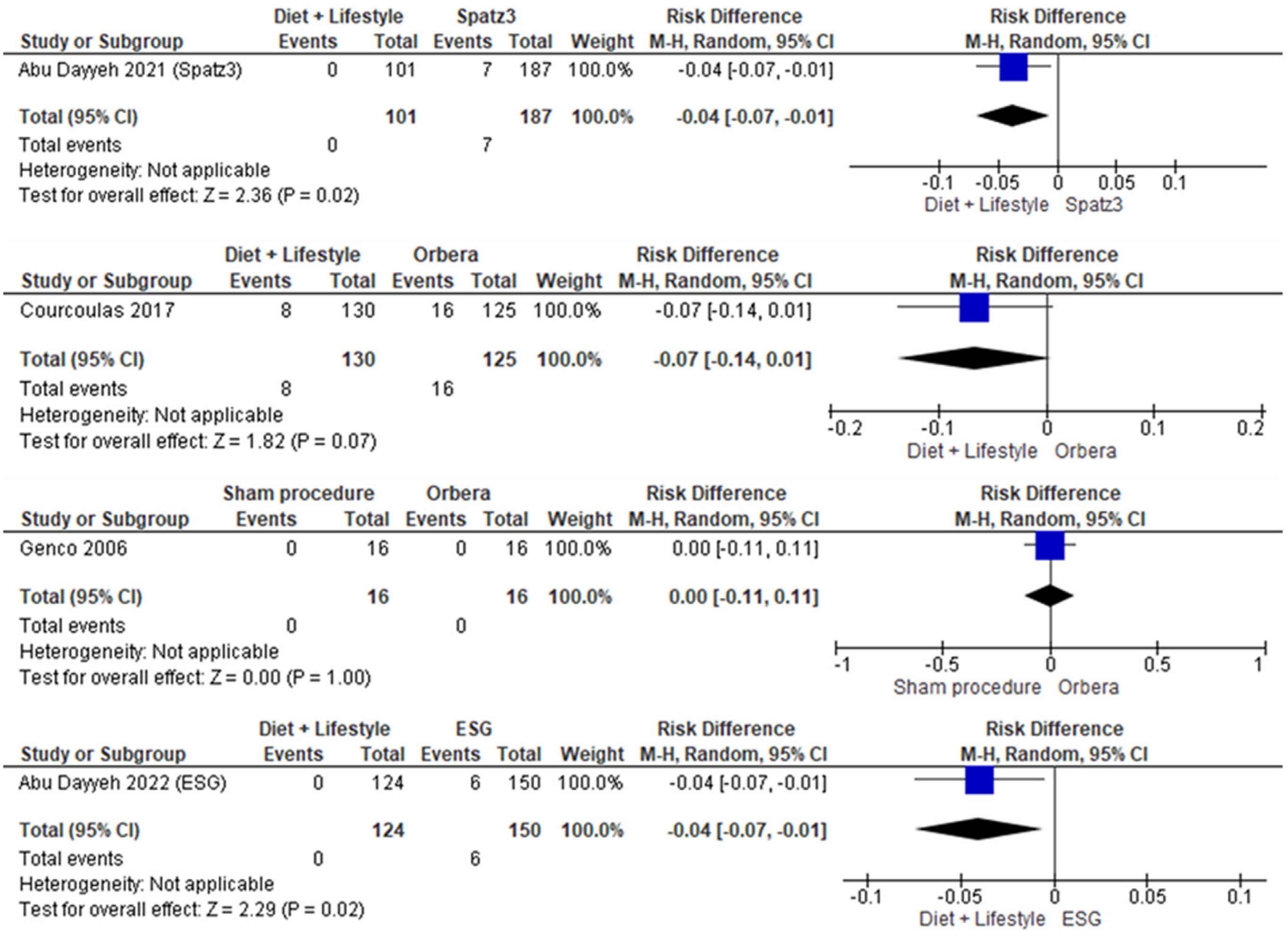
Study or Subgroup	Sham procedure Mean	SD	Total	Orbera Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Genco 2006	2.6	0.9	16	12.7	0.9	16	39.4%	-10.10 [-10.72, -9.48]
Martinez-Brocca 2007	6.4	7	11	8.8	3.8	10	32.2%	-2.40 [-7.16, 2.36]
Mathus-Vliegen 2021	9	4	7	11.3	7.4	7	28.4%	-2.30 [-8.53, 3.93]
Total (95% CI)			**34**			**33**	**100.0%**	**-5.40 [-11.68, 0.87]**

Heterogeneity: Tau² = 25.94; Chi² = 15.65, df = 2 (P = 0.0004); I² = 87%
Test for overall effect: Z = 1.69 (P = 0.09)

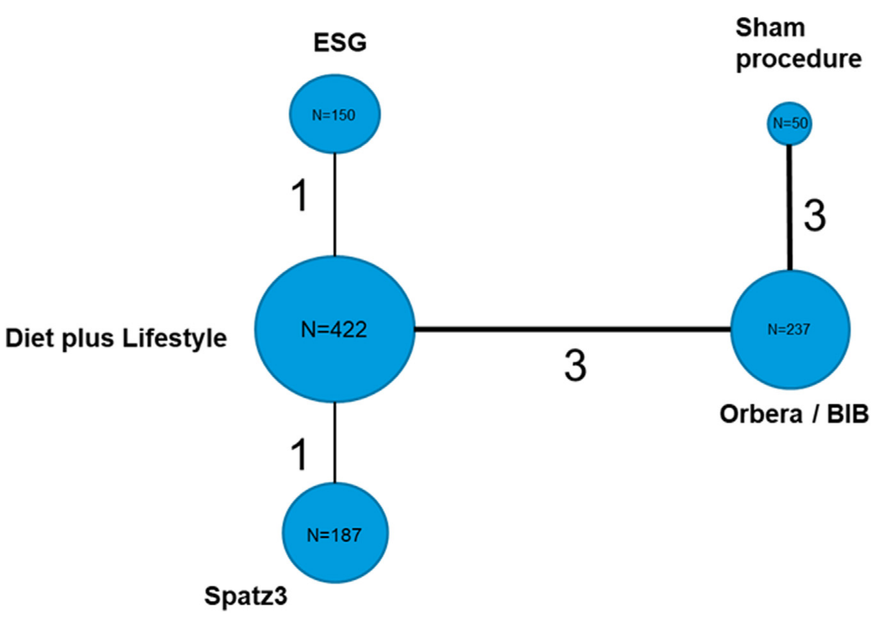
Study or Subgroup	Diet + Lifestyle Mean	SD	Total	ESG Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Abu Dayyeh 2022 (ESG)	0.8	5	89	13.6	8	68	100.0%	-12.80 [-14.97, -10.63]
Total (95% CI)			**89**			**68**	**100.0%**	**-12.80 [-14.97, -10.63]**

Heterogeneity: Not applicable
Test for overall effect: Z = 11.58 (P < 0.00001)

Supplementary Figure 1. Forest plots for percentage of total weight loss at the follow-up closest to 12 months. *CI*, confidence interval; *ESG*, endoscopic sleeve gastroplasty; *IV*, inverse variance.



Supplementary Figure 2. Forest plots for serious adverse events.



Supplementary Figure 3. Geometry of the network.

SUPPLEMENTARY TABLE 1. Characteristics of studies included in the qualitative analysis

Country	Study reference	Population	Intervention	Comparison	Indwelling time mo	Balloon volume mL
Italy	Genco 2006[20]	Adults BMI >40 kg/m^2	BIB/Orbera (n = 16)	Sham procedure (n = 16)	3	500 mL (saline solution) + methylene blue (10 mL)
Spain	Martinez-Brocca 2007[21]	Adults BMI >40 kg/m^2	BIB/Orbera (n = 11)	Sham procedure (n = 11)	4	600ml (saline solution) + methylene blue (10 mL)
Singapore	Lee 2012[24]	Adults (21-65 y) BMI >27 kg/m^2 Histologic evidence of nonalcoholic steatohepatitis	BIB/Orbera (n = 8)	Sham procedure (n = 10)	6	500 mL (saline solution) + methylene blue (10 mL)
Australia	Fuller 2013[34]	Adults (18-60 y) Stable BMI ≥30 and ≤40 kg/m^2	BIB/Orbera (n = 31)	Diet + lifestyle (n = 35)	6	450-700 mL (based on BMI and stomach anatomy)
USA	Courcoulas 2017[25]	Adults BMI ≥30 and ≤40 kg/m^2	BIB/Orbera (n = 125)	Diet + lifestyle (n = 130)	6	550 ± 50 mL
Iraq	Ahmed 2019[23]	Single, obese female Ages between 20 and 40 y BMI ≥30 and <40 kg/m^2	BIB/Orbera (n = 40)	Diet + lifestyle (n = 40)	6	600 mL (saline solution) + methylene blue (10 mL)
Netherlands	Mathus-Vliegen 2021[26]	Adults BMI ≥32 kg/m^2	BIB/Orbera (nITT = 20, nPP = 7)	Sham (nITT = 23, nPP = 7)	3	500 mL (saline solution)
Iran	Kashani 2022[35]	Adults BMI >30 kg/m^2	Supposedly BIB/Orbera (n = 34)	Diet + lifestyle (n = 32)	6	NR
USA	Abu Dayyeh 2021[22]	22-65 y BMI ≥30 and ≤40 kg/m^2	Spatz (n = 187)	Diet + lifestyle (n = 101)	8	400 mL: (height <162.56 cm, with GERD) 450 mL: (height <162.56 cm, no GERD) 500 mL: (height ≥162.56 cm, with GERD) 550 mL (height ≥162.56 cm, no GERD)
USA	Abu Dayyeh 2022[11]	Adults BMI ≥30 and ≤40 kg/m^2	ESG (n = 85; nmITT = 77)	Diet + lifestyle (n = 124; nmITT = 110)	NA	NA

BMI, Body mass index; *IGB*, intragastric balloon; *NR*, not reported; *BIB*, BioEnteric Intragastric Balloon; *IQR*, interquartile range; *nITT*, narrowed intent-to-treat; *nmITT*, non-modified intent-to-treat; *nPP*, narrow per protocol; *ESG*, endoscopic sleeve gastroplasty; *aIGB,* adjustable intragastric balloon.
*Values are mean ± standard deviation, median (IQR), or n (%).

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Age* (y)	Sex	BMI* (kg/m^2)	Diabetes mellitus n (%)	Hypertension n (%)	Dyslipidemia n (%)
IGB: 36.2 ± 5.2 Sham: 36.3 ± 5.9	IGB: 12/16 Sham: 12/16	IGB: 43.9 ± 1.1 Sham: 43.6 ± 1.8	NR	NR	NR
IGB: 34.8 ± 10.8 Sham: 37.7 ± 8.8	IGB: 8/11 Sham: 9/11	IGB: 49.5 ± 9.5 Sham: 51.3 ± 6.1	BIB: 3 (27.3) Sham: 4 (36.4)	BIB: 3 (27.3) Sham: 4 (36.4)	BIB: 6 (54.6) Sham: 8 (72.7)
IGB: median 43 (IQR, 19.75) Sham: median 47 (IQR, 15)	IGB: 5/8 Sham: 8/10	IGB: 30.3 (5.7) Sham: 32.4 (9.1)	IGB: 1/8 (12.5) Sham: 1/10 (10)	NR	IGB: 2/8 (25) Sham: 5/10 (50)
IGB: 43.4 (9.4) Control: 48.1 (7.3)	IGB: 21/31 Control: 23/35	IGB: 36.0 (2.7) Control: 36.7 (2.9)	NR	NR	NR
IGB: 38.7 (9.37) Control: 40.8 (9.61)	IGB: 112/12 Control: 117/130	BMI <30: IGB: 2 (1.6) Control: 1 (.8) BMI ≥30 and <35: IGB: 63 (50.4) Control: 57 (43.8) BMI ≥35 and ≤40: IGB: 56 (44.8) Control: 70 (53.8) BMI >40: IGB: 4 (3.2) Control: 2 (1.5)	IGB: 9/125 (7.2) Control: 8/130 (6.1)	IGB: 33/125 (26.4) Control: 37/130 (28.4)	IGB: 49/125 (39.2) Control: 39/130 (30)
IGB: median 27 (range, 20-39) Control: median 29 (range, 20-39)	IGB: 40/40 Control: 40/40	IGB: median 36 (range, 31-39.9) Control: median 36 (31-39.9)	NR	NR	NR
IGB: median 42 (IQR, 30-55) Sham: median 43 (IQR, 39-47)	IGB: 6/7 Sham: 11/11	IGB: median 42.6 (IQR, 38.4-43.8) Sham: median 39.2 (IQR, 35.7-43.1)	NR	NR	NR
IGB: 36.62 ± 11.27 Control: 33.97 ± 8.87	IGB: 29/34 Control: 28/32	IGB: 38.99 ± 6.65 Control: 43.24 ± 7.05	NR	NR	NR
adjustable IGB: 44.4 (8.9) Control: 44.0 (8.9)	aIGB: 162/187 Control: 90/10	aIGB: 35.8 ± 2.6 Control: 35.8 ± 2.7	aIGB: 13 (7) Control: 4 (4)	aIGB: 41 (22) Control: 32 (32)	aIGB: 41 (22) Control: 23 (23)
ESG: 47.3 ± 9.3 Control: 45.7 ± 10	ESG: 68/77 Control: 92/110	ESG: 35.5 ± 2.6 Control: 35.7 ± 2.6	ESG: 18/77 Control: 36/110	ESG: 38/77 Control: 58/110	ESG: 13/77 Control: 27/110

SUPPLEMENTARY TABLE 2. Weight loss outcomes of the studies included in the qualitative analysis

Study reference	Intervention	Comparison	3-mo TWL (%)	3-mo EWL (%)	4-mo TWL (%)	4-mo EWL (%)	6-mo TWL (%)	6-mo EWL (%)	8-mo TWL (%)	8-mo EWL (%)	9-mo TWL (%)	9-mo EWL (%)
Spatz vs diet + lifestyle interventions												
Abu Dayyeh 2021[22]	Spatz (n = 187)	Diet + lifestyle (n = 101)	NR	NR	NR	NR	NR	NR	**(Calculated field) Adjustable IGB: 15.0 ± 7 (n = 156) Control: 3.3 ± 5.7 (n = 75)**	NR	NR	NR
Orbera vs diet + lifestyle interventions												
Fuller 2013[34]	BIB/Orbera (n = 31)	Diet + lifestyle (n = 35)	(Inputted data) (Calculated field) IGB: 10.2 ±5.4 Control: 3.3 ± 5.5	IGB: 36.4 Control: 12.1	NR	NR	**(Inputted data) (Calculated field) IGB: 14.2± 5.7 (n = 29) Control: 4.8 ± 4.9 (n = 30)**	IGB: 50.3 (n = 29) Control: 16.9 (n = 30)	NR	NR	NR	IGB: 39.0 Control: 19.2
Courcoulas 2017[25]	BIB/Orbera (n = 125)	Diet + lifestyle (n = 130)	NR	NR	NR	NR	**IGB: 10.2 ± 6.5 (n = 119) Control: 3.3 ± 5.0 (n = 121)**	NR	NR	NR	IGB: 9.1 ± 6.8 Control: 7.6 ± 7.4	IGB: 26.5 ± 20.7 Control: 9.7 ± 15.1
Ahmed 2019[23]	BIB/Orbera (n = 40)	Diet + lifestyle (n = 40)	NR	NR	NR	NR	ESG: 30/40 lost >22.2 Control: 0/40	NR				
Kashani 2022[35]	Supposedly BIB/ Orbera (n = 34)	Diet + lifestyle (n = 32)	NR	NR	NR	NR	**(Calculated field) IGB: 12.22 ± 5.7 (n = 34) Control: 5.67 ± 4.05 (n = 32)**	IGB: 40.98 ± 1.25 Control: 15.28 ± 1.19				
Orbera vs sham procedure												
Genco 2006[20]	BIB/Orbera (n = 16)	Sham procedure (n = 16)	**(Calculated field) IGB: 12.7 ± .9 Sham: 2.6 ± .9**	IGB: 34.0 ± 4.8 Sham: 2.1 ± 1								
Lee 2012[24]	BIB/Orbera (n = 8)	Sham procedure (n = 10)	NR	NR	NR	NR	BMI reduction: IGB median 1.52 (range, .36-3.37) Sham: median .8 (range, –.74 to –1.33)					
Martinez-Brocca 2007[21]	BIB/Orbera (n = 11)	Sham procedure (n = 11)	NR	NR	**(Calculated field) IGB: 8.8 ± 3.8 (n = 10) Sham: 6.4 ± 7 (n = 11)**	**(Calculated field) IGB: 17.5 ± 7 Sham: 12.4 ± 3.4**						
Mathus-Vliegen 2021[26]	BIB/Orbera (nITT = 20, nPP = 7)	Sham (nITT = 23, nPP = 7)	**(Calculated field) IGB: 11.3 ± 7.4 Sham: 9 ± 4.0**	NR								
ESG vs diet + lifestyle interventions												
Abu Dayyeh 2022	ESG (n = 85, nmITT = 77)	Diet + lifestyle (n = 124, nmITT = 110)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Bold values indicate time of removal.

AE, Adverse event; *SAE*, serious adverse event; *TWL*, total weight loss; *EWL*, estimated weight loss; *BMI*, body mass index; *IGB*, intragastric balloon; *NR*, not reported; *BIB*, BioEnteric Intragastric Balloon; *nITT*, narrowed intent-to-treat; *nmITT*, non-modified intent-to-treat; *nPP*, narrow per protocol; *ESG*, endoscopic sleeve gastroplasty; *aIGB,* adjustable intragastric balloon.

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

12-mo TWL (%)	12-mo EWL (%)	>5% TWL at 12mo n/N (%)	>10% TWL at 12 mo n/N (%)	>25% EWL at 12 mo n/N (%)	Observations	AEs n/N (%)	SAEs n (%)	No. with early removal	No. of deaths
Spatz vs diet + lifestyle interventions									
NR	NR	171/187 (91.7) at 8 mo	135/187 (72.4) at 8 mo	157/187 at 8 mo	Improvements in alkaline phosphatase, aspartate and alanine aminotranferases, white blood cell count, 25-OH-vitamin D, and vitamin B_{12} improved at 36 wk; 130 patients with upward adjustment = additional 3.1% TWL	52/187 (28) requiring consideration of device adjustment/extraction; non-SAEs: nausea (90%), dyspepsia (74%), vomiting (72%), abdominal pain (56%)	Device-related: 7/187 (4)	31/187 (16.5%)	0
Orbera vs diet + lifestyle interventions									
(Calculated field) IGB: 9.2 ± 5.1 (n = 23) Control: 5.2 ± 5.3 (n = 22)	IGB: 32.7 Control: 17.8	IGB: 11 Control: 6	IGB: 8 Control: 4	NR	—	IGB: nausea (25/31), vomiting (24/31), abdominal pain (19/31) Control: nausea (3/35), vomiting (3/35), abdominal pain (2/35)		3 /31 (9.6)	0
IGB: 7.6 ± 7.4 (n = 125) Control: 3.1 ± 5.9 (n = 130)	NR	IGB: 75 (60) Control: 39 (30)	IGB: 40 (32) Control: 21 (16.2)	NR	—	IGB: 157/160 (98.1) ≥1 AE (5 severe non-SAE); 139 (86.9) nausea, 121 (75.6) vomiting, 92 (57.5) abdominal pain Control: 92/130 (70.8) ≥1 AE (6 severe non-SAE)	IGB: 16/125 (10) Control: 8/130 (6.1)	30 (18.8) because of AE or patient request	0
					Significant improvement in quality of life	NR	NR	NR	0
					—	NR	NR	1/34	0
Orbera vs sham procedure									
					—	Epigastric pain, nausea, vomiting IGB: 13/16, 12/16, 13/16 Sham: 1/16, 3/16, 0/16 No other AEs	0	0	0
					Significant improvement in nonalcoholic fatty liver disease activity score in IGB group compared with sham	NR	NR	3/11 (not included in the PP results) (27.2)	0
					No significant changes in fasting or postprandial ghrelin	NR	NR	1/11 (9.0)	0
					No significant changes in fasting or postprandial ghrelin Increase in no. of ghrelin cells in sham group, returning to baseline after IGB placement	NR	NR	2/20 (10)	0
ESG vs diet + lifestyle interventions									
ESG: 13.6 ± 8.0 (n = 68) Control: .8 ± 5.0 (n = 89)	ESG: 49.2 ± 32 (n = 68) Control: 3.2 ± 18.6 (n = 89)	70/77	48/77	ESG: 59/77 Control: 13/110	—	927 AEs in 138/150 (92) ESG patients	6/150 (includes crossover)	1 reversal/150 ESGs (.66)	0

SUPPLEMENTARY TABLE 3. Comorbidity outcomes of the studies included in the qualitative analysis

Study reference	Metabolic syndrome	Fasting glucose level (mg/dL)	Diabetes mellitus	Hb_{A1c} improvement	Fasting insulin level (mIU/mL)	Homeostasis model assessment for insulin resistance
Spatz vs diet + lifestyle interventions						
Abu Dayyeh 2022	NR	n = 156 –3.2 (95% CI, –6.5 to .2) to baseline	NR	Among diabetics: –.73% (95% CI, –1.49 to .02) to baseline	NR	NR
Orbera vs diet + lifestyle interventions						
Fuller 2013[34]	Remission rates: IGB 51.6% and 45.2% (6 and 12 mo) Control: 34.3% and 28.6% (6 and 12 mo)	NR	NR	NR	NR	NR
Courcoulas 2017[25]	NR	No significant reduction for both groups	IGB: resolution 4/9 at 9 mo Control: resolution 5/8 at 9 mo	NR	NR	NR
Ahmed 2019[23]	NR	NR	NR	NR	NR	NR
Kashani 2022[35]	NR	NR	NR	NR	NR	NR
Orbera vs sham procedure						
Genco 2006[20]	NR	NR	NR	NR	NR	NR
Lee 2012[24]	NR	NR	NR	NR	NR	NR
Martinez-Brocca 2007[21]	NR	NR	NR	NR	NR	NR
Mathus-Vliegen 2021[26]	NR	NR	NR	NR	IGB: median 18 (IQR, 11-56) baseline vs median 15 (IQR, 11-32) at 3 mo Sham: median 17 (IQR, 12-30) baseline vs median 14 (IQR, 10-18) at 3 mo	NR
ESG vs diet + lifestyle interventions						
Abu Dayyeh 2022	Improvement: ESG: 35/42 Control: 10/29	Significant reduction compared with control	Improvement: ESG: 25/27 Control: 4/27	Significant reduction for diabetic patients in ESG group compared with control	Significant reduction compared with control	Improvement in ESG patients compared with control subjects

IGB, Intragastric balloon; *NR*, not reported; *CI*, confidence interval; *IQR*, interquartile range; *ESG*, endoscopic sleeve gastroplasty; *IW,* impact of weight; *BDI-II,* Beck's depression Inventory II.

(*continued on the next page*)

SUPPLEMENTARY TABLE 3. Continued

Blood pressure improvement	Triglyceride improvement	Total cholesterol improvement	High-density-lipoprotein cholesterol improvement	Low-density-lipoprotein cholesterol improvement	Quality of life
Spatz vs diet + lifestyle interventions					
Diastolic blood pressure: –3.7 mm Hg (–6.4 to –1.0, *P* = .0078) vs control and –6.1 mm Hg (–9.8 to –2.3) to baseline	NR	–6.8 mg/dL (–11.1 to –2.6) to baseline	NR	NR	NR
Orbera vs diet + lifestyle interventions					
No between-group difference	NR	NR	NR	NR	Significant improvement at 6 and 12 mo compared with control
IGB: resolution 19/33 at 9 mo Control: 17/37 at 9 mo	NR	No significant reduction for both groups	No significant reduction for both groups	No significant reduction for both groups	Significant improvement compared with control (IW quality of life and BDI-II)
NR	NR	NR	NR	NR	Significant improvement in quality of life
NR	NR	NR	NR	NR	NR
Orbera vs sham procedure					
NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR
ESG vs diet + lifestyle interventions					
Improvement ESG: 39/65 Control: 19/48	ESG: overall reduction	NR	ESG: overall increase	No improvement	Improvement in most domains