Evidence Synthesis Program

Endoscopic Bariatric Interventions versus Lifestyle Interventions or Surgery for Weight Loss in Patients with Obesity: A Systematic Review and Meta-analysis

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted health care topics of importance to clinicians, managers, and policymakers as they work to improve the health and health care of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program comprises four ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, interface with stakeholders, and address urgent evidence needs. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee composed of health system leadership and researchers. The program solicits nominations for review topics several times a year via the program website.

The present report was developed in response to a request from the National Gastroenterology and Hepatology Program Office. The scope was further developed with input from Operational Partners (below), the ESP Coordinating Center, the review team, and the technical expert panel (TEP). The ESP consulted several technical and content experts in designing the research questions and review methodology. In seeking broad expertise and perspectives, divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Ultimately, however, research questions, design, methodologic approaches, and/or conclusions of the review may not necessarily represent the views of individual technical and content experts.

ACKNOWLEDGMENTS

The authors are grateful to Marika Booth for statistical analysis, Alireza Sedarat, MD and Erik Dutson, MD for conceptualization support, and the following individuals for their contributions to this project:

Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

Jason A. Dominitz, MD, MHS
National Program Director
National Gastroenterology and Hepatology Program Office
Veterans Health Administration

Technical Expert Panel

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

Luke Funk, MD, MPH, FACS
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Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence (see Appendix B for disposition of comments). Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center works to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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ABBREVIATIONS TABLE

Abbreviation	Name
AGB	Adjustable Gastric Band
ASMBS	American Society of Metabolic and Bariatric Surgery
BMI	Body Mass Index
DM	Diabetes Mellitus
EBW	Excess Body Weight
EBWL	Excess Body Weight Loss
ESG	Endoscopic Sleeve Gastroplasty
FDA	US Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation working group
GERD	Gastroesophageal Reflux Disease
HTN	Hypertension
IGB	Intragastric Balloon
LAGB	Laparoscopic Adjustable Gastric Banding
LSG	Laparoscopic Sleeve Gastrectomy
LOS	Length of Stay
NAFLD	Nonalcoholic fatty liver disease
NH	Non-Hispanic
POSE	Primary Obesity Surgery Endolumina
RCTs	Randomized controlled trials
ROBINS-I	Cochrane Risk of Bias In Non-randomized Studies – of Interventions
RYGB	Roux-en-Y Gastric Bypass
TBWL	Total Body Weight Loss
QOL	Quality of Life

EXECUTIVE SUMMARY

INTRODUCTION

According to the World Health Organization (WHO), over 500 million adults are obese. Obesity contributes to a range of harmful comorbidities and its economic burden approximates $150 billion dollars per year. Bariatric surgery remains a gold-standard treatment of morbid obesity and is effective at reducing weight, along with obesity-related conditions. Despite the prevalence of obesity and the proven efficacy of surgery, few who qualify ultimately receive this intervention, and surgery has associated risks. Endoscopic bariatric therapy is an alternative offering a less invasive, possibly cost-effective approach for patients who otherwise would not qualify for, or who are hesitant about or do not have access to, surgical bariatric therapy. An estimated 78% of Veterans are overweight or obese, however Veterans Affairs (VA) medical centers perform only 500 bariatric surgeries annually. If endoscopic bariatric interventions are to be increasingly utilized, it is important for the VA to understand the evidence of how they compare to surgical and pharmacologic therapies. In this review, we assess the impact of endoscopic bariatric therapies on weight loss, morbidity, mortality, and resolution of comorbid conditions compared to surgery and lifestyle modification.

METHODS

Data Sources and Searches

We conducted broad searches using terms relating to "gastric balloon" or "bariatric surgical procedure" or "endoscopic gastroplasty." We searched PubMed (1/1/2014-7/2/2021), Embase (1/1/2014-7/2/2021), and Cochrane (1/1/2014-7/2/2021). We limited the search to 2014 onwards, as these therapies were being approved by FDA in 2015-2017. Studies published prior to 2014 would have been based on data from procedures done in 2012 or earlier, and we did not consider evidence from this period to be relevant to current practice.

Study Selection

Two team members working independently screened the titles and abstracts; full-text review was conducted in duplicate. Disagreements were resolved through group discussion.

Studies were included if they were randomized controlled trials (RCTs) or observational studies comparing a bariatric endoscopic procedure to alternate bariatric therapies (pharmaceutical, endoscopic, or surgical) or lifestyle management. We included all RCTs regardless of outcomes studied or sample size. Observational studies were subjected to additional selection criteria. Studies with a comparative arm (regardless of sample size) were included. All cases series (*eg*, studies with no comparison treatment arm) were excluded. We excluded studies where similar endoscopic mechanisms were compared to each other (*eg*, intragastric balloon [IGB] vs IGB, primary obesity surgery endoluminal (POSE) vs endoscopic sleeve gastroplasty (ESG), *etc*), as well as investigational procedures (*ie*, duodenal-jejunal bypass liner, Endomina, botulinum injection, duodenal mucosal resurfacing).

Data Abstraction and Assessment

Data extraction was completed in duplicate. All discrepancies were resolved with full group discussion. We abstracted data on study design, sample size, perioperative outcomes (weight

loss, reoperations/revisions, 30-day readmissions, adverse events, effects on obesity-related comorbid conditions, mortality), and some outcomes that were procedure specific. We also abstracted data needed for the Cochrane Risk of Bias tool or Cochrane Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I). We reported outcomes for weight loss at 6 months, 12 months, 24 months, 36 months, 48 months, and last follow up if longer than 48 months, or the time closest to these follow-up periods.

Synthesis

Pooled Data

For comparisons with at least 3 studies of the same intervention and similar patient populations and the same outcome, we performed random-effects meta-analyses. We conducted a meta-analysis of 6-month weight loss outcomes (mean percent total body weight loss [%TBWL] and mean percent excess body weight loss [%EBWL]) for RCTs and observational studies of IGB vs lifestyle, and for observational studies of ESG versus laparoscopic sleeve gastrectomy (LSG). Pooled estimates of effect are reported as mean difference (MD) with their 95% confidence intervals (CI). Random-effects meta-analyses were conducted using the Hartung-Knapp-Sidik-Jonkman method. The presence of publication bias was evaluated using Begg rank correlation and Egger regression tests. p-values < .05 were considered statistically significant.

Non-pooled Data

A narrative analysis was performed for the remainder of our outcomes. Continuous outcomes were analyzed using the mean or median along with a measure of dispersion (*ie,* standard deviation or inter-quartile range) to calculate the difference and 95% CI between arms. For binary outcomes, the number of subjects with the outcome was collected and a risk difference was derived with its 95% CI.

We created figures for adverse events with 3 or more studies and report these data in Appendix H. Graphical representations of the outcomes' risk and mean differences and 95% CI were plotted when available or able to be estimated using counts and sample sizes. We noted where significance differed between the study-reported p-value and calculated risk or mean differences and 95% CI. For rare outcome events, risk differences were preferentially used during analysis.

RESULTS

Results of Literature Search

The literature search identified 3,541 potentially relevant citations (including 1 recommended by a subject matter expert), 500 of which were included at the abstract screening level. From these, a total of 385 abstracts were excluded, leaving 115 publications for full-text review. On detailed review of the full text of these 115, 79 publications were excluded, leaving 36 publications meeting eligibility criteria. Among these there were 4 RCTs and 2 observational studies comparing intragastric balloon therapy to lifestyle therapy; 1 RCT and 8 observational studies comparing ESG to various other treatments, including lifestyle therapy, adjustable gastric band, and LSG; and 2 RCTs and 1 observational study comparing the device AspireAssist to lifestyle therapy or to gastric bypass surgery.

Summary of Results for Key Questions

Key Question 1: What is the comparative effectiveness of endoscopic bariatric interventions versus lifestyle interventions or bariatric surgery?

Treatment with IGBs was associated with significantly more weight loss compared to lifestyle therapy at multiple short- and intermediate-term follow-up time points (6 and 12 months). These results were consistent across RCTs and observational studies. Treatment with ESG was associated with significantly more weight loss compared to lifestyle therapy, again at 6- and 12-months follow-up. Treatment with ESG was associated with less weight loss than LSG; this conclusion is based solely on observational studies, although results are consistent. Treatment with the AspireAssist was associated with more weight loss than lifestyle therapy in 1 RCT. There was insufficient evidence on associations between treatments and quality of life or HbA1C measures to reach conclusions. Studies describing long-term durability of weight loss after endoscopic therapies have not yet been published.

Results for the most measured outcome, total body weight loss (reported by 14 of the 36 studies), are presented in Figure ES1.

Key Question 2: What are the comparative harms of endoscopic bariatric interventions versus lifestyle interventions or bariatric surgery?

All studies comparing endoscopic bariatric therapy to lifestyle reported more total complications and 30-day readmission or re-intervention rates, which is expected given these patients underwent invasive interventions. There were no or borderline significant differences in total complications between patients treated with LSG compared to ESG, although all studies reported more complications with LSG.

Key Question 3: Do the comparative effectiveness and/or harms vary by patient or intervention characteristics (ie, age, BMI, type of procedure [intragastric balloon, endoscopic gastric reduction, etc])?

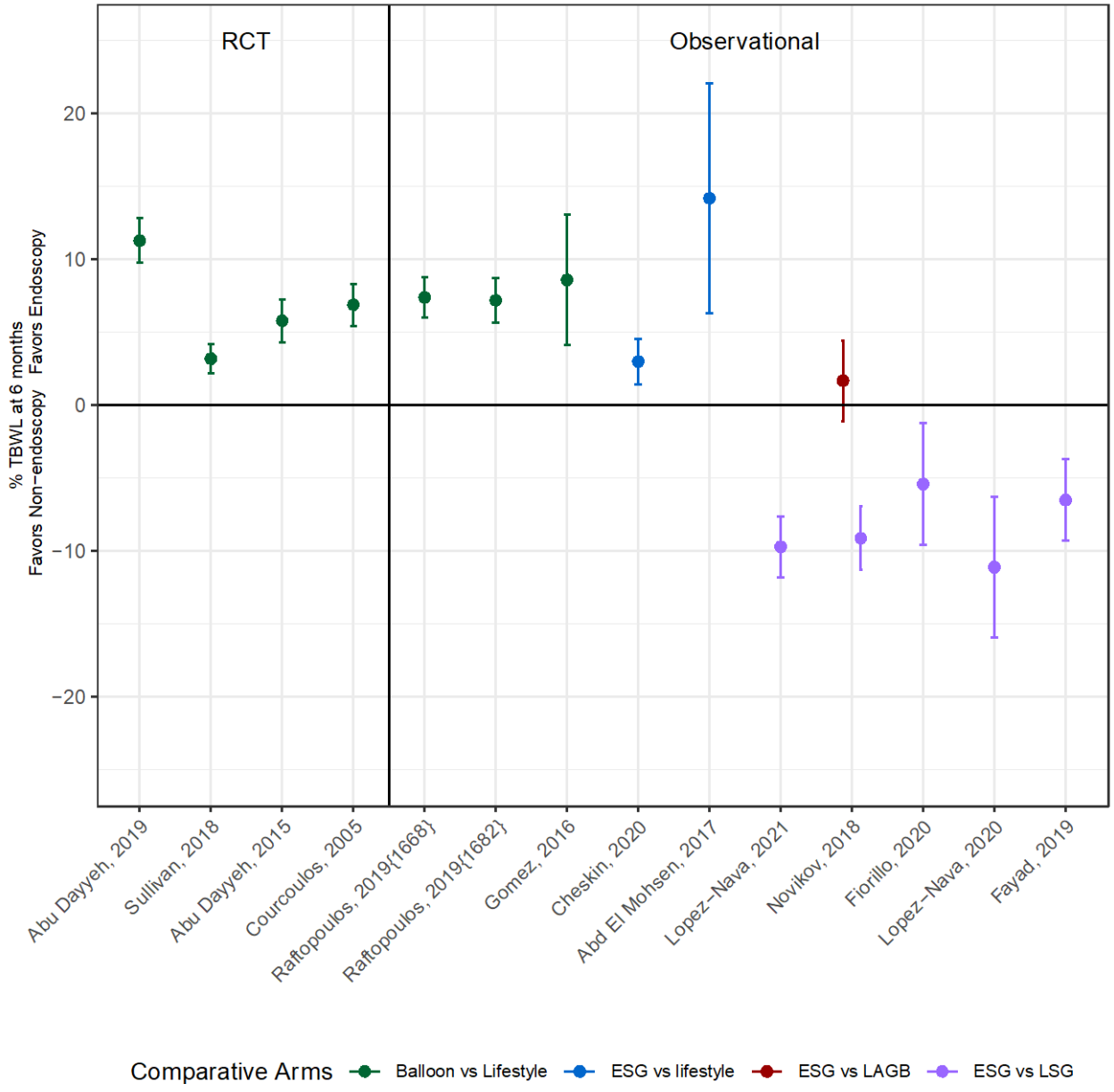
Evidence is insufficient to answer this question.

DISCUSSION

Key Findings and Strength of Evidence

We judged 7 conclusions as being high certainty of evidence, and all were in comparisons between endoscopic interventions and lifestyle therapies. These include: 1) IGB therapy achieves greater %TBWL than lifestyle therapy at 6 and 12 months; 2) IGB therapy achieves more %EBWL than lifestyle therapy at 6 months; 3) ESG achieves more %TBWL than lifestyle therapy at 6 months; and 4) AspireAssist, IGB therapy, and ESG therapy each have greater total complications than lifestyle therapy. Other conclusions were judged to be of moderate or low certainty of evidence due to limitations of the original studies or the presence of only a single study reporting the outcome.

Figure ES1. Total Body Weight Loss at 6 Months for Bariatric Endoscopic Procedures Compared to Lifestyle or Surgery



Abbreviations. %TBWL=mean percent total body weight loss; ESG=endoscopic sleeve gastroplasty; LAGB=laparoscopic adjustable gastric banding; LSG=laparoscopic sleeve gastrectomy.

Applicability

No studies were specific to VA populations. The applicability of these results to VA populations may depend on both the similarity of the patients studied in the trials to VA patients as well as the experience of the gastroenterologists performing endoscopic bariatric therapies in the examined studies compared to VA team experience.

Future Research

The history of weight loss interventions is one of innovation and dissemination prior to evaluation. Vertical banded gastroplasty, a prior version of the gastric balloon, and the combination medication of fenfluramine and phentermine ("Fen-Phen") are all examples of interventions developed and widely used before sufficient studies had been done to establish their risk-benefit profile. These interventions have since been removed following research showing the benefit not to be worth the risk. It would behoove the VA to not repeat this history, and to adequately assess new interventions before they are made widely available. Several specific research gaps are noted in the main text of the report.

Conclusions

In conclusion, the endoscopic therapies IGB, ESG, and AspireAssist are associated with greater short- and intermediate-term weight loss in patients with obesity compared to lifestyle management alone. However, various complications are also more likely in patients treated with endoscopic therapies compared with lifestyle management. No long-term studies of weight loss have been published. The degree of weight loss with endoscopic therapies is probably less than their surgical counterparts. As the field continues to grow, future research should include more robust RCTs or well-designed prospective matches studies with adequate power and follow-up to assess long-term weight loss and the effects on obesity-related comorbid conditions.

EVIDENCE REPORT

INTRODUCTION

PURPOSE

The Evidence Synthesis Program (ESP) developed the present report in response to a request from the Veterans Health Administration (VHA) National Gastroenterology and Hepatology Program Office.

BACKGROUND

The growing prevalence of obesity worldwide is notable. According to a 2016 study by the World Health Organization (WHO), over 1.9 billion adults are considered overweight and another 500 million adults are obese.[1] Obesity contributes to a range of harmful comorbidities spanning cardiovascular disease, type 2 diabetes, cancer, osteoarthritis, non-alcoholic fatty liver disease, and sleep apnea.[2,3] The economic burden on the United States healthcare system, when including direct and indirect costs, approximates $150 billion dollars per year.[4] Targeted pharmacologic, endoscopic, and surgical therapies have been developed in the effort to expand therapeutic options for treating obesity.

Bariatric surgery remains a gold-standard treatment of morbid obesity and is effective at reducing weight, along with obesity-related conditions, which translates into improved long-term survival.[5] The American Society of Metabolic and Bariatric Surgery (ASMBS) estimates that in 2019, laparoscopic sleeve gastrectomy (LSG) represented 60% of all bariatric procedures performed domestically, with Roux-en-Y gastric bypass (RYGB) encompassing 18%, and adjustable gastric band (AGB) and duodenal switch each constituting only 0.9%. The only endoscopic bariatric therapy tracked by ASMBS, intragastric balloon (IGB), comprised 1.8% of total bariatric procedures.[6] There is strong evidence from observational studies and randomized controlled trials (RCTs) that bariatric surgery is an effective intervention for substantial and durable weight loss. Long-term studies with 10-year follow-up have demonstrated mean percent excess weight loss of 60% following RYGB, 49% following AGB, and 57% following LSG in certain populations.[7] Though rare, surgery is associated with a risk of severe morbidity and mortality for an elective operation, approximately 4% and 0.1%, respectively. Additionally, most of these operations are not easily reversible.[8]

Despite the prevalence of obesity and the proven efficacy of surgery, few who qualify ultimately receive this intervention.[9] It is estimated that 256,000 bariatric surgeries were performed in 2019, which accounts for less than 1% of American patients eligible based on BMI.[6] This gap is even more pronounced in the VA population. According to the 2014 VA/Department of Defense obesity guideline summary, 78% of Veterans are overweight or obese resulting in an annual cost of $370 per patient due to medical- or non-medical-related care.[10] The VA performs approximately 500 bariatric surgeries annually across 17-21 centers. Comprehensive and interdisciplinary management thus far has focused on lifestyle modification and medications through programs like MOVE! (MOVE! Weight Management Program) or referral to bariatric surgery. However, given the large percentage of Veterans who are obese receiving care through the VA and the strong association of obesity with comorbid conditions, detailed evaluation of less-invasive therapeutic options is requested by VA stakeholders.

There remains a treatment gap for patients who experience limited weight loss with conservative therapies (*eg*, lifestyle modification, medications), and at the same time, do not qualify for or otherwise do not have access to surgery, or are reluctant because of the potential operative risks. Endoscopic bariatric therapy is a viable alternative to traditional therapies.[11] Over the past 10 years, various endoscopic modalities have been developed that focus on either primary gastric (IGB, endoscopic sleeve gastroplasty [ESG], aspiration therapy) or small bowel (luminal liners, resurfacing or shuttles) interventions. Preliminary studies have shown promising results, including mean percent total body weight loss (%TBWL) of 18-20% 1 year following ESG[1,12] and 8-12% following IGB.[13,14] Endoscopic therapies came to market quickly, as compared to their surgical counterparts, and questions remain about their efficacy and safety. Additionally, the differences in efficacy between therapies are not well described, which may lead practitioners to be uncertain about recommending them to patients who may qualify.

Systematic reviews comparing endoscopic bariatric therapies to surgical intervention, lifestyle intervention, and other endoscopic treatments have methodological variations and inconsistent reporting of obesity and metabolic syndrome-related outcomes.[14-16] This is complicated further by the wide variety of existing therapies available, as well additional novel therapies that are being considered for US Food and Drug Administration (FDA) approval in the near future. Endoscopic bariatric interventions are increasingly being utilized for a broad population of patients with morbid obesity, and it is imperative to examine how they compare to surgical and lifestyle therapies. We conducted a systematic review to help clinicians, patients, and policymakers understand these new approaches in comparison to traditional bariatric surgery. In this review, we aim to assess the impact of endoscopic bariatric therapies on weight loss, morbidity, mortality, and resolution of comorbid conditions.

METHODS

TOPIC DEVELOPMENT

This topic was developed in response to a nomination by Jason A. Dominitz, MD, MHS National Program Director, National Gastroenterology and Hepatology Program Office, Veterans Health Administration. Key questions were then developed with input from the topic nominator, the ESP Coordinating Center, the review team, and a technical expert panel (TEP).

KEY QUESTIONS

The following key questions (KQs) were the focus of this review:

KQ1: What is the comparative effectiveness of endoscopic bariatric interventions versus lifestyle interventions or bariatric surgery?

KQ2: What are the comparative harms of endoscopic bariatric interventions versus lifestyle interventions or bariatric surgery?

KQ3: Do the comparative effectiveness and/or harms vary by patient or intervention characteristics (*ie*, age, BMI, type of procedure [intragastric balloon, endoscopic gastric reduction, *etc*])?

PROTOCOL

A preregistered protocol for this review can be found on the PROSPERO international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO/; registration number CRD42021270205).

DATA SOURCES AND SEARCHES

We conducted broad searches using terms relating to "gastric balloon" or "bariatric surgical procedure" or "endoscopic gastroplasty." We searched PubMed (1/1/2014-12/7/2021), Embase (1/1/2014-12/7/2021), and Cochrane (1/1/2014-12/7/2021). A search focusing on "endoscopic bariatric therapy" was conducted January 23, 2022, and utilized the same databases and search parameters as the initial search. We limited the search to 2014 onwards, as these therapies were being approved by FDA in 2015-2017. Studies published prior to 2014 would have been based on data from procedures done in 2012 or earlier, and we did not consider evidence from this period to be relevant to current practice. See Appendix A for complete search strategy.

STUDY SELECTION

Two team members working independently screened the titles of retrieved citations. For titles deemed relevant by at least 1 person, abstracts were then screened independently in duplicate by 2 team members. All disagreements were reconciled through group discussion. Full-text review was conducted in duplicate by 2 independent team members with any disagreements resolved through discussion. Studies were included at either the abstract or the full-text level if they were RCTs or observational studies comparing a bariatric endoscopic procedure to alternate bariatric therapies (pharmaceutical, endoscopic, or surgical) or lifestyle management. Studies with fewer than 10 participants were excluded during screening.

We included all RCTs regardless of outcomes studied or sample size. Observational studies were subjected to additional selection criteria. Studies with a comparative arm (regardless of sample size) were included. All cases series (*eg*, studies with no comparison treatment arm) were excluded, regardless of sample size, for analysis of the primary outcomes; however, case series with greater than 500 participants were included for complication outcomes. Additionally, observational studies from the same data source, either large databases or single institutional databases, were considered to have a large overlap if >50% of the same subjects were included in multiple publications or if there was >50% overlap in the enrollment period. In this instance, the publication with the most recent data and the most outcomes of interest was included.

We excluded studies where the bariatric procedure was used solely as a bridge to weight loss prior to bariatric surgery, as this fell outside the scope of interest of VA stakeholders. We also excluded studies where similar endoscopic mechanisms were compared to each other (*eg*, IGB vs IGB, primary obesity surgery endoluminal vs endoscopic sleeve gastroplasty, *etc*), as well as those that compared adjustments of endoscopic bariatric therapies in unapproved ways (*eg*, variable balloon inflation volume, number of intragastric balloons, *etc*) or investigational procedures (*ie*, duodenal-jejunal bypass liner, Endomina, botulinum injection, duodenal mucosal resurfacing).

DATA ABSTRACTION AND ASSESSMENT

Data extraction was completed in duplicate. All discrepancies were resolved with full group discussion. We abstracted data on study design, sample size, perioperative outcomes (weight loss, reoperations/revisions, 30-day readmissions, adverse events, effects on obesity-related comorbid conditions, mortality) and some outcomes that were procedure specific (IGB-related complications such as premature removal due to intolerance, fistula or gastric ulceration; AspireAssist-related stomal irritation, *etc*). We also abstracted data needed for the Cochrane Risk of Bias tool or Cochrane Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I). We looked for outcomes for weight loss at 6 months, 12 months, 24 months, 36 months, 48 months, and last follow-up if longer than 48 months, or the time closest to these follow-up periods.

RCTs were assessed for quality (risk of bias) with the Cochrane Risk of Bias tool. This tool requires an assessment of whether a study is at high or low (or unknown) risk of bias in 7 domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other (see Appendix C for tool; Appendix E for table). We used ROBINS-I for observational studies. This tool requires an assessment of whether a study is at critical, serious, moderate, or low risk of bias (or no information) in 7 domains: confounding, selection bias, bias in measurement classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported result (see Appendix D for tool; Appendix F for table). Since observational studies are not required to have published an a priori protocol, we operationalized the last domain (bias in selection of the reported result) as requiring that studies report the most common variables.

We used the criteria of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group.[19] GRADE assesses the certainty of the evidence based on

the assessment of the following domains: risk of bias, imprecision, inconsistency, indirectness, and publication bias. This results in categories as follows:

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/Insufficient: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

SYNTHESIS

Pooled Data

For comparisons with at least 3 studies of the same intervention and similar patient populations and the same outcome, we performed random-effects meta-analyses. We conducted a meta-analysis of 6-month weight loss outcomes (%TBWL and mean percent excess body weight loss [%EBWL]) for RCTs and observational studies of IGB versus lifestyle, and for observational studies of ESG versus LSG. Pooled estimates of effect are reported as mean difference (MD) with their 95% confidence intervals (CI). Random-effects meta-analyses were conducted using the Hartung-Knapp-Sidik-Jonkman method. The presence of publication bias was evaluated using Begg rank correlation[17] and Egger regression tests.[18] p-values < .05 were considered statistically significant.

Non-pooled Data

A narrative analysis was performed for the remainder of our outcomes. Continuous outcomes were analyzed using the mean or median along with a measure of dispersion (standard deviation, inter-quartile range) to calculate the difference and 95% CI between arms. For binary outcomes, the number of subjects with the outcome was collected and a risk difference was derived with its 95% CI.

We created figures for adverse events with 3 or more studies and included all in Appendix H. Graphical representations of the outcomes' risk and mean differences and 95% CI were plotted when available or estimable using counts and sample sizes. We noted where significance differed between the study-reported p-value and calculated risk or mean differences and 95% CI. For rare outcome events, risk differences were preferentially used during analysis.

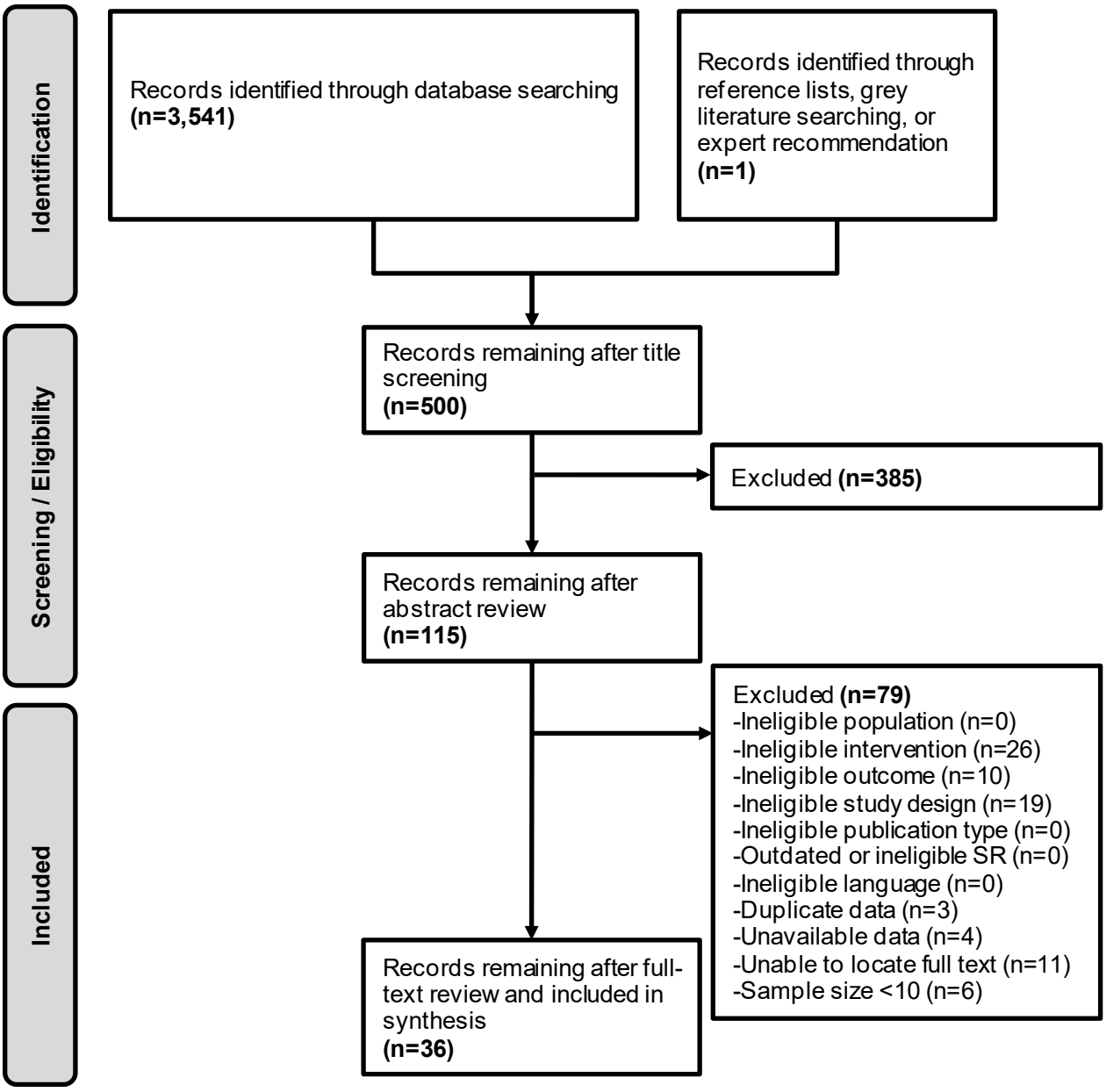
All analyses were carried out with the *metafor* package in R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

LITERATURE FLOW

The literature flow diagram (Figure 2) summarizes the results of the study selection process (full list of excluded studies available in Appendix B).

Figure 1. Literature Flowchart



LITERATURE OVERVIEW

The literature search identified 3,541 potentially relevant citations (including 1 recommended by a subject matter expert), 500 of which were included at the abstract screening level. From these, a total of 385 abstracts were excluded for the following reasons: study design (*N* = 276), no outcomes (*N* = 53), bridging therapy (*N* = 24), duplicate (*N* = 22), modified procedures (*N* = 3), adjunct therapies (*N* = 2), pediatric (*N* = 2), procedure type not included (*N* = 2), and no data available (*N* = 1). This left 115 publications for full-text review, of which 79 publications were excluded for the following reasons: study design (*N* = 19), unavailable (*N* = 11), procedure type not included (*N* = 10), adjunct therapies (*N* = 8), modified procedures (*N* = 7), non-bariatric outcomes (*N* = 6), sample size (*N* = 6), no data available (*N* = 4), short follow-up (*N* = 4), duplicate data (*N* = 3), and bridging therapy (*N* = 1). A full list of excluded studies from the full-text review is in Appendix I. A total of 36 publications were identified at full-text review as meeting initial inclusion criteria. Descriptions of included publications are available in the Evidence Table (Appendix G).

Intragastric Balloon

A total of 12 RCTs were identified, all of which compared IGB to lifestyle therapy. An additional 3 observational studies were identified comparing IGB to lifestyle therapy.

Endoscopic Sleeve Gastroplasty

One RCT was identified comparing ESG to lifestyle therapy. An additional 11 observational studies were identified, of which 5 compared ESG to lifestyle therapy, 1 compared to AGB, and 7 compared ESG to LSG (1 study compared ESG to both AGB and LSG).

Aspiration Therapy

A total of 3 RCTs were identified that compared AspireAssist to lifestyle therapy. One additional observation study compared AspireAssist to RYGB.

Risk of Bias

For the RCTs, the most common sources of bias were lack of blinding of participants and personnel, incomplete outcome data, and blinding of outcome assessment. All studies were high risk of bias in at least 1 domain. For the observational studies, the most common sources of bias were bias due to confounders, selection of participants, missing data, and measurement of outcomes. All but one observational study has unknown or high risk of bias in at least 1 domain.

KEY QUESTION 1: What is the comparative effectiveness of endoscopic bariatric interventions versus lifestyle interventions or bariatric surgery?

6 Month Total Body Weight Loss

A total of 10 studies compared %TBWL with IGB to control groups at 6 months (Figure 2).[13,20-28] All of these studies compared IGB to lifestyle; 7 were RCTs and 3 were observational studies. All of these studies but 1 found significantly greater %TBWL in patients treated with IGB. The size of weight loss benefit was mostly similar between studies, with 95% CIs for the results overlapping in 9 of the 10 studies. We pooled the 7 RCTs in a random-effects meta-analysis (Figure 3). The pooled estimate of the mean difference in %TBWL at 6 months was 6.37% (95% CI [3.94, 8.80]). There was no evidence of publication bias (Egger's test $p = 0.903$, Begg's test $p = 0.239$). For the 3 observational studies, the random effect pooled estimate of mean difference in %TBWL at 6 months was 7.37% (95% CI [6.36, 8.39]), favoring treatment with balloon. There was no evidence of publication bias (Egger's test $p = 0.595$, Begg's test $p = 1$).

A total of 9 studies compared %TBWL with ESG to control groups at 6 months (Figure 2).[29-37] One RCT and 2 observational studies[29-31] compared ESG to lifestyle, and all found significantly greater %TBWL in the patients treated with ESG. The size of the weight loss benefit was very different in the 3 studies, with the 95% CIs for the results non-overlapping. The 1 study comparing ESG to laparoscopic adjustable gastric banding (LAGB) reported no significant differences in total body weight loss at 6 months. Six observational studies compared ESG to LSG at 6 months.[32-37] These studies all reported significantly greater total body weight loss in the patients treated with LSG. We pooled these 6 observational studies in a random-effects meta-analysis (Figure 4). The pooled estimate of the mean difference in %TBWL at 6 months was 10.44% (95% CI [6.08, 14.80]), favoring treatment with LSG. There was no evidence of publication bias (Egger's test $p = 0.691$, Begg's test $p = 0.817$).

No studies compared AspireAssist %TBWL at the 6-month interval.

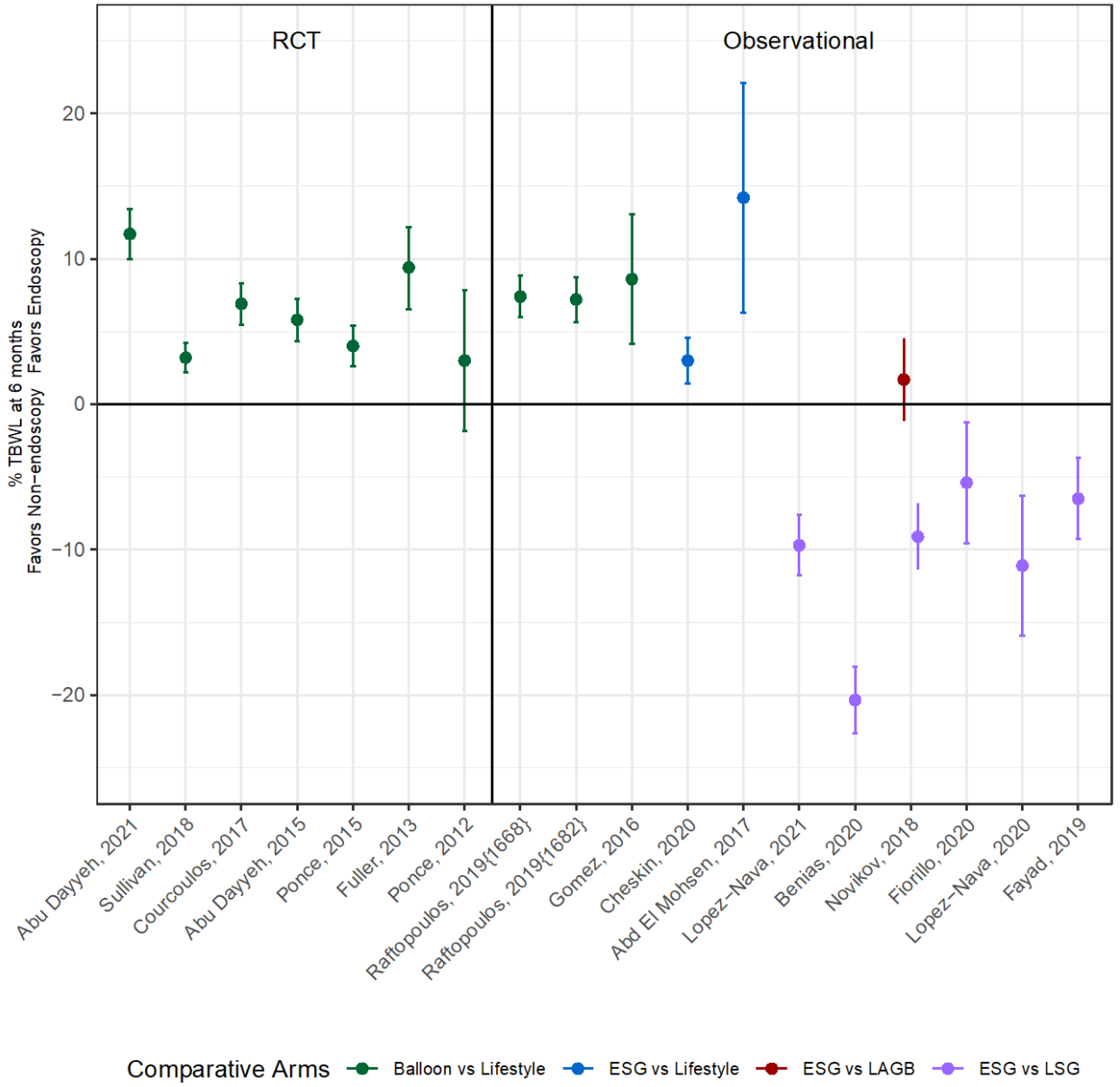
6 Month Excess Body Weight Loss

A total of 6 studies compared %EBWL with IGB to control groups at 6 months (Figure 5).[20,22,26-28,38] All of these studies compared IGB to lifestyle, and all were RCTs. All of these studies but 1 found significant %EBWL in patients treated with IGB at 6 months. The size of weight loss benefit was mostly similar between studies, with 95% CIs for the results overlapping across all studies. A random-effects meta-analysis was performed examining %EBWL after IGB versus lifestyle (Figure 6). The pooled estimate of the mean difference in %EBWL at 6 months was 17.11% (95% CI [11.65, 22.57]). There was no evidence of publication bias (Egger's test $p = 0.618$, Begg's test $p = 0.333$).

A total of 2 studies compared excess body weight loss with ESG to control groups at 6 months: 1 RCT comparing ESG to lifestyle and 1 observational study comparing ESG to LSG.[31,34] The study comparing ESG to lifestyle found significantly superior %EBWL in patients treated with ESG, whereas the observational study comparing ESG to LSG found significant %EBWL with LSG compared to ESG.

No studies compared AspireAssist %EBWL at the 6-month interval.

Figure 2. Total Body Weight Loss at 6 Months for Bariatric Endoscopic Procedures Compared to Lifestyle or Surgery



Abbreviations. %TBWL=mean percent total body weight loss; ESG=endoscopic sleeve gastroplasty; LAGB=laparoscopic adjustable gastric banding; LSG=laparoscopic sleeve gastrectomy.

Figure 3. Meta-analysis of IGB versus Lifestyle for the Outcome of Total Body Weight Loss at 6 Months

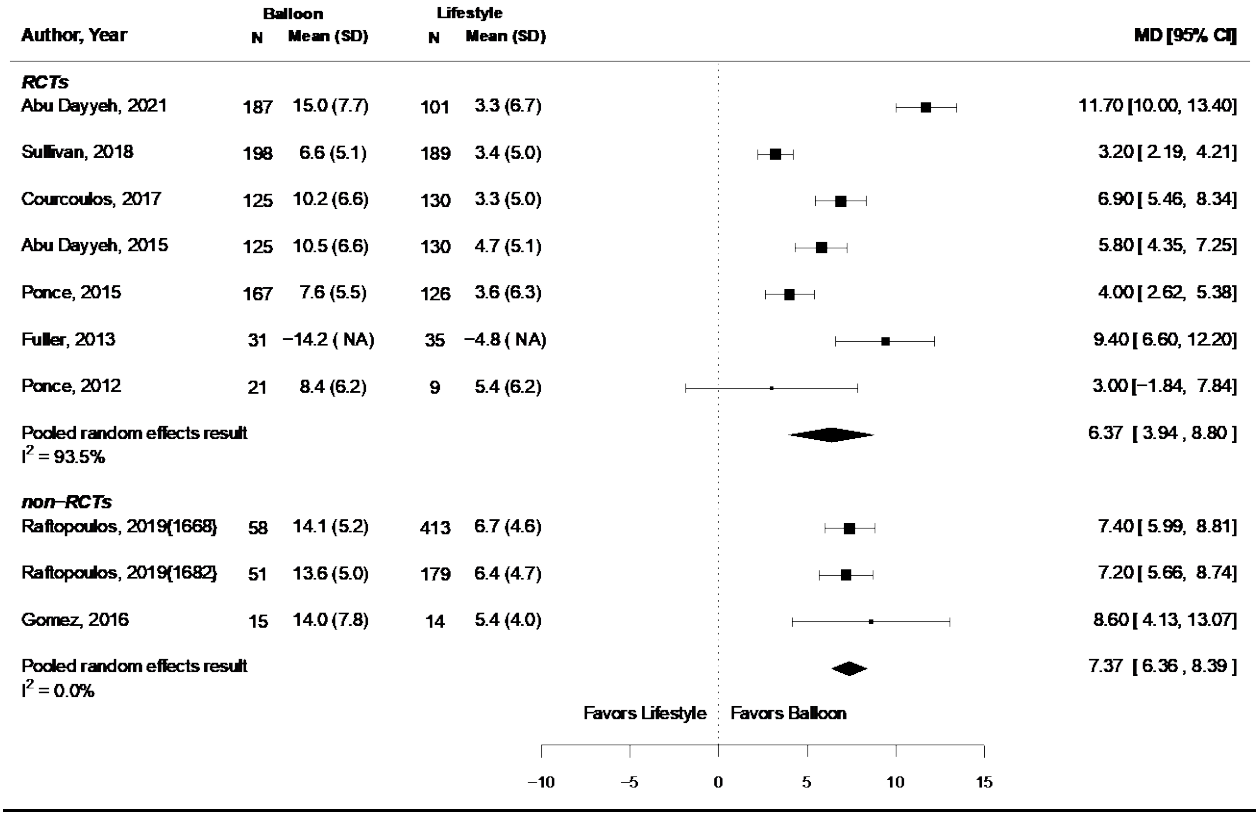
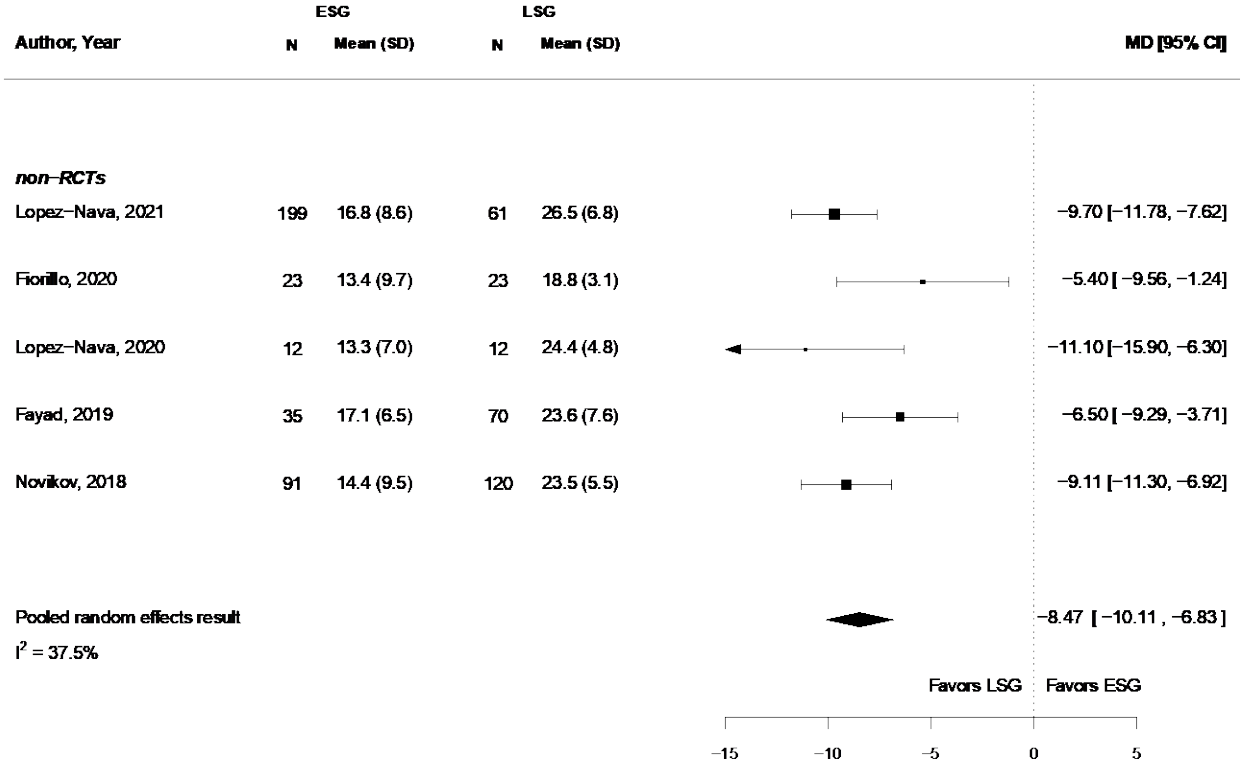
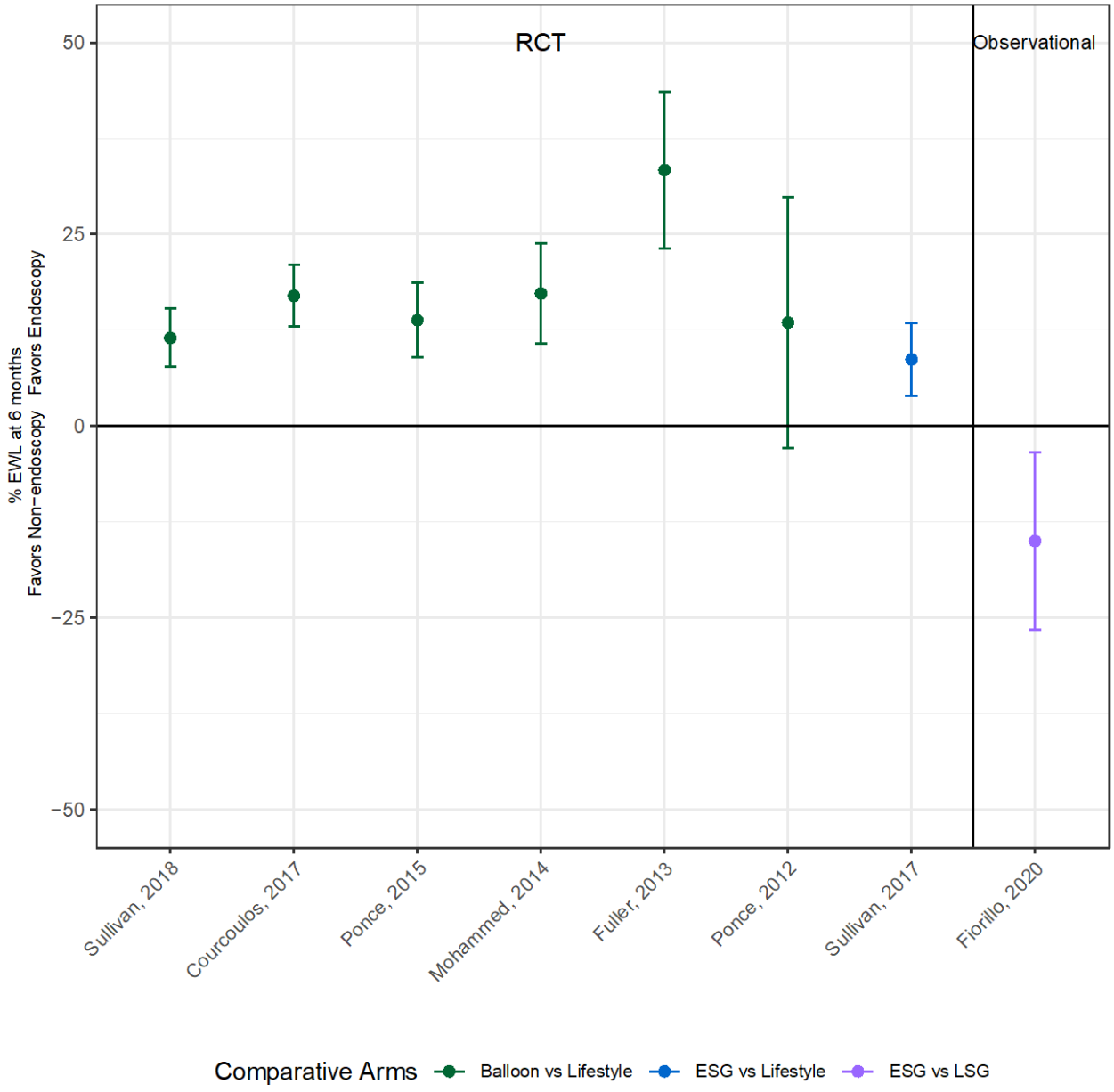


Figure 4. Meta-analysis of ESG versus LSG for the Outcome of %TBWL at 6 Months



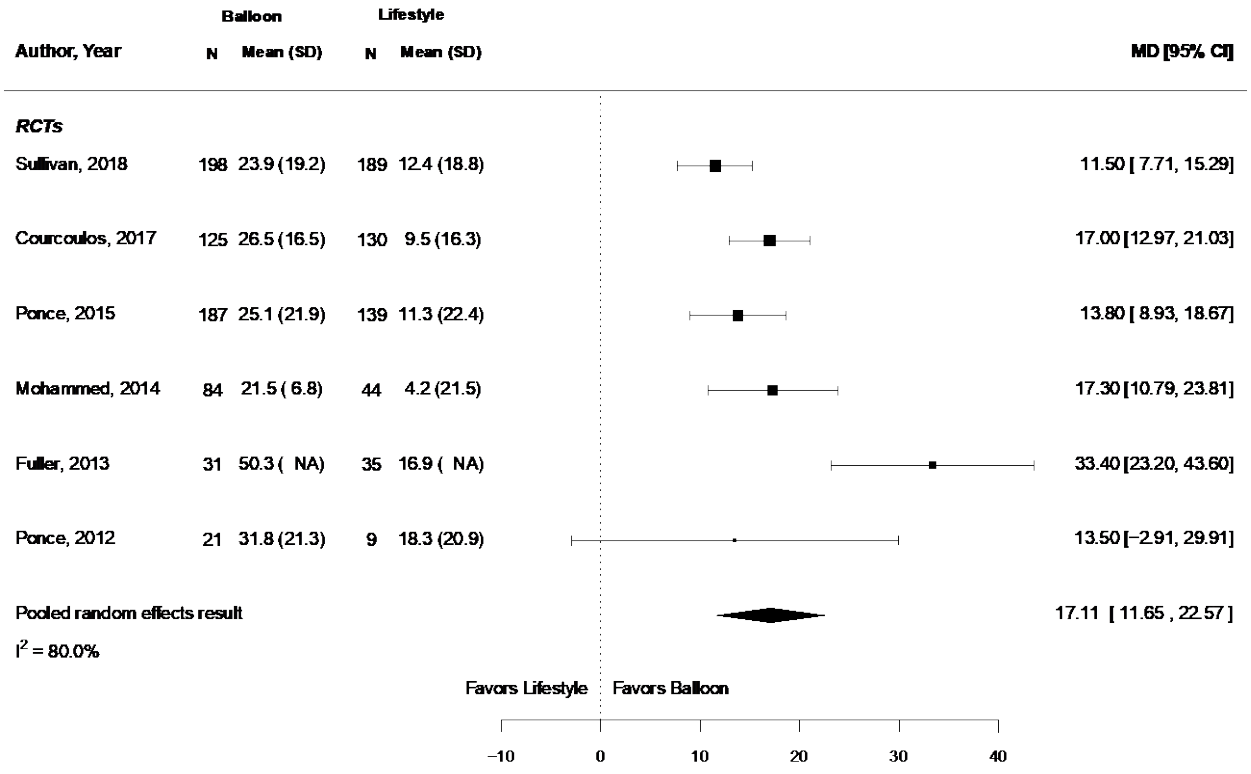
Abbreviations. ESG=endoscopic sleeve gastroplasty; LSG=laparoscopic sleeve gastrectomy.

Figure 5. Excess Body Weight Loss at 6 Months for Bariatric Endoscopy as Compared to Lifestyle or Surgery



Abbreviations. %EWL=excess weight loss; ESG=endoscopic sleeve gastroplasty; LSG= laparoscopic sleeve gastrectomy.

Figure 6. Meta-analysis of Intragastric Balloon versus Lifestyle for the Outcome of %EBWL at 6 Months



12 Month Total Body Weight Loss

A total of 5 studies compared ESG to control groups at 12 months (Figure 7).[29,31-33,37] Two studies compared ESG to lifestyle.[29,31] Both of these studies found significantly greater %TBWL in the patients treated with ESG. One study compared ESG to LAGB, reporting significant differences in weight loss at 12 months with those treated with the gastric band.[32] Three observational studies compared ESG to LSG at 12 months.[32,33,37] These studies reported significantly greater %TBWL in the patients treated with LSG.

A total of 6 studies compared IGB to lifestyle at 12 months, 4 of which were RCTs.[13,20,21,24,26,27] All studies except 1 RCT reported significant %TBWL with IGB compared to control. Of these studies, 4 used the Orbera endoscopically placed balloon, 1 reported results from the swallowable Ellipse balloon, and 1 study reported results with the Reshape dual balloon. The Reshape dual balloon result was the only trial not to be significant. We pooled these 4 RCTs in a random-effects meta-analysis (Figure 9). The pooled estimate was 4.13% (95% CI [2.99, 5.27]. There was no evidence of bias (Egger's test $p = 0.198$, Begg's test $p = 0.469$)

A total of 3 studies compared AspireAssist to control at 12 months, 1 of which was an RCT.[39-41] Two RCTs compared longitudinal outcomes from AspireAssist to lifestyle therapy at 12 months, both reporting significant %TBWL with aspiration therapy versus control.[39,41] One observational study compared AspireAssist to RYGB.[40] This study demonstrated significantly more weight loss at 12 and 24 months with RYGB compared to AspireAssist.

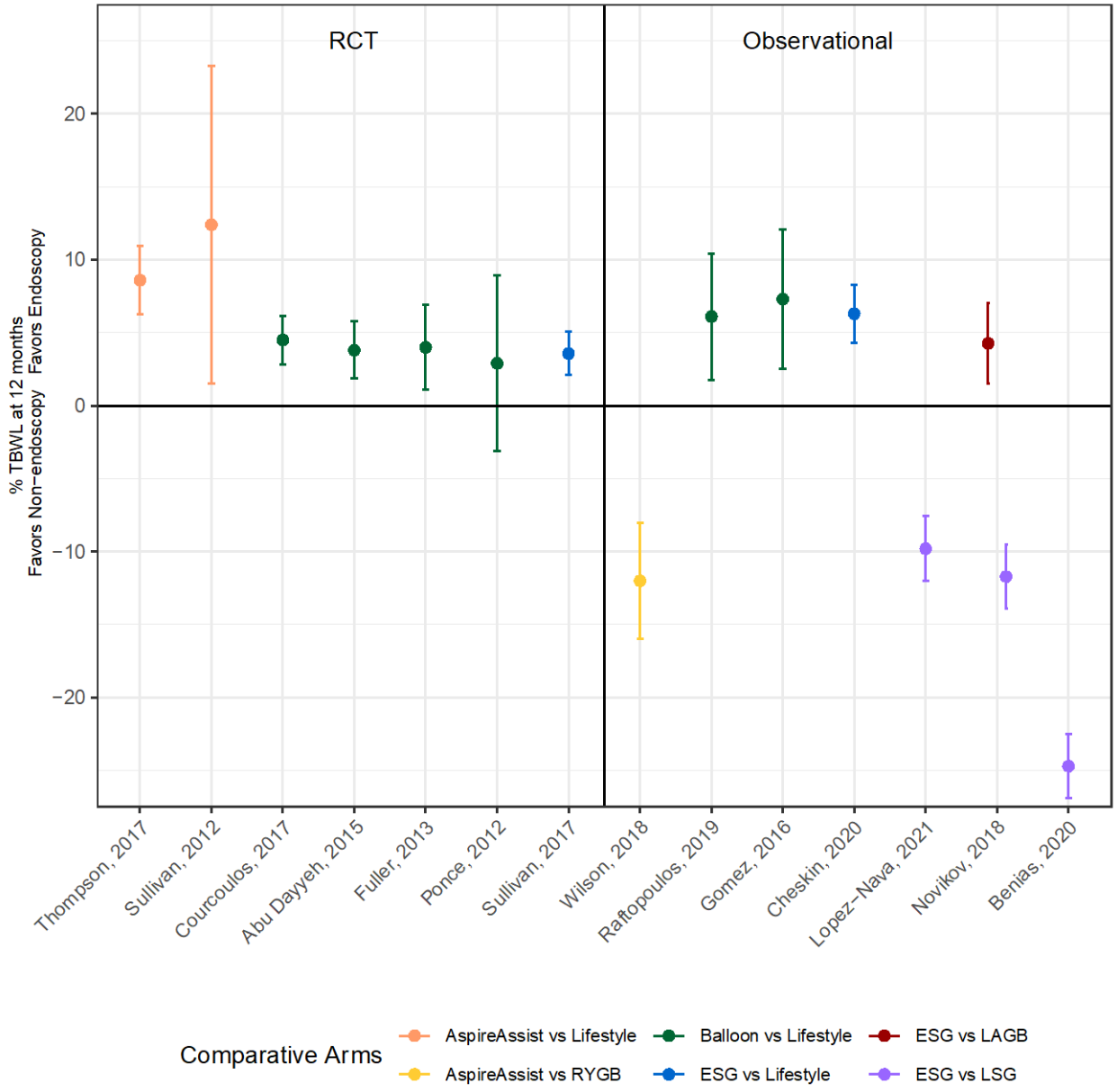
12 Month Excess Body Weight Loss

A total of 4 studies compared %EBWL with IGB versus lifestyle at 12 months, all of which were RCTs (Figure 8).[20,26,27,38] Of these studies, all but 1 demonstrated significant excess body weight loss at 12 months, and all 95% CIs overlapped.

One study reported %EBWL after ESG vs lifestyle therapy.[31] This RCT reported statistically greater excess body weight loss at 12 months with ESG compared to control.

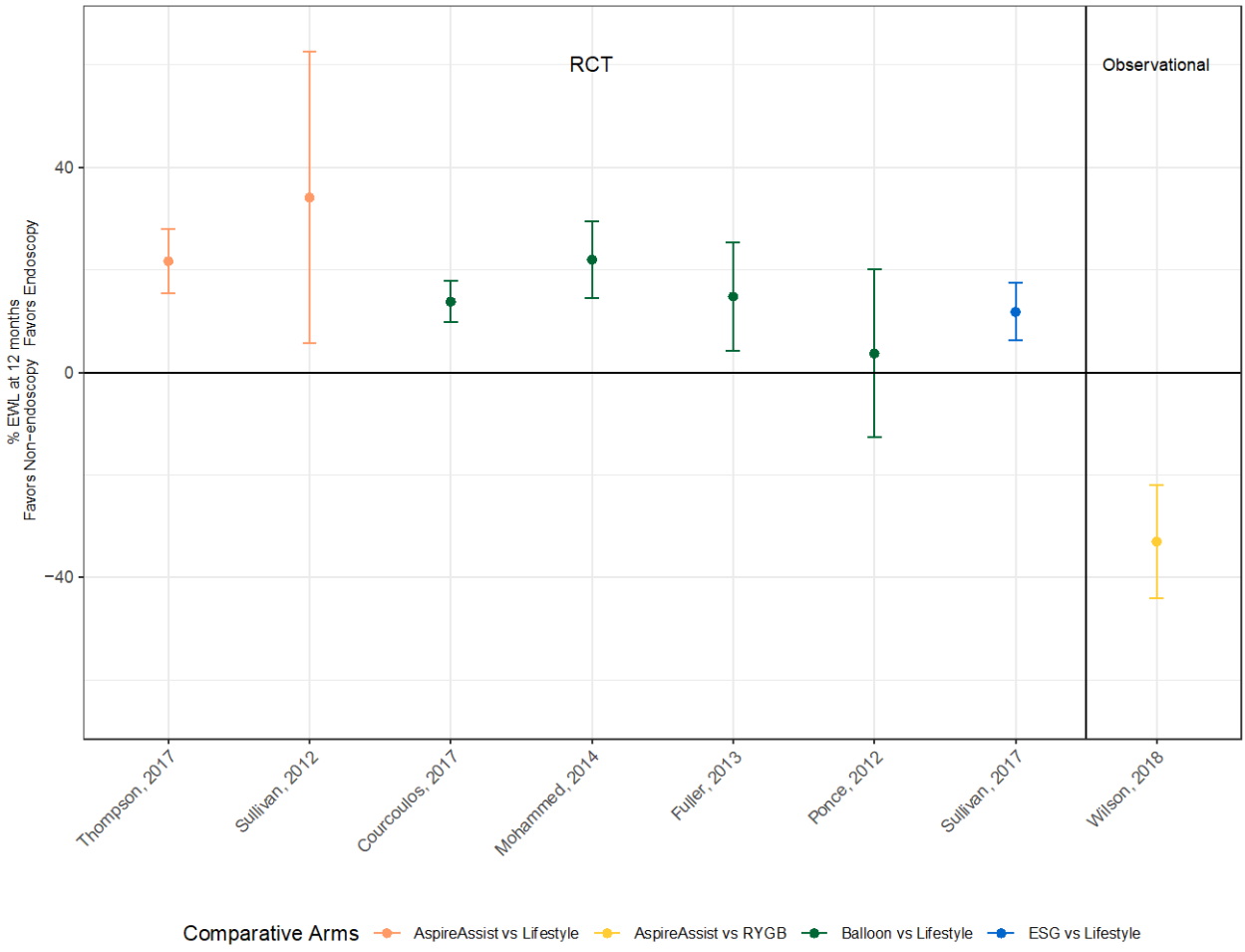
A total of 3 studies compared %EBWL with aspiration therapy to control at 12 months.[39-41] Two RCTs compared AspireAssist to lifestyle, both reporting significantly increased %EBWL with aspiration therapy at 12 months.[39,41] One observational study compared aspiration therapy to RYGB and reported significantly greater %EBWL at 12 months with RYGB compared to AspireAssist. [40]

Figure 7. Total Body Weight Loss at 12 Months for Bariatric Endoscopy as Compared to Lifestyle or Surgery



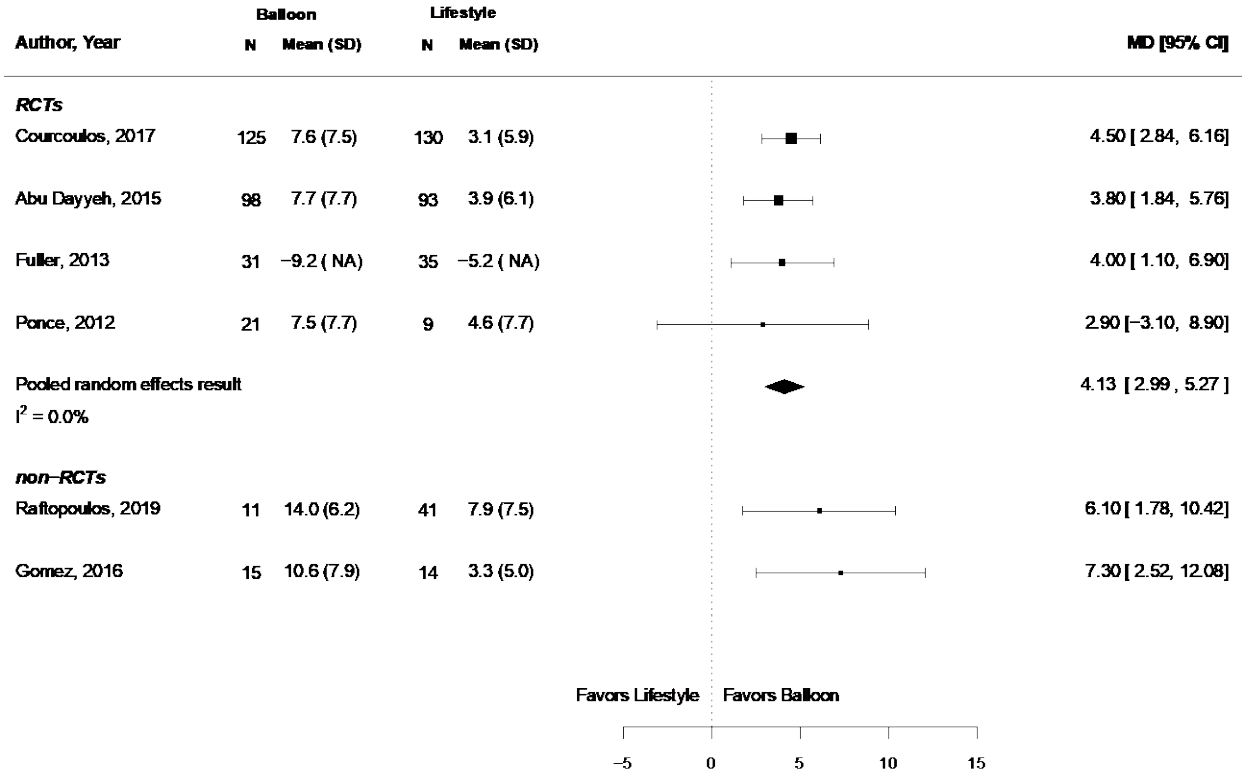
Abbreviations. %TBWL=mean percent total body weight loss; ESG=endoscopic sleeve gastroplasty; LAGB=laparoscopic adjustable gastric banding; LSG=laparoscopic sleeve gastrectomy.

Figure 8. Excess Body Weight Loss at 12 Months for Bariatric Endoscopic Procedures as Compared to Lifestyle or Surgery



Abbreviations. %EWL=excess weight loss; ESG=endoscopic sleeve gastroplasty; RYGB=Roux-en-Y gastric bypass.

Figure 9. Meta-analysis of IGB versus Lifestyle Outcome %TBWL at 12 Months



Quality of Life Outcomes (Table 1)

IGB versus Lifestyle

One study reported quality of life (QOL) outcomes at both 6 and 12 months.[20] This study found mean difference in IWQOL-Lite scores 7.5 points greater at 6 months and 6.4 points greater at 12 months after IGB compared to lifestyle treatment, but a confidence interval could not be determined (higher scores indicate better QOL).

ESG versus Lifestyle

One study reported QOL outcomes at 6 months, and 1 reported QOL outcomes at 12 months.[31,42] Courcoulos et al found mean difference in IWQOL-Lite scores 3.11 points greater after 6 months and 3.88 points greater at 12 months after ESG compared to lifestyle treatment. This study found significantly higher QOL at 12 months compared to lifestyle. Ahmed et al found significantly higher risk differences of increased QOL in the balloon group at 6 months.

ESG versus LSG

Two studies reported QOL outcomes at 6 months.[34,43] One study reported no significant difference in GIQOL scores between the 2 procedures.[34] Another study reported 7.9% less improvement in QOL after ESG compared to LSG when subjectively rated on a scale of 1-10 at 6 months.[43] This result was not statistically significant in 1 study, and in the other, no confidence interval could be determined.

Table 1. Hemoglobin A1c and Quality of Life Outcomes for Bariatric Endoscopic Procedures Compared to Lifestyle or Surgery

	HbA1c Negative is better for endoscopic treatment *MD [95% CI]*	**Quality of Life** Positive is better for endoscopic treatment *MD [95% CI]*
IGB vs Lifestyle		
Abu Dayyeh, 2021, 9 mo (RCT)	-0.73 [-1.49, 0.02][a]	
Sullivan 2018, 6 mo (RCT)	0.00 [-0.14, 0.14]	—
Courcoulos 2017, 6 mo (RCT)	—	7.5 [NR]
Courcoulos 2017, 12 mo (RCT)	—	6.40 [NR]
ESG vs Lifestyle		
Ahmed 2019, 6 mo (RCT)		0.13 [0.02, 0.231][c]
Sullivan 2017, 6 mo (RCT)	-0.03 [-0.9, 0.04]	—
Sullivan 2017, 12 mo (RCT)	-0.03 [-0.11, 0.05]	2.9 [1.6, 4.2]
AspireAssist vs Lifestyle		
Thompson 2017, 12 mo (RCT)	-0.14 [NR]	—
ESG vs LSG		
Benais 2020, 12 mo (Obs)	-7.7 [-11.0, -4.8][b]	
Fiorillo 2020, 6 mo (Obs)	—	1.00 [-8.6, 10.64]
Sadek 2017, 6 mo (Obs)	—	7.9 [NR]

Notes. [a]Only among those with type 2 diabetes and baseline HbA1c >7.5%. [b]Mean difference percent change from baseline. [c]Risk difference (different between percent reporting high QOL).
Abbreviations. ESG=endoscopic sleeve gastroplasty; IGB=intragastric balloon; LSG=laparoscopic sleeve gastrectomy.

Hemoglobin A1c (Table 1)

IGB versus Lifestyle

Two studies reported changes in HbA1c after IGB.[22,25] These studies found no significant differences in HbA1c after IGB compared to lifestyle.

ESG versus Lifestyle

One study reported changes in HbA1c after ESG compared to lifestyle.[31] At both 6 and 12 months, there was no significant improvement in HbA1c compared to lifestyle therapy.

AspireAssist versus Lifestyle

One study reported changes in HbA1c after AspireAssist compared to lifestyle.[39] This study reported a 12-month improvement in HbA1c 0.14 mg/dL greater after aspiration therapy compared to lifestyle, but statistical significance could not be calculated.

ESG versus LSG

One study reported changes in HbA1c after ESG compared to LSG.[37] This study reported significantly greater mean percent decrease in HbA1c after ESG compared to LSG.

KEY QUESTION 2: What are the comparative harms of endoscopic bariatric interventions versus lifestyle interventions or bariatric surgery?

Reporting of details of procedural adverse events was inconsistent across studies, limiting interpretation of relative harm when comparing techniques.

Total Complications

A total of 12 studies reported total complication rates, defined as any complication in any patient (Figure 10, Table 2).[20,22,25,26,28,29,31-34,36,39] One randomized trial comparing AspireAssist to lifestyle reported statistically significantly fewer complication rates with lifestyle therapy.[39] Five randomized trials looking at IGB versus lifestyle all demonstrated statistically significantly fewer complications with lifestyle therapy.[20,22,25,26,44] Two studies comparing ESG versus lifestyle found significantly fewer complication rates with lifestyle therapy.[29,31] There were 4 observational studies focusing on ESG compared to LSG.[32-34,36] Three of these studies reported no difference in complications between ESG and LSG, while 1 reported significantly higher rates of complications with ESG compared to LSG. A total of 2 case series reported total complication rates after IGB of 5.9% and 14.3%, respectively.[45,46] One study reported complication rates after IGB in terms of Clavien-Dindo classification, reporting an 89.3% rate of Grade 1 complications, 10% rate of grade 2 complications, and 0.7% rate of grade 3 complications.[47] Another case series reported major complication rates of 0.83% with IGB.[48] No large volume case series reported total complication rates after ESG or AspireAssist.

A total of 4 studies reported total complication rates at 12 months.[29,31,32,39] The 3 studies comparing intervention to lifestyle, ESG and AspireAssist, all reported significantly higher complication rates with intervention compared to lifestyle.[29,31,39] The 1 study comparing ESG to LSG noted significantly higher complication rates with LSG compared to ESG.[32]

30-day Readmissions

The 1 study comparing intervention versus lifestyle therapy that assessed readmissions between groups noted higher 30-day readmission rates with IGB placement compared to lifestyle.[22]

A total of 3 studies compared 30-day readmissions between ESG and LSG, and none found significant differences in 30-day readmissions between the groups.

30-day Reinterventions

One study reported 30-day reintervention rates comparing IGB to lifestyle, reporting no differences. However, there is low confidence in this finding given the number of patients requiring premature balloon removal noted in other studies.[40] One study of AspireAssist reported that there was 1 reintervention out of a trial of 137 patients who received AspireAssist therapy due to a skin port malfunction.[49] Two studies compared 30-day reintervention rates between ESG and LSG, 1 noting no difference between the groups and the other noting fewer 30-day

reinterventions amongst ESG compared to LSG.[32,36] One case series reported a 30-day reintervention rate of 2.4%.[50]

Abdominal Pain

Four studies compared patient-reporting of abdominal pain between IGB and lifestyle.[20,22,27,40] Three studies noted significantly higher reporting of abdominal pain among IGB patients compared to lifestyle, while the third reported no abdominal pain among its cohort. One study compared patient reporting of abdominal pain between AspireAssist and lifestyle therapy, noting a higher rate of abdominal pain among patients receiving aspiration therapy compared to lifestyle. No studies compared abdominal pain reporting after ESG to LSG. One case series reported a 5.29% incidence of abdominal pain after IGB.[46]

Gastric Ulceration

A total of 3 studies compared rates of gastric ulceration between IGB and lifestyle,[22,28,49] all reporting significantly higher rates among IGB patients compared to lifestyle. One study compared rates of gastric ulceration in ESG patients to lifestyle, also noting higher rates with intervention.[51] No studies reported rates of gastric ulceration compared to LSG or with aspiration therapy. Two case series reported rates of gastric ulceration after IGB placement as 0.82% and 0.9%, respectively.[45,46]

Bleeding

One study reported higher rates of bleeding after IGB compared to lifestyle, although not statistically significant.[22] One study reported significantly higher rates of bleeding after ESG compared to lifestyle.[31] One study reported bleeding rates after aspiration therapy, finding no significantly different rates of bleeding amongst aspiration therapy compared to lifestyle.[52] Three studies compared bleeding rates between ESG and LSG, all finding no significantly different rates of bleeding between interventions.[34-36] Two case series reported rates of bleeding after IGB placement as 0.01% and 0.6%, respectively.[45,53] One case series reported bleeding rates of ESG as 0.7%.[50]

Gastroesophageal Reflux Disease (GERD)

One study compared GERD rates between IGB and lifestyle, finding significantly higher rates of GERD after IGB.[20] One study compared GERD rates between ESG and lifestyle, finding no significant differences between interventions.[31] A total of 2 studies compared rates of GERD between ESG and LSG, 1 finding no significant difference while another found less GERD after ESG compared to LSG.[34,36] One case series reported a rate of GERD after IGB placement of 0.82%.[46]

Nausea

Four studies compared nausea rates between IGB and lifestyle, finding significantly higher rates of nausea after IGB.[20,22,25,27] One study compared nausea rates between ESG and lifestyle, finding significantly higher rates of nausea after ESG.[31] One case series reported a rate of nausea after IGB placement of 63%.[46] One additional case series reported nausea rates after ESG as 92.4%.[50]

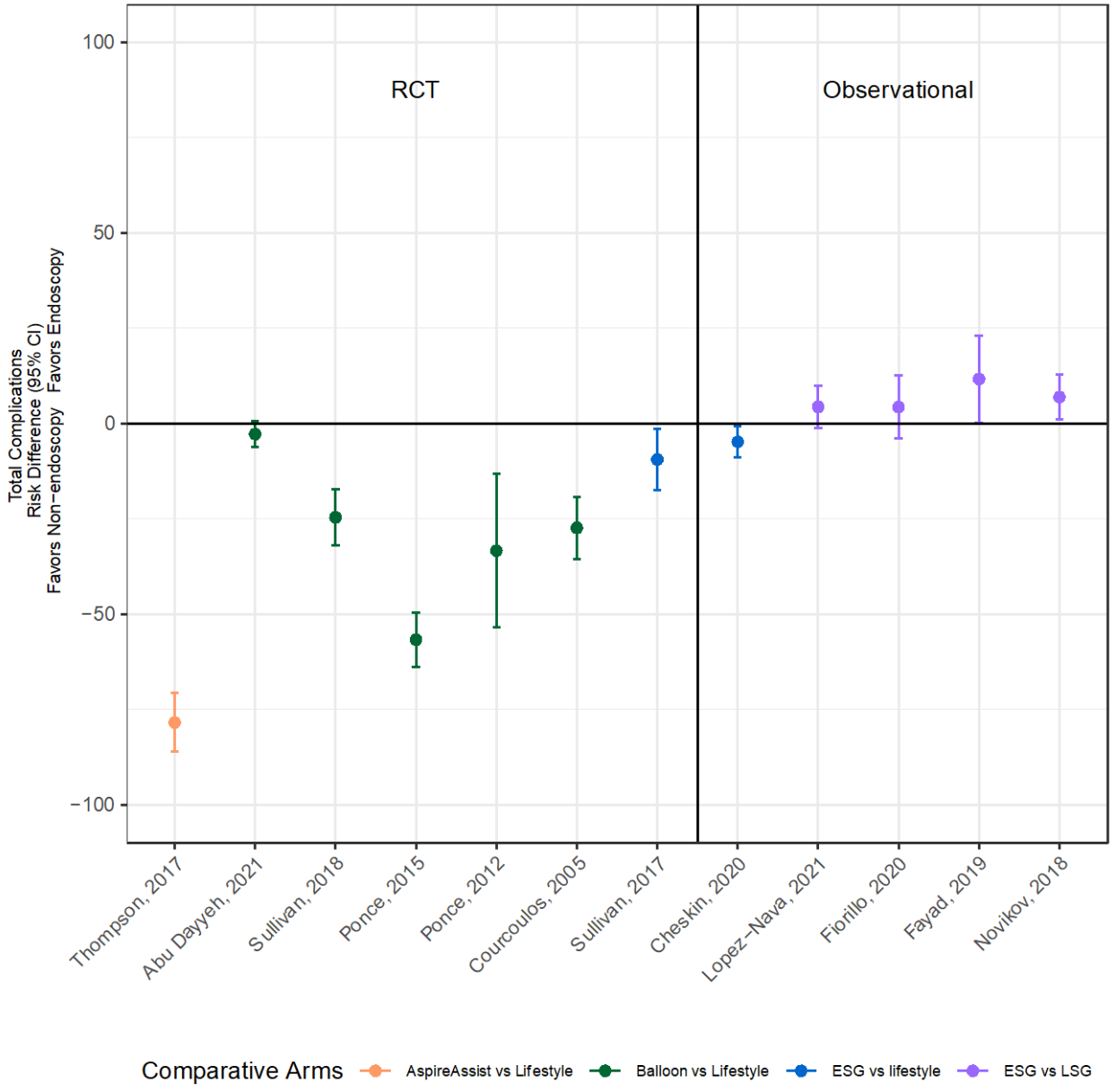
Vomiting

Four studies compared vomiting rates between IGB and lifestyle, finding significantly higher rates of vomiting after IGB.[20,22,25,27] One study compared vomiting rates between ESG and lifestyle, finding significantly higher rates of vomiting after ESG.[31] One study compared vomiting rates after AspireAssist compared to lifestyle, finding significantly higher rates after AspireAssist.[52] A total of 2 studies compared vomiting rates between ESG and LSG, one finding significantly higher rates after ESG and another finding no significant difference.[32,36] One case series reported vomiting rates after IGB placement as 31%.[46]

Dehydration

Four studies compared dehydration rates between IGB and lifestyle therapy, 2 finding significantly higher rates of dehydration after IGB while the other 2 found no significant difference.[20,22,25,27] One study compared dehydration rates after ESG versus lifestyle therapy, finding no significant difference in rates.[29] One study compared dehydration rates after ESG versus LSG, finding no significant difference.[36] Two case series reported rates of dehydration after IGB placement of 0.07% and 0.2%, respectively.[45,46]

Figure 10. Total Complications for Bariatric Endoscopic Procedures Compared to Lifestyle or LSG



Abbreviations. %TBWL=mean percent total body weight loss; ESG=endoscopic sleeve gastroplasty; LAGB=laparoscopic adjustable gastric banding; LSG=laparoscopic sleeve gastrectomy.

Table 2. Adverse Events for Bariatric Endoscopic Procedures as Compared to Lifestyle or Surgery

Study, Year *Design*	Total Complication	30-day Readmission	30-day Reintervention	Nausea	Vomiting	Dehydration	Abdominal Pain	Gastric Ulceration	Bleeding	GERD
IGB vs Lifestyle										
Moore 2019 *Case series*	14.3%			63%	31%	0.07%	5.29%	0.82%		0.82%
Sander 2017 *Case series*									0.01%	
Mathus-Vliegen 2015 *Case series*	5.9%		0.2%			0.2%		0.9%	0.6%	
Sullivan 2018 *RCT*	Risk Diff (CI) 0.25 (0.17, 0.32)			0.38 (0.29, 0.46)	0.07 (0.01, 0.14)	-0.01 (-0.02, 0.01)	0.49 (0.41, 0.58)	0.01 (0, 0.01)	0.06 (0.03, 0.09)	
Courcoulos 2017 *RCT*	0.27 (0.19, 0.35)	7.5		0.82 (0.75, 0.88)	0.70 (0.62, 0.78)	0.14 (0.09, 0.2)	0.54 (0.45, 0.62)			0.25 (0.17, 0.33)
Abu Dayyeh 2021 *RCT*	0.03 (0, 0.06)		0.00 (0, 0)	0.90 (0.86, 0.95)	0.71 (0.65, 0.78)	0.02 (0, 0.04)	0.56 (0.49, 0.63)	0.02 (0, 0.04)		
Ponce 2012 *RCT*	0.33 (0.13, 0.53)									
Pone 2015 *RCT*	0.57 (0.5, 0.64)							0.35 (0.28, 0.42)		
Fuller 2013 *RCT*				0.72 (0.55, 0.89)	0.69 (0.51, 0.86)	0.26 (0.1, 0.41)	0.56 (0.37, 0.74)			
ESG vs Lifestyle										
Alqahtani 2019 *Case series*		2.4%		92.4%					0.7%	

Sullivan 2017 *RCT*	0.09 (0.01, 0.17)			0.14 (0.07, 0.21)	0.19 (0.13, 0.24)			0.01 (0, 0.01)	0.04 (-0.02, 0.09)
Cheskin 2020 *Observ.*	0.05 (0.01, 0.09)					0.01 (-0.01, 0.03)	0.03 (0, 0.06)		
AspireAssist vs Lifestyle									
Thompson 2017 *RCT*	0.78 (0.71, 0.86)		0.01 (-0.01, 0.03)		0.17 (0.1, 0.24)		0.38 (0.29, 0.47)	0.02 (-0.01, 0.04)	
ESG vs LSG									
Fayad 2019 *Observ.*	-0.12 (-0.23, 0)	-0.06 (-0.18, 0.07)	0.00 (0, 0)		0.01 (0.01, 0.16)	-0.01 (-0.04, 0.01)		-0.03 (-0.07, 0.01)	-0.13 (-0.22, -0.03)
Fiorillo 2020 *Observ.*	-0.04 (-0.13, 0.04)	-0.04 (-0.13, 0.04)						-0.04 (-0.13, 0.04)	-0.30 (-0.49, -0.12)
Lopez-Nava 2021 *Observ.*	-0.04 (-0.1, 0.01)							-0.04 (-0.1, 0.01)	
Novikov 2018 *Observ.*	-0.07 (-0.13, -0.01)	-0.02 (-0.04, 0.01)	-0.04 (-0.09, -0.01)		-0.01 (-0.02, 0.01)				

Note. Data are presented as mean difference between comparative arms when appropriate, where positive values favor endoscopic therapy and negative values favor comparative arm. For case series, complication data are presented in percentages.
Abbreviations. ESG=endoscopic sleeve gastroplasty; IGB=intragastric balloon; LSG=laparoscopic sleeve gastrectomy.

KEY QUESTION 3: Do the comparative effectiveness and/or harms vary by patient or intervention characteristics (*ie*, age, BMI, type intragastric balloon, gastroplasty technique, *etc*)?

Study designs and procedures varied considerably, making the ability to compare effectiveness and harm of interventions based on patient characteristics or procedural technique limited. For all the studies included in this review, factors such as baseline age or BMI were not variables that were prospectively assessed or reported in terms of their association with clinical outcomes.

Intragastric Balloon

There were 7 RCTs with detailed demographic and pre-procedural data available for review. Four studies examined the Orbera intragastric balloon[13,20,38,54] and 1 the Obalon IGB[55] against lifestyle modification. Two studies investigated the Reshape dual intragastric balloon.[26,28] One study investigated the Spatz adjustable balloon.[26] There was no direct comparison between the Orbera and Obalon; therefore, conclusions about which type of IGB is more effective based on these 3 trials are limited.

We identified 1 small comparative study looking at the BioEnterics Intragastric Balloon against the Spatz Adjustable Balloon.[56] This single center experience of 20 patients showed equivocal differences in weight loss at 6 months (20kg for both) and adverse events rate. However, given the small sample size, no conclusions can be drawn. Two small observational studies assessed the effects of IGB on liver stiffness, function, and fibrosis in patients with nonalcoholic fatty liver disease (NAFLD), finding significant improvements in liver abnormalities in patients with this condition who undergo IGB placement.[57,58]

Endoscopic Sleeve Gastroplasty

There were multiple cohort studies comparing ESG to LSG.[32-34,36,37] Across all studies, the mean age was similar, ranging from 40-48 years. There were notable differences in baseline characteristics for 3 studies.[32,34,36] In the study by Novikov et al,[32] LSG patients had baseline higher BMIs (47.2 vs 38.6, respectively) and a higher percentage of patients had diabetes (20.5% vs 3.7%) compared to ESG patients. In 3 observational studies,[32,34,36] LSG patients also had significantly higher rates of hypertension. These studies demonstrate that patients with higher BMI with or without metabolic syndrome are more likely to get bariatric surgery overall, but no conclusion can be drawn regarding whether higher BMI or metabolic syndrome affects percent weight loss.

Aspiration Therapy

There are 2 RCTs evaluating AspireAssist to lifestyle with no significant baseline differences.[39,41]

High-quality randomized trials are necessary to assess these key questions in order to optimize patient selection for various bariatric therapies.

CERTAINTY OF EVIDENCE

Our assessments of the certainty of evidence, using the GRADE Framework, are presented in Table 3. In making these determinations, we factored in our assessments of risk of bias for the

studies when judging the degree of study limitations. We considered all the studies to satisfy the directness domain, as all studies measured weight loss, QOL, a metabolic outcome, or complications in standard ways. We considered the consistency and precision domains in the context of the conclusion about each outcome. As an example, for the conclusion that %TBWL is greater in patients treated with an IGB than with lifestyle therapy, we considered the results across studies as consistent and precise if they all had the same finding – that weight loss was significantly greater in patients treated with intragastric balloon therapy – even if the studies found values of %TBWL favoring balloon therapy between 4% and 12%. We did this because we judged the practice-relevant decision was "will this therapy result in greater weight loss?" and not on the precise amount of weight loss. Also, in studies where the comparison was lifestyle therapy, we drew on the large body of literature about lifestyle therapy for weight loss to conclude that complications like reintervention, bleeding, and gastric ulceration can safely be assumed to be negligible, such that the presence of any of these in the intervention groups receiving balloon therapy, gastric sleeve therapy, *etc*, can be more strongly attributed to the intervention. Likewise, the limited effectiveness of lifestyle therapies to yield sustained weight loss increases our certainty that statistically significant benefits favoring an interventional therapy are likely to be causal.

We judged 7 conclusions as being high certainty of evidence, and all were in comparisons between endoscopic interventions and lifestyle therapies: 1) IGB achieves greater %TBWL than lifestyle therapy at 6 and 12 months; 2) IGB achieves more %EBWL than lifestyle therapy at 6 months; 3) ESG achieves more %TBWL than lifestyle therapy at 6 months; and 4) AspireAssist, IGB, and ESG each have greater total complications than lifestyle therapy.

Table 3. GRADE Certainty of Evidence

Outcome	Study Limitations	Consistency	Directness	Precision	Certainty of Evidence
%TBWL					
At 6 months					
IBG > Lifestyle	RCT: No serious limitations Unmatched observational studies: Serious	Consistent	Direct	Precise	High
ESG > Lifestyle	Matched observational studies: Serious Unmatched observational studies: Serious	Consistent	Direct	Imprecise	Low
ESG < LSG	Matched observational studies: Serious Unmatched observational studies: Serious	Consistent	Direct	Precise	Low
At 12 months					
AspireAssist > Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	Moderate
AspireAssist < RYGB	Unmatched observational studies: Serious limitations	N/A	Direct	Precise	Low
IGB > Lifestyle	RCT: No serious limitations	Consistent	Direct	Precise	High

Outcome	Study Limitations	Consistency	Directness	Precision	Certainty of Evidence
	Unmatched observational studies: Serious limitations				
ESG > Lifestyle	RCT: No serious limitations	Consistent	Direct	Precise	High
ESG < LSG	Unmatched observational studies: Serious limitations	Consistent	Direct	Precise	Low
%EBWL					
At 6 months					
IGB > Lifestyle	RCT: No serious limitations	Consistent	Direct	Precise	High
ESG > Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	Moderate
ESG < LSG	Matched observational studies: Serious limitations	N/A	Direct	Precise	Low
At 12 months					
AspireAssist > Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	Moderate
AspireAssist < RYGB	Unmatched observational studies: Serious limitations	N/A	Direct	Precise	Low
IGB > Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	Moderate
ESG > Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	Moderate
HbA1C					
At 6 months					
IGB = Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	Moderate
ESG = Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	Moderate
AspireAssist = Lifestyle	RCT: Very serious limitations	N/A	Direct	N/A	Very low
Quality of Life					
At 12 months					
ESG > Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	Low
ESG = LSG	Unmatched observational studies: Serious limitations	N/A	Direct	Imprecise	Very Low
Total Complications					
At 6 months					
AspireAssist > Lifestyle	RCT: No serious limitations	N/A	Direct	Precise	High
IGB > Lifestyle	RCT: No serious limitations	Consistent	Direct	Precise	High
ESG > Lifestyle	RCT: No serious limitations	Consistent	Direct	Precise	High
ESG = LSG	Matched observational studies: Serious limitations Unmatched observational studies: Serious limitations	Consistent	Direct	Precise	Low

Abbreviations. ESG=endoscopic sleeve gastroplasty; IGB=intragastric balloon; LSG=laparoscopic sleeve gastrectomy; RYGB=Roux-en-Y gastric bypass.

DISCUSSION

SUMMARY OF EVIDENCE BY KEY QUESTION

Key Question 1

Treatment with IGBs was associated with significantly more weight loss compared to lifestyle therapy at multiple short- and intermediate-term follow-up time points (6 and 12 months). These results were consistent across RCTs and observational studies. Treatment with ESG was associated with significantly more weight loss compared to lifestyle therapy, again at 6- and 12-months follow-up. Treatment with ESG was associated with less weight loss than LSG; this conclusion is based solely on observational studies, although results are consistent. Treatment with the AspireAssist was associated with more weight loss than lifestyle therapy in 1 RCT. There was insufficient evidence on associations between treatments and QOL or HbA1C measures to reach conclusions. There are fewer studies assessing the durability of weight loss with endoscopic therapies, such as at 5 years or even 10 years following the intervention, than exist for some established bariatric surgeries (such as gastric bypass). One study by Chan et al compared IGB to sibutramine, a now discontinued weight loss medication. This RCT found no difference between IGB and sibutramine weight loss at 10 years.[59]

Key Question 2

All studies comparing endoscopic bariatric therapy to lifestyle reported more total complications and 30-day readmission or re-intervention rates in the intervention arm, which is expected given these patients underwent an invasive intervention. There were no or borderline statistically significant differences in total complications between patients treated with LSG compared to ESG, although all studies reported more complications with LSG.

Key Question 3

Regarding demographic or interventional factors that improve weight loss outcomes or increase risk for adverse events, there was insufficient evidence to answer this question. It is possible that certain patient variables may contribute to more profound weight loss post-therapy. A multicenter study asserted that younger patients may have more profound weight loss 1 year after gastric plications.[60] This study was not included in this review because the plications were performed with the RESTORe suturing system, which is no longer widely used. However, some have speculated that younger age at the time of intervention may allow for shortened recovery and quicker introduction of exercise back into the lifestyle regimen post-therapy. Higher initial BMI may be associated with more profound weight loss after intervention; however, it is unclear if this would translate to a substantial difference in %TBWL. Patients with underlying gastric motility disorders are poorer candidates for endoscopic therapy given higher complication rates of nausea, vomiting, and oral intolerance due to potentiating delayed gastric emptying with ESG or IGB therapy.[21]

LIMITATIONS

Publication Bias

In the few places where we were able to statistically test for the possibility of publication bias, no such evidence was found. It is possible, however, that the tests employed were underpowered in

the present analyses, as is commonly the case, and the large *p*-values produced by the tests are suggestive of low statistical power. Nevertheless, we feel it is unlikely that there exist high-quality randomized trials or comparative observational studies of endoscopic bariatric therapies compared to surgical or pharmacologic therapies that were not identified and similarly escaped detection by other experts in this field. On the other hand, it is likely that a large volume of case series on endoscopic bariatric therapies from individual practices and institutions exists but has not been published, especially as endoscopic bariatric therapies are often paid for out of pocket, and the available literature likely represents only a small fraction of what could have been known using case series. The decision to exclude case series was due to concerns about limited follow-up and single-institution bias present in studies of this type.

Study Quality

The RCTs were judged to have low risk of bias for outcomes such as weight loss, HbA1c, QOL, and complications. True blinding of participants is difficult with bariatric interventions, and even with a high-quality sham swallowable balloon protocol, it is likely patients were able to feel if they were given an IGB or placebo. Additionally, blinding of outcome assessment was rarely discussed, and it is unclear how weight was reported; it is also unlikely participants could remain blinded to changes in their weight. Incomplete outcome data remains a difficult challenge in bariatric studies, as was frequently seen in these RCTs with suboptimal long-term follow-up. The observational studies were judged to have moderate risk of bias due to their non-random assignment of treatments, which increases risk of procedure selection bias. Many of the observational studies did not state how patients were directed towards either endoscopic or surgical bariatric interventions, causing a risk of selection bias. However, of these studies, 4 used propensity matching to mitigate selection bias, which corresponded to a reduction in the rating of this risk from high to moderate.

Methodological Inconsistency

Included studies compared IGB to lifestyle therapy, ESG to lifestyle therapy, ESG to LSG, ESG to AGB, AspireAssist to lifestyle therapy, and AspireAssist to RYGB. Of these, only IGB versus lifestyle, ESG versus lifestyle, ESG versus LSG, and AspireAssist versus lifestyle were examined in multiple studies. Although we evaluated each comparison group separately, there were remaining inconsistencies among studies within comparison groups. For example, studies varied in choice of intragastric balloon (Obalon, Orbera, Reshape, Spatz, and Ellipse were all used); balloon placement (some balloons were endoscopically placed, whereas others were swallowable capsules); and, in the case of ESG, some procedures were traditional ESG whereas others were the Primary Obesity Surgery Endolumina (POSE) method. Additionally, lifestyle therapy represents a wide range of interventions, from providing patients with reading regarding healthy lifestyle choices, to scheduled meetings with registered dieticians, physical therapists, and psychologists.

Patient population such as age, BMI, and gender were largely similar among intervention and control groups. However, especially in endoscopic versus surgical review studies, the patient population undergoing surgery tended to have more significant metabolic comorbidities, such as higher rates of diabetes, hypertension, and super obesity, introducing heterogeneity into these comparisons in both outcomes and adverse events. This phenomenon was seen in nearly every identified endoscopic versus surgery study.

Although obesity intervention outcomes, such as weight loss and HbA1c, are largely standardized, adverse event reporting appeared more inconsistent. Multiple articles reported no adverse events among their intervention cohorts, which is possibly due to a true lack of adverse events or a study-specific definition of threshold of adverse event severity. Other studies had lower thresholds for adverse event reporting but may have had differing definitions of adverse events such as dehydration, abdominal pain, and dyspepsia.

Applicability

No studies were specific to VA populations. The applicability of these results to VA populations may depend on both the similarity of the patients studied in the trials to VA patients as well as the experience of the gastroenterologists performing endoscopic bariatric therapies in the examined studies compared to VA team experience. Additionally, management of bariatric patients requires extensive multidisciplinary care and follow-up, as often represented by the control group of lifestyle treatment. However, the benefits of endoscopic bariatric therapies may still be realized or even amplified given the population health differences among the general population in comparison to the VA, as the VA population has greater burden of comorbidities than the general population. Further studies are warranted to examine efficacy of endoscopic bariatric therapies in the VA system. Endoscopic bariatric procedures, though still representing a small fraction of all bariatric procedures performed in the US, are becoming more widely adopted and studied, which will likely translate to the VA setting.

FUTURE RESEARCH

The history of weight loss interventions is one of innovation and dissemination prior to evaluation. Vertical banded gastroplasty, prior versions of the gastric balloon, and the combination medication of fenfluramine and phentermine ("Fen-Phen") are all examples of interventions developed and widely used before sufficient studies had been done to establish their risk-benefit profile. These interventions have since been removed following research showing the benefit not to be worth the risk. It would behoove the VA to not repeat this history, and to adequately assess new interventions before they are made widely available. Several research gaps are highlighted below.

First, a majority of the endoscopic studies have follow-up timelines that terminate between the 1- to 2-year mark. There are 2 studies at present with follow up of >4 years.[52,61] Compared to the existing literature on bariatric surgeries, with some reporting follow-up data spanning past a decade, these novel endoscopic therapies lack long-term data. Studies are necessary to firmly establish the durability of weight loss following endoscopic therapy including rates of repeat or alternative endoscopic or surgical interventions due to weight recidivism.

Second, there are no high-quality RCTs comparing endoscopic bariatric procedures to surgery. We identified 3 propensity-matched trials comparing ESG to surgical procedures, mostly LSG.[29,34,36] We recognize that performing such studies has logistical limitations, but these head-to-head trials are essential. Currently, bariatric surgery is indicated per guidelines for patients with BMI >35 with at least 1 comorbid condition or BMI > 40. However, given the millions of patients who qualify under these parameters and the limited number of bariatric surgeons, endoscopic therapies could be an alternative. Trials enrolling patients with the above BMI criteria to compare effectiveness of endoscopic therapy to surgery also need to assess impact on comorbid conditions, along with long-term cost benefits. Financial impacts on closed health care

systems, such as the VA or Kaiser, offer an important opportunity for comprehensive assessments of long-term care costs related to obesity treatments.

Third, additional direct endoscopic and surgical comparisons of post-procedure complications and adverse events are also necessary to improve patient selection for certain procedures. For example, RCTs are scarce in the "super obese" population (BMI >50), who have elevated risk profiles given their baseline comorbidities and anesthesia requirements. These patients theoretically would benefit more from the aggressive mean percent weight loss provided by the surgical interventions, but greater understanding is needed of the perioperative risks and adverse events associated with surgery compared to IGB or ESG as primary therapy to better weigh risks against the extent of potential weight loss.

Additional dedicated studies are required in other subpopulations of patients:

A. *Class I Obesity*. Patients with class I obesity (BMI 30-35) are not current candidates for bariatric surgery. However, data suggest early targeted intervention prior to the development of comorbid conditions should be a goal both for morbidity prevention and decreasing health care expenditures. In these patients, comparative trials of the various endoscopic options as well as medications will be valuable.

B. *Underserved populations*. Given the financial limitations with endoscopic bariatric therapies, largely due to lack of insurance coverage, the studied patient populations for most trials are primarily privately insured and white, as seen in Appendix G. More research is needed on the effectiveness and risks of all bariatric interventions in underserved and/or underrepresented populations.

C. *Patients with obesity-related comorbid conditions such as diabetes, hypertension, non-alcoholic fatty liver disease*. Sharaiha et al demonstrated significant reduction in hypertension, lipid panel, ALT as marker for fatty liver, and HbA1c at the 12-month timepoint following ESG, with sustained results up to 5 years post-procedure.[61] Other available evidence suggests that that as little as 10% TBWL improves metabolic factors including markers for fatty liver disease.[62,63] Studies are required to distinguish which endoscopic bariatric therapies can achieve these outcomes.

D. *VA patients*. There are currently no studies evaluating endoscopic therapies in the VA population.

E. *Bridging therapy*. We did not include studies assessing the efficacy of endoscopic bariatric therapy as a bridge to definitive treatment. Studies have described using IGB as a bridge to bariatric surgery, and it remains to be determined if this use reduces cost or adverse events.

Fourth, there are limited data evaluating the effectiveness of medications on weight loss when combined with endoscopic therapy. A recently published clinical trial demonstrated optimistic results with semaglutide use in patients, with obesity resulting 15% mean TBWL.[64] There is a single study, which was excluded from our analysis due to lack of a non-endoscopic comparative arm, which demonstrated enhanced weight loss of +4% TBWL at the 4- and 7-month marks when ESG was combined with liraglutide as compared to ESG alone.[65] Prior to any invasive procedure including endoscopy, patients should be trialed on pharmacologic management if tolerated. Many patients therefore will present for endoscopic therapies while on medications

such as phentermine, orlistat, liraglutide, or semaglutide. Further studies evaluating efficacy of combination therapy are needed to assist in management of patients with obesity.

Fifth, because there are multiple bariatric endoscopy devices in development for future trials or FDA approval, standardization of primary outcomes (%TBWL, % EBWL, percentage of patients achieving >10% EBWL, percentage of patients achieving >25% EBWL, *etc*) would be beneficial to evaluate efficacy across studies. The same consideration arises when evaluating secondary outcomes associated with resolution of comorbid conditions.

CONCLUSIONS

In summary, the endoscopic therapies IGB, ESG, and AspireAssist are associated with greater short- and intermediate-term weight loss in patients with obesity compared to lifestyle management alone. However, various complications are also more likely in patients treated with endoscopic therapies than with lifestyle management. No long-term studies of weight loss have been published. The degree of weight loss with endoscopic therapies is likely less than more invasive surgical interventions, but with fewer adverse events. The field of endoscopic bariatric therapy continues to innovate and expand, with multiple devices in the pipeline for FDA approval. The MERIT trial, a multicenter randomized trial evaluating ESG vs lifestyle, reported initial 1-year follow-up data in late 2021. As the field continues to grow, future research should include more robust RCTs or well-designed prospective matched studies with adequate power and follow-up to assess long-term weight loss and the effects on obesity-related comorbid conditions.

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APPENDIX A. SEARCH STRATEGIES

PubMed
((("Aspiration therapy"[Title/Abstract] OR AspireAssist[Title/Abstract] OR "Intragastric balloon"[Title/Abstract] OR "endoscopic sleeve gastroplasty"[Title/Abstract] OR "endoscopic sleeve"[Title/Abstract] OR "Endoscopic gastroplasty"[Title/Abstract] OR "primary obesity surgery endoluminal"[Title/Abstract] OR "Endoscopic gastric plication"[Title/Abstract] OR "gastric volume reduction"[Title/Abstract] OR OverStitch[Title/Abstract] OR ORBERA[Title/Abstract] OR Obalon[Title/Abstract] OR "Gastric Balloon"[Title/Abstract] OR Gastrostomy[Title/Abstract] OR Gastroplasty[Title/Abstract] OR "Collis Gastroplasty"[Title/Abstract] OR "Vertical Banded Gastroplasty"[Title/Abstract] OR "Gastrostomies"[Title/Abstract] OR "Gastric Bubble"[Title/Abstract] OR IGB[Title/Abstract] OR ESG [Title/Abstract])) OR ((Gastric Balloon [MeSH] OR Gastrostomy [MeSH] OR Gastroplasty [MeSH]))) AND ((("metabolic Surgery"[Title/Abstract] OR "Bariatric Surgery"[Title/Abstract] OR "Bariatric Surgical Procedure"[Title/Abstract] OR "Stomach Stapling"[Title/Abstract] OR "gastric bypass"[Title/Abstract] OR MGB[Title/Abstract] OR OAGB[Title/Abstract] OR lifestyle[Title/Abstract] OR "life style"[Title/Abstract] OR lifestyles[Title/Abstract] OR "life styles"[Title/Abstract] OR “Lifestyle therapy”[Title/Abstract])) OR (("Bariatric Surgery"[Mesh] OR "gastric bypass"[Mesh] OR Life Style[MESH])))

Filters: from 2014/1/1 - 2021/12/07 [1599]

AND

“endoscopic bariatric therapy”[Title/Abstract]
Filters: from 2014/1/1 – 2022/01/23 [45]

Embase
('aspiration therapy':ab,ti OR aspireassist:ab,ti OR 'intragastric balloon':ab,ti OR 'endoscopic sleeve gastroplasty':ab,ti OR 'endoscopic sleeve':ab,ti OR 'endoscopic gastroplasty':ab,ti OR 'primary obesity surgery endoluminal':ab,ti OR 'endoscopic gastric plication':ab,ti OR 'gastric volume reduction':ab,ti OR overstitch:ab,ti OR orbera:ab,ti OR obalon:ab,ti OR 'gastric balloon':ab,ti OR gastrostomy:ab,ti OR gastroplasty:ab,ti OR 'collis gastroplasty':ab,ti OR 'vertical banded gastroplasty':ab,ti OR 'gastrostomies':ab,ti OR 'gastric bubble':ab,ti OR igb:ab,ti OR esg:ab,ti OR (“gastric balloon”/exp) OR 'gastrostomy'/exp OR 'gastroplasty'/exp) AND ('metabolic surgery':ab,ti OR 'bariatric surgery':ab,ti OR 'bariatric surgical procedure':ab,ti OR 'stomach stapling':ab,ti OR 'gastric bypass':ab,ti OR mgb:ab,ti OR oagb:ab,ti OR lifestyle:ab,ti OR 'life style':ab,ti OR lifestyles:ab,ti OR 'life styles':ab,ti OR 'lifestyle therapy':ab,ti OR ‘endoscopic bariatric therapy’:ab,ti OR (('bariatric surgery'/exp OR 'gastric bypass'/exp OR “life style”/exp))

Filters: from 2014/1/1 - 2021/12/07 [1533]

AND
‘endoscopic bariatric therapy’:ab,ti
Filters: from 2014/1/1 – 2022/01/23 [36]

Cochrane
("Aspiration therapy" OR AspireAssist OR "Intragastric balloon" OR "endoscopic sleeve gastroplasty" OR "endoscopic sleeve" OR "Endoscopic gastroplasty" OR "primary obesity surgery endoluminal" OR "Endoscopic gastric plication" OR "gastric volume reduction" OR OverStitch OR ORBERA OR Obalon OR "Gastric Balloon" OR Gastrostomy OR Gastroplasty OR "Collis Gastroplasty" OR "Vertical Banded Gastroplasty" OR "Gastrostomies" OR "Gastric Bubble" OR IGB OR ESG) in Title Abstract Keyword OR (mh Gastroplasty OR mh Gastrostomy OR mh "Gastric Balloon") in All Text OR (mh "Bariatric Surgery" OR mh "gastric bypass" OR mh "Life Style") in All Text AND ("metabolic Surgery" OR "Bariatric Surgery" OR "Bariatric Surgical Procedure" OR "Stomach Stapling" OR "gastric bypass" OR MGB OR OAGB OR lifestyle OR "life style" OR lifestyles OR "life styles" OR "Lifestyle therapy") in Title Abstract Keyword - with Cochrane Library publication date Between Jan 2014 and Dec 1 [985]

AND
"endoscopic bariatric therapy"
Between Jan 2014 and Jan 2022 [5]

APPENDIX B. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Reviewer #	Reviewer Comment	Authors Responses
1	Are there any published or unpublished studies that we may have overlooked? Yes - Abu Dayyeh BK, Maselli DB, Rapaka B, Lavin T, Noar M, Hussan H, Chapman CG, Popov V, Jirapinyo P, Acosta A, Vargas EJ, Storm AC, Bazerbachi F, Ryou M, French M, Noria S, Molina D, Thompson CC. Adjustable intragastric balloon for treatment of obesity: a multicentre, open-label, randomised clinical trial. Lancet. 2021 Nov 27;398(10315):1965-1973. doi: 10.1016/S0140-6736(21)02394-1. Epub 2021 Nov 15. Erratum in: Lancet. 2021 Nov 27;398(10315):1964. PMID: 34793746.	We have included this article in the updated search.
2	Make sure that abbreviations are defined when first used. a. For example, ESG should be defined on page 6 before it is used on page 7	Completed.
	Page 8: The following line seems a bit awkward. "There are no studies assessing the durability of the weight loss with endoscopic therapies, such as at 5 years or even 10 years following the intervention, as does exist for some established surgical weight loss therapies (such as gastric bypass)." a. Consider rephrasing the portion “such as at 5 year or even 10 years…” It may be better to drop the “or even 10 years”. I understand that you are trying to say that surgery has data out to 10 years, but the way it is written seems awkward.	Completed.
	Page 17: there is an error: “Error!...”	Thank you for this comment; there was a technical glitch and has been corrected.
	Page 27, line 8: This statement about statistical significance is a bit confusing. Consider revising to include this information in the earlier sentences on that page. I presume the 7.9% less improvement is the result that has no confidence interval. Since the other result is presented as non-significant, I don’t think that point merits repeating.	We adapted the description of these studies to make this more clear.
	Page 28, line 47: It would help the reader if the 1 reintervention was put in the context of the overall sample size. Is this one out of 10 participants or 1 out of 100, etc.?	Fixed.
	Page 28, lines 53-60 and all of page 29: Along the same lines, the discussion of abdominal pain and other adverse events is difficult to interpret without some information about the	We agree with the comments made by the reviewer. Most of the included studies do not detail severity or symptom specifics in

Reviewer #	Reviewer Comment	Authors Responses
	overall proportion and ideally, severity of the symptoms. a. Table 2 should be called out on the prior page as this would have helped answer my question. The table would benefit from changing "Total Complications" to "Any Complication" and clarification that these are risk differences, not absolute rates of nausea, etc. b. The analysis of adverse events doesn't delve into any issues of severity or duration of these events. Many of these symptoms may be transitory as the patient adapts to the intervention. If nausea and vomiting require removal of the device, then that is much more important than a day or two of nausea immediately following the initial intervention. Even if it is not feasible to detail the severity and duration of symptoms, it would seem appropriate to acknowledge this as a limitation of the review.	regards to abdominal discomfort. Therefore we are limited in our ability to further characterize abdominal pain in our review. We have added a statement regarding limitation of interpretation on page 28 as suggested.
	Page 29, Figure 8: This is labelled as "Total Complications" but then presented as risk differences. This is a bit confusing because "Total" makes it seem like this is a count of complications, but I suspect you mean "Any Complication". As such, for the Thompson study, it would seem that almost 100% of the endoscopic group had a complication versus very few in the lifestyle group. Consider if there is a way to clarify this presentation through revision of the labels and/or adding explanatory text.	We have written a definition for total complications as a total of any complication in any patient.
	Page 37, line 6: This should read "Primary Obesity Surgery Endoluminal (POSE)"	Complete.
	Page 38, line 26: Consider revising as: "Financial impacts on closed…"	Complete.
	Page 39, line 47: The Conclusion states that endoscopic therapy is more effective than lifestyle, but has more complications. This is followed by a statement that surgery is probably more effective than endoscopy therapy but there is no mention of the increased risk of complications with surgery (ref 30). It would seem that this trade-off of risk/reward should also be clearly stated in the conclusion. This one aspect gives at least a hint of surgical bias in the presentation of the review.	We appreciate this input and have changed the sentence in conclusion to reflect the decreased relative adverse events rate of endoscopy as compared to surgery.
3	Review for VA Evidence Synthesis Program Endoscopic bariatric interventions versus lifestyle interventions or surgery for weight loss in obese patients: A systematic review and meta-analysis Overall, based on the available evidence I	On the updated search following submission, we are including the data in regards to the newly FDA-approved Spatz balloon which will include the data as suggested by the reviewer.

Reviewer #	Reviewer Comment	Authors Responses
	agree with the conclusions of the report. The report is limited by not including some of the registry studies, which for US data includes the largest number of patients and are likely more representative of clinical practice. For example, Moore RL. SOARD. 2019;15(3):417-423 included over 1300 patients from 108 practices with data collected and entered into the registry prospectively. However, I understand that the questions posed were specific to comparator groups, which is why registry data was not included. There were a few studies listed below that were not included in this analysis and there were some study populations that were reported more than once, which are outlined below. I would also highly recommend adding the data on safety included in FDA's Summary of Safety and Efficacy Data for the Spatz3 balloon, which is can be found on FDA's website (I can also provide you a PDF if you cannot find it). Although the data on non-serious adverse events wasn't included in the abstract, all of that data is included in the SSED and it would be good if that can be included in the analysis.	
	Please change all language to people first: patients with obesity instead of obese patients. This is the required terminology for most obesity and bariatric surgery related journals as well as The Obesity Society and ASMBS.	Completed.
	Page 17 lines 20-21 include a grammatical error message,	Thank you for this comment; there was a technical glitch and has been corrected.
	Citations 14, 21, and 22 are from the same study population (IGB and control groups)	These references were continuations of a similar study population, for which we only included additional data for later published studies with longer followup. We were cognizant to not double count any overlapping data.
	Citations 31 and 33 are from the same patient population for ESG	These references were continuations of a similar study population, for which we only included additional data for later published studies with longer followup. We were cognizant to not double count any overlapping data.
	Citations 27 and 34 are from the same patient population for ESG (This may or may not be an issue because the comparator groups are different)	These references had overlapping study populations but we were cognizant to not double count any overlapping data.

Reviewer #	Reviewer Comment	Authors Responses
	In table 2 and other points in the manuscript the Courcoulos 2017 study is incorrectly listed as Courcoulos 2005.	Complete.
	No studies of the ReShape balloon were included in the analysis. This balloon is no longer commercially available, but both a pilot study and randomized sham-controlled study took place in the US leading to FDA approval. The data support the use of intragastric balloons for weight loss, but would not otherwise change your conclusions.	We include FDA approved and currently available devices/techniques in this review.
	Randomized sham-controlled study design has been shown to reduce weight loss in endoscopic bariatric therapies (Swei E. The American Journal of Gastroenterology. 2021;116:S584). While this doesn't change your overall conclusions, it should be noted in your introduction and summary that this may limit the ability of this analysis to determine the full extent of efficacy since some of the studies included in this analysis were sham controlled.	We appreciate this insight and will address this in the methods.
	There are 2 randomized controlled trials for Aspire Assist. You are missing: Sullivan S. Gastroenterology. 2013;145(6):1245-1252	This title was included in our updated search but has been excluded as it is a pilot study of a later Sullivan RCT of AspireAssist patients with likely patient overlap.
	Reference 36 is not an RCT. It is a comparative analysis.	We have updated this in our study.
	Page 28 line 19, this should be reference 36	We have confirmed that this reference is appropriate
	Reference 26 is only an abstract. The full data can be seen on the FDA's Summary of Safety and Effectiveness Data report for the Spatz3 balloon, which is available publicly on line. I understand this got approval one week before completing this report. If possible this data should be included in all of the sections on AE outcomes in Key Question 2 indicating data is available for these outcomes in 3 studies.	We have added these data to our study.
	Page 28 line 46 – I don't believe this is the correct reference.	We have changed the reference to the appropriate study.
	Page 29 line 5, I believe 36 is the incorrect reference	We have changed the reference to the appropriate study.
	Page 29 line 14. There was one bleeding event in the study of reference 23. That should be noted since the rate is 0.3% compared with 0%, which actually may not reach statistical significance.	Thank you for the reference and we have adjusted the results in the manuscript.

Reviewer #	Reviewer Comment	Authors Responses
	Page 32 paragraph 2. There is a comparative analysis of Obera vs Obalon balloon: Almuh aidb A. Comparison of the efficacy and safety of the FDA-Approved Intragastric Balloon systems in a clinical setting. Gastrointestinal Endoscopy. 2020;91(6):AB222.	We excluded studies that compared endoscopic to endoscopic therapies given that this was beyond the scope of this query.
4	Very nicely done. This will be a helpful addition to the literature. Some suggestions for improvements: General - Many organizations and journals are trying to move away from the phrase "obese patients" or "obese adults" and instead use "patients with obesity." For example, in the title, would rephrase to "patients with obesity." There are numerous places in the manuscript too.	Complete.
	Terminology - Instead of "surgical bariatric therapy" would just say "bariatric surgery"; I get that you're drawing a comparison to "endoscopic bariatric therapy," but that term is awkward.	Complete.
	Are you comparing endoscopy to surgery and "lifestyle modification" only? What about pharmacologic therapy? This typically would not be considered in the same boat as behavior weight management, which typically includes dietary and physicial activity changes. Would be clear about these therapies throughout. In my mind, there are 4 therapies: behavioral weight management, pharmacologic, endoscopic, and surgery. Also, would use the term "pharmacologic" since previous obesity workgroups (e.g., Weight Management SOTA in 2015) used the terminology "pharmacologic"	We agree that pharmacotherapy is a crucial part of management. We did not find any randomized or comparative studies directly studying endoscopic methods to pharmacotherapy in our search. This is a key question that should be explored further in future research.
	Data abstraction - Who was involved in the "full group discussion"?	Phan, Shekelle, Weitzner, Gibbons, Girgis
	Exec summary Intro - Is that economic burden in the US alone?	Yes the burden is in regards to the United States alone.
	Rationale for excluding studies where similar mechanisms were compared to one another (balloon vs. balloon). Wouldn't data from those participants still be useful in a meta-analysis?	We agree that comparing similar mechanisms is valuable, as it warrants investigation in future papers. However, this was outside the scope of our paper for the purposes of TEP review.
	I like including the main outcome as % TWL as opposed to another metric such as % EWL. The first figure is excellent.	We appreciate this feedback.
	Key question 2 - "more total complications....." in which group?	Completed.
	Research gap - Can you be more specific about a "prior version of the gastric balloon." Are you referring to laparoscopic adjustable gastric	Thank you for the comments, clarification has been added to the research gaps.

Reviewer #	Reviewer Comment	Authors Responses
	banding or another type of endoscopically placed intra-gastric balloon? LAGB has not been "removed" although it is much lower in frequency than it was previously.	
	Literature flow - There is a comment that includes "Error!"	Thank you for this comment; there was a technical glitch and has been corrected.
	The interpretation of Table 1 is challenging. It's not immediately clear what the mean difference in hemoglobin and QoL represents. For QoL, presumably a higher number means QoL is higher for IGB compared to lifestyle? It's not clear if these scales are all the same. For HgbA1c diff, a higher number would presumably be bad for IBG because it would imply that post-intervention HbgA1c is higher than that of lifestyle? The interpretation is quite challenging here. Would consider just describing this in the text.	We have clarified this for the reader.
	Same with Table 2. I struggle with interpretability. Maybe it would be helpful to add a legend describing what a couple of numbers in the various cells means.	A legend has been added to help explain table values.
	The authors note that "the history of weight loss interventions is one of innovation and dissemination prior to evaluation." This seems misleading and inaccurate. Yes, there are some examples that the authors highlight. There is also a 30+ year history of a lack of D&I of evidence-based obesity treatment - including the 2 gold standard operations (lap sleeve and lap bypass) and numerous FDA-approved obesity medications such that we're severely underutilizing evidence-based obesity treatments in the U.S. I think it's totally justifiable to cite those examples (VBG, LABG?, phenteramine) as interventions within the field where evidence was lacking prior to D&I, but would not characterize the entire field of obesity treatment (meds, bariatric surgery) as fitting that description.	Thank you for this comment; the statement has been rephrased.
1	The authors are to be congratulated on this important and well-executed systematic review and meta-analysis. Given the rapid increase in obesity over the past few decades, and projected further increase in obesity, new interventions available to veterans are needed. Amongst the currently available options, bariatric surgery appears to be the most effective in reducing weight and improving metabolic comorbidities in the long term, however, its uptake is limited due to perceived surgical risks and limited access. A new class of interventions that are less invasive than	Thank you for this comment. We have included the Spatz balloon in our updated review after its approval.

Reviewer #	Reviewer Comment	Authors Responses
	surgery, endoscopic bariatric therapies (EBTs), have become available to veterans in recent years. This systematic review focuses on a few specific questions related to the efficacy of FDA-approved EBTs, looking at studies published since 2014. These include two of the four FDA-approved intragastric balloons(IGBs), Orbera and Obalon; aspiration therapy, and endoscopic gastroplasty (not approved for treatment of obesity but device approved for use). Another balloon that was approved in 2015, the Reshape balloon, currently is not available in the US. A fourth balloon, the Spatz balloon, was approved in October 2021, but data was published after this review was completed. However, the pivotal trial results were presented as an abstract in 2018-2019, and likely should have been included. The FDA submission documents were also available for review since earlier in 2021. Overall, well-executed review looking at three questions: Key Question 1: What Is the Comparative Effectiveness Of Endoscopic Bariatric Interventions Versus Lifestyle Interventions Or Bariatric Surgery? Key Question 2: What Are the Comparative Harms Of Endoscopic Bariatric Interventions Versus Lifestyle Interventions Or Bariatric Surgery? Key Question 3: Do The Comparative Effectiveness And/Or Harms Vary By Patient Or Intervention Characteristics(ie, Age, BMI, Type Intragastric Balloon, Gastroplasty Technique, etc)?	
	Given the general lack of RCTs involving EBTs, I would recommend including the recently published high quality RCT of Spatz balloon in this meta-analysis. PMID 34793746	This study has been included in our updated search.
	The authors have used overlapping data of three presentations looking at the same IGB trial population: References 14,20,21 are all presentations of data from the Orbera pivotal trial, here presented as different studies. I would argue that this may be allowed if they document complimentary data, such as reporting different adverse events, but would not use them separately to report the same outcome measure such as weight loss or nausea, for example.	These references had overlapping study populations but we were cognizant to not double count any overlapping data.
	References 1 and 12 are the same.	Thank you for catching this error. The references have been changed.
	Additionally, ref 1/12 and 30 have overlapping patients; 1/12, 30 and 43 – same.	These references had overlapping study populations but we were

Reviewer #	Reviewer Comment	Authors Responses
		cognizant to not double count any overlapping data.
	Regarding Figures 2 and 6, I am not sure why the authors decided to pool both surgery and lifestyle as comparators to EBTs. I would argue that these should be two different figures : 2a and 2b, and 6a and 6b,with lifestyle and surgery, respectively.	The data are not pooled, just displayed on the same graph to allow better visual interpretation.
	The adverse events associated with Orbera and Obalon differ widely, and one could argue that they should be analyzed separately and not pooled together. Rate of serious adverse events (SAE) with fluid-filled gastric balloons such as Spatz, Reshape and Orbera, is reported to be around 10%, while rate of SAE with Obalon(gas-filled) is 0.2%. To me, it is not clinically relevant to pool these together in the same meta-analysis. Rather, these should be discussed separately in comparison to lifestyle or surgery.	While each procedure has its own benefits and shortcomings, the scope of our review was to compare overall effects of treatment types in comparison to each other. Further studies can tease out these nuances.
	Since the approval of semaglutide, weight loss medications have become a viable option for treatment of obesity, apparently similar in efficacy to the EBTs, with its own set of adverse events, cost issues, and attrition rate. Additionally, combination of GLP-1 and GIP-agonists are pending and expected next year. Thus, weight loss medications should be included in the discussion of future directions for studies.	We agree and have included the importance of pharmacotherapy in the future directions.
	Some data from outside of the US points to a beneficial more sustained effect of EBTs in patients with lower BMIs in the overweight range. Thus, studies of early weight reduction interventions in patients who are overweight and at risk for metabolic decompensation could represent a future direction.	We agree, but aimed this review at those who qualify for procedures in the US. Future studies can address this.
	Finally, in our experience, combination therapies involving EBTs and weight loss medications may be a viable long-term option for patients unwilling to undergo surgery. We use IGB of ESG as a tool for selected patients as part of a lifelong obesity therapy with an initial weight reduction that, in turn, could positively influences lifestyle choices and allow weight stabilization in the long term.	We agree and have expanded this in our discussion.

APPENDIX C. COCHRANE RISK OF BIAS TOOL

The Cochrane Collaboration's Tool for Assessing Risk of Bias*

Domain	Support for judgment	Review authors' judgment
Selection bias		
Random sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
Performance bias		
Blinding of participants and personnel *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Detection bias		
Blinding of outcome assessment *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.
Attrition bias		
Incomplete outcome data *Assessments should be made for each main outcome (or class of outcomes).*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.
Reporting bias		
Selective reporting	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.

Other bias		
Other sources of bias	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Bias due to problems not covered elsewhere in the table.

* http://handbook.cochrane.org/ in Table 8.5.a

APPENDIX D. RISK OF BIAS IN NON-RANDOMISED STUDIES – OF INTERVENTIONS (ROBINS-I)

Bias domains included in ROBINS-I

Pre-intervention	Risk of bias assessment is mainly distinct from assessments of randomised trials
Bias due to confounding	Baseline confounding occurs when one or more prognostic variables (factors that predict the outcome of interest) also predicts the intervention received at baseline ROBINS-I can also address time-varying confounding, which occurs when individuals switch between the interventions being compared and when post-baseline prognostic factors affect the intervention received after baseline
Bias in selection of participants into the study	When exclusion of some eligible participants, or the initial follow-up time of some participants, or some outcome events is related to both intervention and outcome, there will be an association between interventions and outcome even if the effects of the interventions are identical This form of selection bias is distinct from confounding—A specific example is bias due to the inclusion of prevalent users, rather than new users, of an intervention
At intervention	Risk of bias assessment is mainly distinct from assessments of randomised trials
Bias in classification of interventions	Bias introduced by either differential or non-differential misclassification of intervention status Non-differential misclassification is unrelated to the outcome and will usually bias the estimated effect of intervention towards the null Differential misclassification occurs when misclassification of intervention status is related to the outcome or the risk of the outcome, and is likely to lead to bias
Post-intervention	Risk of bias assessment has substantial overlap with assessments of randomised trials
Bias due to deviations from intended interventions	Bias that arises when there are systematic differences between experimental intervention and comparator groups in the care provided, which represent a deviation from the intended intervention(s) Assessment of bias in this domain will depend on the type of effect of interest (either the effect of assignment to intervention or the effect of starting and adhering to intervention).
Bias due to missing data	Bias that arises when later follow-up is missing for individuals initially included and followed (such as differential loss to follow-up that is affected by prognostic factors); bias due to exclusion of individuals with missing information about intervention status or other variables such as confounders
Bias in measurement of outcomes	Bias introduced by either differential or non-differential errors in measurement of outcome data. Such bias can arise when outcome assessors are aware of intervention status, if different methods are used to assess outcomes in different intervention groups, or if measurement errors are related to intervention status or effects
Bias in selection of the reported result	Selective reporting of results in a way that depends on the findings and prevents the estimate from being included in a meta-analysis (or other synthesis)

APPENDIX E. QUALITY ASSESSMENT FOR INCLUDED RANDOMIZED CONTROLLED TRIALS

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data at 6, 12 months, longest	Selective reporting	Other sources of bias
Abu Dayyeh, 2015 [13]	Unknown risk	Unknown risk	High risk	High risk	High risk (70-75% follow up at 1 year)	Low risk	Moderate risk
Abu Dayyeh, 2019 [49]	Unknown risk	Unknown risk	High risk	High risk	Low risk	Low risk	Moderate risk
Chan, 2021 [59]	Unknown risk	Unknown risk	High risk	High risk	Moderate risk	Low risk	Low risk
Courcoulas, 2017 [20]	Low risk (Trial is FDA approved)	Unknown risk	High risk	Unknown risk for weight Unclear how weight measured Moderate risk for QOL	Low risk at 9 months (80% follow up) High risk at 12 months (75% follow up)	Low risk	Moderate risk
Fuller, 2013 [27]	Unknown risk	Unknown risk	High risk	High risk	Low risk	Low risk	Moderate risk
Gomez, 2016 [21]	Low risk (Trial is FDA approved)	Unknown risk	High risk	Unknown risk for weight Unclear how weight measured Moderate risk for QOL High risk for gastric emptying	Low risk (100% follow up)	High risk Weight is not primary endpoint of study	Moderate risk
Lee, 2012 [58]	Unknown risk	Unknown risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data at 6, 12 months, longest	Selective reporting	Other sources of bias
Mohammed, 3220 [38]	Unknown risk	Unknown risk	High risk	Moderate risk	Low risk	Low risk	Low risk
Ponce, 2013 [26]	Unknown risk	Unknown risk	Moderate risk	Moderate risk	Low risk	Low risk	Moderate risk
Ponce, 2015 [28]	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Moderate risk
Raftoupoulos, 2019 [24]	Unknown risk	Unknown risk	High risk	High risk	High risk	Low risk	Low risk
Sullivan, 2012 [41]	Unknown risk	Unknown risk	High risk	High risk	Low risk	Low risk	Low risk
Sullivan, 2017 [31]	Low risk (Trial is FDA approved)	Unknown risk	Low risk	Unknown risk for weight Unclear how weight measured Moderate risk for QOL	Low risk	Low risk	Moderate risk
Sullivan, 2018 [22]	Low risk (Trial is FDA approved)	Unknown risk	Low risk	Unknown risk for weight Unclear how weight measured Moderate risk for QOL	Los risk	Low risk	Moderate risk
Thompson, 2017 [39]	Low risk (Trial is FDA approved)	Unknown risk	High risk	Unknown risk for weight Unclear how weight measured Moderate risk for QOL	High risk	Low risk	Moderate risk

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data at 6, 12 months, longest	Selective reporting	Other sources of bias
Thompson, 2019 [52]	Low risk (Trial is FDA approved)	Unknown risk	High risk	Unknown risk for weight Unclear how weight measured Moderate risk for QOL	High risk	Low risk	Moderate risk

APPENDIX F. QUALITY ASSESSMENT FOR INCLUDED OBSERVATIONAL STUDIES

Author, year	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of reported results
Abd El Mohsen, 2017 [30]	Unknown risk	Unknown risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Abeid, 2019 [47]	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Ahmed, 2019 [42]	Moderate risk	Moderate risk	Low risk	Low risk	Low risk	High risk	Low risk
Alqahtani, 2019 [50]	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Benias, 2020 [37]	Low risk	Moderate risk	Low risk	Low risk	Unknown risk	Moderate risk	Low risk
Cheskin, 2020 [29]	Low risk	Low risk	Low risk	Low risk	High risk	Moderate risk	Low risk
Espinet Coll, 2017 [48]	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Fayad, 2019 [36]	Moderate risk	Low risk	Low risk	Low risk	High risk	Moderate risk	Low risk
Fiorillo, 2020 [34]	Low risk	High risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Lopez-Nava, 2020 [35]	Low risk	Unknown risk	Low risk	Low risk	Low risk	Low risk	Low risk
Lopez-Nava, 2021 [33]	Low risk	High risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Mathus-Vliegen, 2015 [45]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Novikov, 2018 [32]	High risk	High risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Raftopoulos, 2019 [23]	Moderate risk	Unknown risk	Low risk	Low risk	Unknown risk	Moderate risk	Low risk
Raftopoulos, 2019 [24]	Unknown risk	Unknown risk	Low risk	Low risk	Unknown risk	Moderate risk	Unknown risk
Sadek, 2017 [43]	Unknown risk	Unknown risk	Low risk	Low risk	Unknown risk	Moderate risk	Low risk
Salomone, 2021 [57]	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk

Author, year	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of reported results
Sander, 2017 [53]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Wilson, 2018 [40]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk

APPENDIX G. EVIDENCE TABLES

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop					
				ESG	Balloon	AspireAssist	RYGB	LSG	Lifestyle
Cheskin, 2020 [29]	Obs / Y	Single	Yes	n: 105 Age: 47.58 (11.97) Female: 75 (71.42) BMI: 40.50 (7.89)					n: 281 Age: 48.17 (12.18) Female: 189 (67.26) BMI: 39.85 (7.62)
Courcoulas, 2017 [20]	RCT / Y	Multi	No		n: 125 Age: 38.7 (9.37) Race White: 101 (80.8) Black: 13 (11.2) Asian: 0 Hispanic: 9 (7.2) Female: 112 (89.6) BMI: <30: 2 (1.6) 30-35: 63 (50.4) 35-40: 56 (44.8) >40: 4 (3.2) EBW: 36# (11) DM: 9 (7) HTN: 33 (26)				n: 130 Age: 40.8 (9.61) Race White: 106 (81.5) Black: 15 (11.5) Asian: 0 Hispanic: 7 (5.4) Female: 117 (90.0) BMI: <30: 1 (0.8) 30-35: 57 (43.8) 35-40: 70 (53.8) >40: 2 (1.5) EBW: 36# (9) DM: 8 (6) HTN: 37 (28)
Fayad, 2019 [36]	Obs / Y	Single	Yes	n: 54 Age: 48 (24-72) Female: 57.4% BMI: median				n: 83 Age: 47 (30-67) Female: 59 (71.1) BMI: 44.12 (29.73-64.46)	

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop			
				BMI 43.07 DM: 3.7% HTN: 27.8%		DM: 20.48% HTN: 50.60%	
Fiorillo, 2020 [34]	Obs / N	Single	Yes	n: 23 Age: 41 (35-43) Female: 16 (30.4) BMI: 39.5 (36.7-44.7) DM: 2 (8.7) HTN: 3 (13)		n: 23 Age: 37 (25-43) Female: 17 (73.9) BMI: 41 (38.3-43.4) DM: 3 (13) HTN: 7 (30.4)	
Gomez, 2016 [21]	RCT / Y	Single	No		n: 15 Age: 38.1 (8.8) Race White: 60% Female: 87% BMI: 34.7 (3.42)		n: 14 Age: 38.2 (8.78) Race White: 85.7% Female: 93% BMI: 35.6 (2.84)
Lopez-Nava, 2021 [33]	Obs / N	Multi	No	n: 199 Age: 44.6 (10) Female: 141 (71) BMI: 39.4 (5.4)		n: 61 Age: 44.6 (11.2) Female: 36 (59) BMI: 40.1 (3.7)	
Novikov, 2018 [32]	Obs / Y	Single	No	n: 91 Age: 43.86 (11.26) Female: 62 (68.13) BMI: 38.61 (6.98)		n: 120 Age: 40.71 (11.95) Female: 94 (78.33) BMI: 47.22 (7.84)	

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop			
				DM: 20 (21.98) A1c: 5.82 (0.98) HTN: 18 (19.78)		DM: 31 (25.83) A1c: 6.3 (1.25) HTN: 61 (50.83)	
Sullivan, 2018 [22]	RCT / Y	Multi	No		n: 198 Age: 42.7 (9.6) Race White: 165 (83.3) Female: 171 (86.4) BMI: 35.2 (2.7) A1c: 5.3 (0.4) HTN: 31 (15.7)		n: 189 Age: 42.5 (9.3) Race White: 155 (82.0) Female: 170 (89.9) BMI: 35.5 (2.7) A1c: 5.3 (0.5) HTN: 28 (14.8)
Sullivan, 2017 [31]	RCT / Y	Multi	No	n: 221 Age: 44.2 (8.6) Race White: 154 (71) Black: 61 (28.1) Female: 195 (88.2) BMI: 36.0 (2.4) EBW: 99.7 (12.2kg) DM: 17 (7.7) HTN: 100 (45.2)			n: 111 Age: 45.3 (9.1) Race White: 70 (64.8) Black: 34 (31.5) Female: 101 (91) BMI: 36.2 (2.2) EBW: 98.7 (11.6kg) DM: 11 (9.9) HTN: 42 (37.8)

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop		
Thompson, 2017 [39]	RCT / Y	Multi	No	n: 111 Age: 42.4 (10.0) Race White: 63 (56.8) Black: 33 (29.7) Hispanic: 11 (9.9) Female: 96 (86.5) BMI: 42.0 (5.1) DM: 3 (2.7) A1c: 5.7 (0.6) HTN: 46 (41.4)		n: 60 Age: 46.8 (11.6) Race White: 31 (51.7) Black: 17 (28.3) Hispanic: 11 (18.3) Female: 53 (88.3) BMI: 40.9 (3.9) DM: 8 (13.3) A1c: 5.8 (0.6) HTN: 24 (40.0)
Thompson, 2018 [52]	RCT / Y	Multi	No	n: 111 Age: 42.4 (10.0) Race White: 63 (56.8) Black: 33 (29.7) Hispanic: 11 (9.9) Female: 96 (86.5) BMI: 42.0 (5.1) DM: 3 (2.7) A1c: 5.7 (0.6)		n: 60 Age: 46.8 (11.6) Race White: 31 (51.7) Black: 17 (28.3) Hispanic: 11 (18.3) Female: 53 (88.3) BMI: 40.9 (3.9) DM: 8 (13.3) A1c: 5.8 (0.6) HTN: 24 (40.0)

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop					
					HTN: 46 (41.4)				
Lopez-Nava, 2020 [35]	Obs / N	Multi	No	n: 12 Age: 49.3 (2.4) Female: 9 (75) BMI: 38.3 (1.8) DM: 0 HTN: 2 (17)			n: 12 Age: 50.5 (1.9) Female: 9 (75) BMI: 39.2 (1.5) DM: 0 HTN: 9 (75)		
Raftopoulos, 2019 [23]	Obs / N	Single	Yes		n: 58 Age: 43.2 (11.8) Female: 70.7% BMI: 36.7 (5.7)			n: 413 Age: 48.3 (12.4) Female: 85.9% BMI: 36.8 (5.0)	
Raftopoulos, 2019 [24]	Obs / N	Single	Yes		n: 79 Age: 43 (10.8) Female: 68.4% BMI: 36.2 (5.4)			n: 413 Age: 48.3 (12.4) Female: 85.9% BMI: 36.8 (5.0)	
Abu Dayyeh, 2019 [49]	RCT / Y	Multi	No						
Wilson, 2018 [40]	Obs / N	Single	No			Unknown	Unknown		
Sadek, 2017 [43]	Obs / Y	Single	Unclear	n: 23				n: 277	

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop					
Abd El Mohsen, 2017 [30]	Obs / Y	Multi	No	n: 5					n: 14
Abu Dayyeh, 2015 [13]	RCT / Y	Multi	No		n: 137 Age: 38.7 (9.4) Female: (89.6) BMI: 35.2 (3.17) EBW: 28.4 (2.7)				n: 136 Age: 40.8 (9.6) Female: (90) BMI: 35.4 (2.7) EBW: 28.7 (8.1) kg
				ESG	Balloon	AspireAssist	RYGB	LSG	Lifestyle
Fuller, 2010 [66]	RCT / N	Single	No		n: 31 Age: 43 Female: (68) BMI: 36.0				n: 35 Age: 48 BMI: 36.7
Ponce, 2012 [26]	RCT / Y	Multi	No		n: 21 Age: 38.9 (9.1) White: (95) Female: (81) BMI: 34.7 (2.6)				n: 9 Age: 45.3 (6.6) White: (100) Female: (100) BMI: 35.6 (2.0)
Lee, 2012 [58]	RCT / N	Single	No		n: 8 Age: 43 (19.75) Female: 5 (62.5) BMI: 30.3 (4.22) Diabetes: 1 (12.5) NAFLD: 8 (100)				n: 10 Age: 47 (15) Female: 2 (20) BMI: 32.4 (6.66) Diabetes: 1 (10) NAFLD: 10 (100)
Ponce, 2015 [28]	RCT / Y	Multi	No		n: 187 Age: 43.8 (9.5) White: (81.8) Black: (13.4)				n: 139 Age: 44.0 (10.2) White: (85.6) Black: (11.5)

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop		
				Hispanic: (8) Female: (95.2) BMI: 35.3 (2.8) Diabetes: (7) HbA1c: 5.7 (0.7) HTN: (28.9)		Hispanic: (5.8) Female: (95.0) BMI: 35.4 (2.6) Diabetes: (7.2) HbA1c: 5.7 (0.88) HTN: (35.3)
Mohammed, 2014 [38]	RCT / N	Single	No	n: 84 Age: 43.96 (8.98) Female: (54) BMI: 47.87 (1.08) EBW: 65.45 (5.04)		n: 44 Age: 42.65 (6.61) Female: (59) BMI: 47.46 (1.85) EBW: 65.23 (6.77)
Ahmed, 2019 [42]	Obs / N	Single	No	n: 40 Female: 40 (100) BMI: 36		n: 40 Female: 40 (100) BMI: 36.5
Sullivan, 2012 [41]	RCT / Y	Single	No		n: 11 BMI: 42 (4.7)	n: 7 BMI: 43.4 (5.3)
Salomone, 2021 [57]	Obs / N	Single	No	n: 26 Age: 53 Female: (31) Diabetes: (38) HbA1c: 7.5 HTN: (65) NAFLD: 26 (100)		
Chan, 2021 [59]	RCT / N	Multi	No	n: 26 Age: 38.1 (7.9) Female (70) BMI: 30.2 (2.3)		n: 23 Age: 35.3 (7.2) Female: (75.5) BMI: 30.2 (2.1)

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop		
Abeid, 2019 [47]	Obs / N	Single	No		n: 1600 Age: 34.1 (10.3) Female: (77) BMI: 40.3 (8.17) Diabetes: (6.8) HTN: (15.06)	
Alqahani, 2019 [50]	Obs / N	Single	No	n: 1000 Age: 34.4 (9.5) Female: (89.7) BMI: 33.3 (4.5) Diabetes: (1.7) HTN: (2.8)		
Mathus, 2014 [45]	Obs / N	Single	No		n: 815 Age: 36.5 (9.8) Diabetes: (2.3) HTN: (15.6)	
Sander, 2017 [53]	Obs / N	Single	No		n: 9763 Age: 31.13 Female: (78) BMI: 33.42	
Benias, 2020 [37]	Obs / N	Single	No	n: 14 Age: 39 (4.2)		n: 11 Age: 47 (3.9)

	Study Design / US	Single vs Multi-center	Propensity Matching	Patient Characteristics Preop	
Fuller, 2019 [27]	RCT / Y	Single	No	n: 37 Age: 43.3 (9.4) White: (83.9) Female: (68) BMI: 36 (2.7)	n: 37 Age: 48.1 (7.3) White: (74.3) Female: (66) BMI: 36.9 (2.7)
Abu Dayyeh, 2021 [25]	RCT / Y	Single	No	n: 187 Age: 44.4 (8.9) White: 132 (71) Black: 49 (26) Asian: 1 (1) Female: 162 (87) BMI: 35.8 (2.6) Diabetes: 13 (7) HTN: 41 (22)	n: 101 Age: 44.0 (8.9) White: 72 (71) Black: 26 (26) Asian: 1 (1) Female: 90 (89) BMI: 35.8 (2.7) Diabetes: 4 (4) HTN: 32 (32)
Moore, 2019 [46]	Obs / Y	Multi	No	n: 1343 Age: 45.7 (10.8) White: 897 (66.8) Female: 1055 (78.6) BMI: 35.4 (5.4)	

APPENDIX H. OUTCOMES

Outcome	f/u Time (months)	# Studies	# RCTs	# nonRCTs
%TBWL	6	19	7	12
%TBWL	12	15	7	8
%EBWL	6	8	7	1
%EBWL	12	8	7	1
BMI	6	8	6	2
total complication	6	7	4	3
weight loss	6	7	6	1
weight loss	12	7	6	1
nausea/vomiting	12	6	3	3
total complication	12	6	3	3
BMI	12	5	3	2
QOL	6	5	3	2
infection	12	5	2	3
GERD	6	4	2	2
at least 10% total body weight	6	4	3	1
at least 5% total body weight	6	4	3	1
bleeding	12	4	2	2
dehydration	6	4	3	1
nausea/vomiting	6	4	3	1
%TBWL	24	3	0	3
30-day readmissions (time not specified)	6	3	1	2
30-day reintervention	12	3	1	2
QOL	12	3	3	0
at least 10% total body weight	12	3	3	0
at least 25% excess body weight	12	3	3	0
at least 5% total body weight	12	3	3	0

Outcome	f/u Time (months)	# Studies	# RCTs	# nonRCTs
bleeding	6	3	1	2
dehydration	12	3	1	2
dyspepsia/abdominal pain	6	3	3	0
dyspepsia/abdominal pain	12	3	2	1
gastric ulceration	6	3	3	0
HbA1C	6	3	3	0
HbA1C	12	3	2	1
30-day reintervention	6	2	1	1
BMI	24	2	0	2
GERD	12	2	2	0
at least 25% excess body weight	6	2	2	0
infection	6	2	1	1
mortality	12	2	1	1
weight loss	24	2	1	1
%EBWL	24	1	0	1
%EBWL	36	1	0	1
%TBWL	36	1	0	1
%TBWL	120	1	1	0
30-day readmissions (only know within 90 days though)	12	1	0	1
30-day readmissions (time not specified)	12	1	1	0
30-day reintervention (don't know time frame)	12	1	0	1
BMI	120	1	1	0
gastric ulceration	12	1	0	1
improvement of diabetes	12	1	1	0
improvement of hypertension	12	1	1	0
weight loss	60	1	1	0
weight loss	120	1	1	0

APPENDIX I. CITATIONS FOR EXCLUDED PUBLICATIONS

Adjunct Therapies, *N* = 8

1. Badurdeen, D., et al., Endoscopic sleeve gastroplasty plus liraglutide versus endoscopic sleeve gastroplasty alone for weight loss. Gastrointestinal endoscopy, 2021. 93(6): p. 1316-1324.e1.
2. Badurdeen, D., et al., ESG PLUS LIRAGLUTIDE IS SUPERIOR TO ESG ALONE FOR WEIGHT LOSS IN OVERWEIGHT AND OBESE PATIENTS. Gastrointestinal Endoscopy, 2020. 91(6): p. AB215.
3. Carolina Hoff, A., et al., SEMAGLUTIDE IN ASSOCIATION TO ENDOSCOPIC SLEEVE GASTROPLASTY: TAKING ENDOSCOPIC BATRIATRIC PROCEDURES OUTCOMES TO THE NEXT LEVEL. Gastrointestinal Endoscopy, 2021. 93(6): p. AB6-AB7.
4. de Souza, T.F., et al., The First Study Evaluating Effectiveness and Safety of the Endoscopic Sleeve Gastroplasty in HIV Patients. Obesity surgery, 2020. 30(3): p. 1159-1162.
5. Hoff, A.C., et al., Endoscopic sleeve gastroplasty and liraglutide: Associating a GLP1-analogue to potentialize weight loss. Digestive Endoscopy, 2020. 32((Hoff A.C.) Angioskope SP, Bariatric Endoscopy, São Paulo, Brazil): p. 14.
6. Kolli, S., et al., THE DUAL EFFICACY OF PHARMACOTHERAPY WITH INTRAGASTRIC BALLOONS FOR SUSTAINED WEIGHT LOSS – A RETROSPECTIVE ANALYSIS. Gastrointestinal Endoscopy, 2020. 91(6): p. AB227.
7. Peker, Y., et al., Comparison of results of laparoscopic gastric banding and consecutive intragastric balloon application at 18 months: a clinical prospective study. Journal of laparoendoscopic & advanced surgical techniques. Part a, 2011. 21(6): p. 471-475.
8. Russo, T., et al., BioEnterics Intragastric Balloon (BIB) versus Spatz Adjustable Balloon System (ABS): Our experience in the elderly. International journal of surgery (London, England), 2017. 38: p. 138-140.

Bridging Therapy, *N* = 1

1. Rzepa, A., et al. (2019). "Selected aspects of intra-gastric balloons use in patients undergoing surgery for morbid obesity." Obesity surgery 29(5): 551.

Duplicate Data, *N* = 3

1. Fuller, N., et al., A prospective, randomised, controlled trial of the BioEnterics® Intragastric Balloon (BIB) in the treatment of obese individuals with metabolic syndrome. Obesity reviews, 2010. 11: p. 436-.
2. Fuller, N.R., et al., An intragastric balloon produces large weight losses in the absence of a change in ghrelin or peptide YY. Clinical obesity, 2013. 3(6): p. 172-179.
3. Klein, S., et al., Aspiration therapy: a novel endoscopic approach for treating obesity. Obesity facts., 2012. 5: p. 203.

Modified Procedures, *N* = 7

1. Alasfar, F.S. and F. Alotaibi, A comparison between swallowable fluid filled and air filled gastric balloon: A single surgeon experience. Surgical Endoscopy, 2019. 33((Alasfar F.S.; Alotaibi F.) Department of Surgery, Faculty of Medicine, Kuwait University): p. S35.
2. Barrichello, S.A., et al., ANALYSIS OF THE EFFICACY AND SYMPTOMATOLOGY OF THE BALLOON IN RELATION TO THE VOLUME OF THE ACCESSORY. "INTRAGASTRIC BALLOON - THE GREATER THE VOLUME, THE BETTER?". Gastrointestinal Endoscopy, 2019. 89(6): p. AB274-AB275.
3. Fittipaldi-Fernandez, R.J., et al., Randomized Prospective Clinical Study of Spatz3® Adjustable Intragastric Balloon Treatment with a Control Group: a Large-Scale Brazilian Experiment. Obesity surgery, 2021. 31(2): p. 787-796.
4. Folini, L., et al., Liver steatosis (LS) evaluated through chemical-shift magnetic resonance imaging liver enzymes in morbid obesity; effect of weight loss obtained with intragastric balloon gastric banding. Acta diabetologica, 2014. 51(3): p. 361-368.
5. Malik, S., et al., INTRA-GASTRIC BALLOON FOR TREATMENT OF OBESITY: SAFETY ANALYSIS OF 2407 PATIENTS PERFORMED BY GASTROENTEROLOGISTS AND SURGEONS. Gastrointestinal Endoscopy, 2019. 89(6): p. AB271-AB272.
6. Mosli, M.M. and M. Elyas, Does combining liraglutide with intragastric balloon insertion improve sustained weight reduction? Saudi journal of gastroenterology : official journal of the Saudi Gastroenterology Association, 2017. 23(2): p. 117-122.
7. Sadek, R. and A. Wassef, Comparative gastric balloon systems: Does size matter? endoscopic and percutaneous interventional procedures. Obesity Surgery, 2017. 27(1): p. 345.

No Data, *N* = 4

1. Nct, Efficacy and Safety of Endoscopic Sleeve Gastroplasty Versus Laparoscopic Sleeve Gastrectomy in Obese Subjects With NASH. https://clinicaltrials.gov/show/NCT04060368, 2019.
2. Pate, P., et al., Impact of combined medical weight loss and intra-gastric balloon therapy on body fat composition following completion of 6 months of treatment punam patel md, michael seger md, jennifer seger md, terive duperier md, richard englehardt md, allison arnett NP-BC, tamara deshazo np. Surgery for obesity and related diseases, 2017. 13(10): p. S198-S199.
3. Plua Marcillo, W., et al., Prospective analysis of results of laparoscopic gastric sleeve and intragastric ball in obese patients. Obesity Surgery, 2019. 29(5): p. 1112.
4. Solmaz, A., et al., Comparison of intragastric balloon and gastric plication. Obesity Surgery, 2015. 25(1): p. S262.

Non-Bariatric Outcomes, *N* = 5

1. Abu Dayyeh, B.K., et al., Baseline gastric emptying and its change in response to diverse endoscopic bariatric therapies predict weight change after intervention. Gastroenterology, 2016. 150(4): p. S86.
2. Fayad, L., et al., ENDOSCOPIC BARIATRIC THERAPIES ASSOCIATED WITH LOWER RATE OF ADVERSE EVENTS AND LENGTH OF STAY THAN LAPAROSCOPIC BARIATRIC THERAPIES. Gastrointestinal Endoscopy, 2020. 91(6): p. AB223-AB224.
3. Goff, J.L., Gastroplasty with stomach plication gp associated with significant psychological support: A real alternative to the sleeve and gastric by-pass. Obesity Surgery, 2014. 24(8): p. 1245-1246.
4. Kolesnikov, E., et al., Comperative ph-monitoring studies after Roux-en-Y gastric bypass, sleeve gastrectomy operations and intragastric balloon insertion in morbidly obese patients. Obesity Surgery, 2015. 25(1): p. S274.
5. Wroblewski, E., et al., Variation in blood levels of hormones in obese patients following weight reduction induced by endoscopic and surgical bariatric therapies. Cytokine, 2016. 77: p. 56-62.

Procedure Type Not Included, *N* = 10

1. Cruz, J., et al. (2017). "Efficacy of weight reduction of endoscopic intrasgastric balloon (IGB) vs oral sibutramine in patients with class i obesity in an asian cohort-a randomized control trial with long term follow up. Surgery and strategies for low BMI." Obesity surgery 27(1): 235-.
2. Durmus, A., et al., The Efficacy Of Intragastric Balloon Versus Botulinum Toxin Injection In Obese Patients. Surgery for Obesity and Related Diseases, 2019. 15(10): p. S187-S188.
3. Familiari, P., et al., Transoral gastroplasty for morbid obesity: a multicenter trial with a 1-year outcome. Gastrointestinal endoscopy, 2011. 74(6): p. 1248-1258.
4. Huberty, V., et al., Endoscopic sutured gastroplasty in addition to lifestyle modification: short-term efficacy in a controlled randomised trial. Gut, 2020.
5. Jonnalagadda, S.S., et al., Preliminary results of a randomized, blinded, sham-controlled trial of transoral gastroplasty for the treatment of morbid obesity. Gastroenterology, 2012. 142(5): p. S78-.
6. Lecumberri, E., et al., Effectiveness and safety of air-filled balloon heliosphere BAG in 82 consecutive obese patients. Obesity surgery, 2011. 21(10): p. 1508-1512.
7. Nanni, G., et al., Effectiveness of the transoral endoscopic vertical gastroplasty (TOGa): a good balance between weight loss and complications, if compared with gastric bypass and biliopancreatic diversion. Obesity surgery, 2012. 22(12): p. 1897-1902.
8. Popov, V., A. Ou, and C.C. Thompson, Intragastric balloons are effective at inducing weight loss: a systematic review and meta-analysis of randomized controlled trials. Gastroenterology, 2015. 148(4): p. S903-.
9. Rothstein, R.I., et al., TRANSPYLORIC SHUTTLE TREATMENT IMPROVES CARDIOMETABOLIC RISK FACTORS AND QUALITY OF LIFE IN PATIENTS WITH OBESITY: RESULTS FROM A RANDOMIZED, DOUBLE-BLIND, SHAM-CONTROLLED TRIAL. Gastroenterology, 2019. 156(6): p. S-237-.

10. Schouten, R., et al., Long-term results of bariatric restrictive procedures: a prospective study. Obesity surgery, 2010. 20(12): p. 1617-1626.

Sample Size, *N* = 6

1. IMPACT OF SINGLE FLUID-FILLED INTRAGASTRIC BALLOON ON METABOLIC PARAMETERS AND NONALCOHOLIC STEATOHEPATITIS: a PROSPECTIVE PAIRED ENDOSCOPIC ULTRASOUND GUIDED CORE LIVER BIOPSY AT THE TIME OF BALLOON PLACEMENT AND REMOVAL. Gastroenterology, 2018. 154(6): p. S-1360-.
2. Genco, A., et al., Safety and efficacy of a new swallowable intragastric ballon not needing endoscopy: earlyitalian experience. Gastrointestinal endoscopy, 2017. 85(5): p. AB271-.
3. Jagtap, N., et al., Endoscopic sleeve gastroplasty for non-alcoholic fatty liver disease. Endoscopy, 2021. 53(SUPPL 1): p. S21-.
4. Lopez-Nava, G., et al., Endoscopic Sleeve Gastroplasty for Obesity: a Multicenter Study of 248 Patients with 24 Months Follow-Up. Obesity surgery, 2017: p. 1-7.
5. Machytka, E., et al., Elipse, the first procedure less gastric balloon for weight loss: a prospective, observational, open-label, multicenter study. Endoscopy, 2016. (no pagination).
6. Maekawa, S., M. Niizawa, and M. Harada, A Comparison of the Weight Loss Effect between a Low-carbohydrate Diet and a Calorie-restricted Diet in Combination with Intragastric Balloon Therapy. Internal medicine (Tokyo, Japan), 2020. 59(9): p. 1133-1139.

Short Follow-Up, *N* = 4

1. Armijo, P.R., et al., Patients undergoing intra-gastric balloon achieve approximately 50% of their target weight loss in the first month postoperatively: a Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program analysis. Surgery for Obesity and Related Diseases, 2018. 14(11): p. S63.
2. Armijo, P.R., et al., Patients undergoing intragastric balloon achieve approximately 50% of their target weight loss in the first month postoperatively: an MBSAQIP analysis. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery, 2019. 15(12): p. 2060-2065.
3. Behzadi, F., et al., Predictors of Early Reintervention Following Intragastric Balloon: An MBSAQIP Analysis. Surgery for Obesity and Related Diseases, 2019. 15(10): p. S74.
4. Jain, S., S. Rajput, and R.K. Jain, Endoscopic Sleeve gastroplasty is safe minimally invasive modality in treatment of obesity with good short term efficacy: Initial experience at single center. Journal of Gastroenterology and Hepatology, 2019. 34((Jain S.; Jain R.K.) Jainamshree Multispecialty Hospital, Bhopal, India): p. 454.

Study Design, *N* = 19

1. Abeid, M., et al., EFFICACY AND SAFETY OF INTRAGASTRIC BALLOON PLACEMENTS IN 1600 CASE, AN EXPERIENCE FROM THE MIDDLE EAST. Gastrointestinal Endoscopy, 2019. 89(6): p. AB263.
2. Deliopoulou, K., et al., The impact of weight loss on depression status in obese individuals subjected to intragastric balloon treatment. Obesity surgery, 2013. 23(5): p. 669-675.
3. Fayad, L., et al., Endoscopic sleeve gastroplasty versus intragastric balloon insertion: efficacy, durability, and safety. Endoscopy, 2019. 51(6): p. 532-539.
4. Fernandez, R.J.F., et al., Intragastric balloon: A critical view in non elective bariatric surgery patients. United European Gastroenterology Journal, 2017. 5(5): p. A830.
5. Fittipaldi-Fernandez, R., et al., Intragastric balloon: A critical view in non elective bariatric surgery patients endoscopic and percutaneous interventional procedures. Obesity Surgery, 2017. 27(1): p. 494-495.
6. Ienca, R., C. Giardiello, and R. Schiano, Virtual follow-up (FU) program enhances weight-loss results post Elipse balloon: an innovative, digital patient-friendly approach. Obesity facts, 2018. 11: p. 49-.
7. Ienca, R., et al., Elipse® swallowable intragastric balloon + very low calorie ketogenic diet (VLCKD): a novel strategy to optimize weight-loss and minimize side effects. Obesity surgery, 2018. 28(1): p. S49-S50.
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