SYSTEMATIC REVIEWS AND META-ANALYSES

Siddharth Singh, Section Editor

Efficacy and Safety of Endoscopic Sleeve Gastroplasty: A Systematic Review and Meta-Analysis

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This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e64. Learning Objective–Upon completion of this activity, successful learners will be able to define the scope of the obesity epidemic worldwide, list comorbid conditions that improve with weight loss, and cite the efficacy (total body weight loss) and adverse event rate of endoscopic sleeve gastroplasty.

BACKGROUND & AIMS: **Bariatric surgery is the most successful treatment for obesity. However, many patients avoid surgery due to its perceived invasive nature and fear of complications. Endoscopic sleeve gastroplasty (ESG) is a seemingly less invasive option for patients with obesity. We performed a systematic review and meta-analysis to evaluate the efficacy and safety of ESG in adults.**

METHODS: **We searched MEDLINE, Embase, Web of Science, and Cochrane Library through July 2019. Investigated outcomes included the percent total body weight loss (TBWL), body mass index reduction, percent excess weight loss (EWL), and adverse events.**

RESULTS: **We extracted data from 8 original studies, published from 2016 through 2019, which included a total of 1772 patients. At 6 months, mean TBWL was 15.1% (95% CI, 14.3–16.0), mean decrease in body mass index was 5.65 kg/m2 (95% CI, 5.07–6.22), and mean excess weight loss was 57.7% (95% CI, 52.0–63.4). Weight loss was sustained at 12 months and 18–24 months with a TBWL of 16.5% (95% CI, 15.2–17.8) and 17.2% (95% CI, 14.6–19.7), respectively. The pooled post-ESG rate of severe adverse events was 2.2% (95% CI, 1.6%–3.1%), including pain or nausea requiring hospitalization (n = 18, 1.08%), upper gastrointestinal bleeding (n=9, 0.56%), and peri-gastric leak or fluid collection (n = 8, 0.48%).**

CONCLUSIONS: **In a systematic review and meta-analysis, we found ESG to produce clinically significant weight loss that was reproducible among independent centers and to have a low rate of severe adverse events. ESG appears to be an effective intervention for patients with obesity, although comparative studies and randomized controlled trials are necessary. PROSPERO Identifier: CRD42019121921**

Keywords: Stomach; Complication; Endoscopy; Overweight.

See related article on page 1070.

In 2016, more than 1.9 billion adults 18 years of age and older were overweight and 650 million were obese.[1] The global prevalence of obesity is alarming, yet data suggests that these staggering statistics will only

Abbreviations used in this paper: **BMI, body mass index; CI, confidence interval; ESG, endoscopic sleeve gastroplasty; EWL, excess weight loss; LSG, laparoscopic sleeve gastrectomy; TBWL, total body weight loss.**

Most current article

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continue to rise.[2] Obesity associated comorbid conditions including type 2 diabetes mellitus, hypertension, coronary heart disease, stroke, and nonalcoholic fatty liver disease all improve with weight loss.[2] Diet, exercise, and medications are often prescribed due to the lower cost and favorable side effect profile, but produce suboptimal results. Bariatric surgery is the gold standard for management of moderate to severe obesity; however, only 1%–2% of eligible patients undergo surgery each year.[3–6] Thus, a large proportion of obese patients who are nonresponsive to lifestyle and pharmacologic interventions are inadequately treated.[3]

Endoscopic bariatric therapies have emerged as a novel method to fill this void.[7] For endoscopic therapies to fulfil the unmet clinical need, there remains a requirement for not only an effective and safe therapy, but also one appealing to patients and clinicians. An endoscopic technique avoiding the placement and removal of a foreign body may result in acceptable tolerability and durability, thus increasing the likelihood of potential adoption. A potential solution was developed termed endoscopic sleeve gastroplasty (ESG). The ESG is an innovative imitation of the laparoscopic sleeve gastrectomy.[8] It is offered to patients who are not candidates for bariatric surgery based on body mass index (BMI) criteria, or are apprehensive of "going under the knife" for fear of complications. The volume of the stomach is reduced by approximately 70% through plication of the greater curvature of the stomach using an endoscopic suturing device (OverStitch, Apollo Endosurgery, Austin, TX).[9] The outpatient procedure is performed under general anesthesia and typically takes 1 hour to perform, after which discharge is possible the same day.

ESG is being increasingly adopted across the globe despite the current evidence being limited to retrospective case series and case-control studies. Comparative studies are lacking with no published data comparing ESG with diet and lifestyle modification therapy and only a few studies comparing ESG to bariatric surgery.[10,11] This is dissimilar to other endoscopic bariatric therapies, including intragastric balloons and aspiration therapy, in which level 1 evidence exists.[12–15] Therefore, there is a need to synthesize the available literature pertaining to ESG to arm the clinician with the data required to facilitate a data driven discussion with patients interested in the procedure. The aim of the systematic review and meta-analysis was to evaluate the efficacy of ESG for significant and sustained weight loss and define the risk of severe adverse events.

What You Need to Know

Background

Endoscopic sleeve gastroplasty (ESG) is an incisionless minimally invasive weight loss therapy that is being used to treat patients with obesity. We performed a systematic review and meta-analysis to evaluate the efficacy and safety of ESG in adults.

Findings

ESG was found to produce clinically significant weight loss that was reproducible across the United States, Europe, and South America. Furthermore, it was associated with a low incidence of serious adverse events.

Implications for patient care

ESG appears to be an effective and safe weight loss intervention for patients with obesity, although comparative studies and randomized controlled trials are necessary.

Methods and Materials

Search Strategy

Adhering to the MOOSE (Meta-analysis of Observational Studies in Epidemiology) guidelines,[16] studies were identified by performing a comprehensive literature search of 3 electronic databases (MEDLINE through PubMed, Web of Science, and the Cochrane library) with the last search performed on July 1, 2019. The search equation for PubMed was ("Gastroplasty" or "Overstitch" or "Endosleeve" or "Endoscopic sleeve gastroplasty" or "Endoscopic bariatric therapy" or "Endoscopic suturing" or "Bariatric endoscopy" or "Endobariatrics") AND ("Weight loss" or "Obesity" or "Bariatric") AND ("Endoscopic"). Queries for other databases were adapted from this search strategy. We attempted to identify additional studies by reviewing the reference list of all included studies, personal collections, and manual search to retrieve other articles that may have been missed by the initial search strategy. Two investigators (A.H., J.F.) screened all titles and abstracts for relevance to the study and reviewed the full text of the relevant studies. Disagreements were resolved by consensus with the intervention of a third reviewer (V.K.) when necessary.

Study Selection and Quality Assessment

Predefined inclusion criteria were retrospective or prospective studies, case-control or cohort studies, or clinical trials (including randomized controlled trials) with more than 20 patients and studies reporting clinical outcomes of ESG in adult patients. Our exclusion criteria were animal studies, commentaries, reviews or surveys, overlapping patients, publications in a language other than English or French, case reports, and letters or comments. If multiple articles were on the same study sample with the same exposure and outcome, the publication with the largest sample size was retained. All studies were evaluated for quality independently by 2 investigators

Table 1. Baseline Characteristics of Included Studies

Author, Year	Setting	Design	Data Period	Cohort Size	Country	Male	Age (y)	BMI (kg/m^2)	Suture
Graus-Morales, 2018	Single center	Retrospective	01/2015–02/2016	148	Spain	27 (18.2)	41.5 ± 10	35.1 ± 5.5	4 ± 0.2
Fayad, 2018	Single center	Retrospective	05/2015–12/2016	54	United States	31 (57.4)	48 ± 12	43.0 ± 8.9	NR
Sartoretto, 2018 (Australia)	Multicenter	Retrospective	02/2016–05/2017	51	Australia	15 (29.4)	43 ± 11.9	36.7 ± 4.9	6.0 ± 1.2
Sartoretto, 2018 (United States)	Multicenter	Retrospective	02/2016–05/2017	19	United States	3 (15.7)	41.9 ± 9,6	33.6 ± 4.0	8.9 ± 1.5
Saumoy, 2017	Single center	Prospective	08/2013–12/2016	128	United States	42 (32.8)	43.6 ± 11.3	38.9 ± 6.9	8 ± 5
Lopez-Nava, 2017	Single center	Prospective	05/2013–03/2016	154	Spain	46 (29.8)	44.9 ± 9.5	38.3 ± 5.5	7 ± 1
Abu Dayyeh, 2016	Single center	Prospective	09/2012–03/2015	25	United States	4 (16.0)	47.6 ± 10	35.5 ± 2.6	16 ± 5
Alqahtani, 2018	Single center	Prospective	12/2016- NR	1000	Saudi Arabia	897 (89.7)	34.4 ± 9.5	33.3 ± 4.5	4.2 ± 0.5
Barrichello, 2019	Multicenter	Prospective	07/2017 – 08/2018	193	Multicenter	45 (23.3)	42.3 ± 9.6	34.11 ± 2.97	NR

Values are n (%) or mean ± SD.
NR, not reported.

(A.H., J.F.) using National Institutes of Health quality assessment for before-after (pre-post) studies.[17]

Data extraction. One investigator (A.H.) using a standardized data extraction sheet extracted data from each study. The data extraction form included (1) author name, (2) year of publication, (3) setting (location), (4) study design, (5) study period, (6) number of patients/lesions, (7) patient demographics (age, sex, BMI, weight, height, waist-circumference), (8) patient comorbidities, (9) number of sutures, (10) total body weight loss (TBWL), (11) excess weight loss (EWL), (12) severe adverse events, and (13) follow-up period. When published information was insufficient, the corresponding author was contacted to obtain further information.

Outcome Measures

The studies reviewed measured weight loss efficacy with different scales, including relative weight loss, absolute decrease in BMI, and relative EWL. To assess the stability of these findings and identify sources of heterogeneity, preplanned subgroup analyses based on study design, cohort size, BMI, and sex proportion were performed. Safety was evaluated by calculating the severe adverse event rate reported in the included studies.

Statistical Analyses

The proportions and 95% confidence intervals (CIs) for each categorical factor and the mean or median for continuous data were obtained or calculated when possible. The pooled means and proportions were then computed using either fixed-effects or random-effects models, depending on study homogeneity or heterogeneity. Statistical heterogeneity was evaluated by means of I^2 statistics and Cochran Q test values.[18] An I^2 value >50% was considered high statistical heterogeneity (I^2 >50% and $P < .05$). For the main outcomes that failed the homogeneity test, we searched for potential sources of heterogeneity, including study setting, average age, sex, number of sutures, baseline BMI and evaluated these via metaregression analysis, where TBWL was the summary outcome. For all analyses, if mean and standard deviation were not available, median was considered equivalent to mean, interquartile range was converted to standard deviation by dividing by 1.35 and range was transformed to standard deviation by dividing by 4, in accordance with the Cochrane handbook.[18] Funnel plots were generated to evaluate the possibility of publication bias.[19] The study was conducted in accordance with the MOOSE recommendations for reporting systematic reviews and meta-analyses for observational studies (Supplementary Table 1).[16] All statistical analyses were performed using R software (version 3.5.3) (R Foundation for Statistical Computing, Vienna, Austria).[20]

Results

Study Selection, Characteristics, and Quality of Included Studies

The flow diagram for study selection is shown in Supplementary Figure 1. In total, 1012 studies were identified through our database query, of which 250 were duplicates. Of the remaining 762 studies, 685 irrelevant articles were excluded based on the titles and abstracts. Full text review was then performed on the remaining 77 studies using the predefined inclusion and exclusion criteria, after which 8 studies were retained.

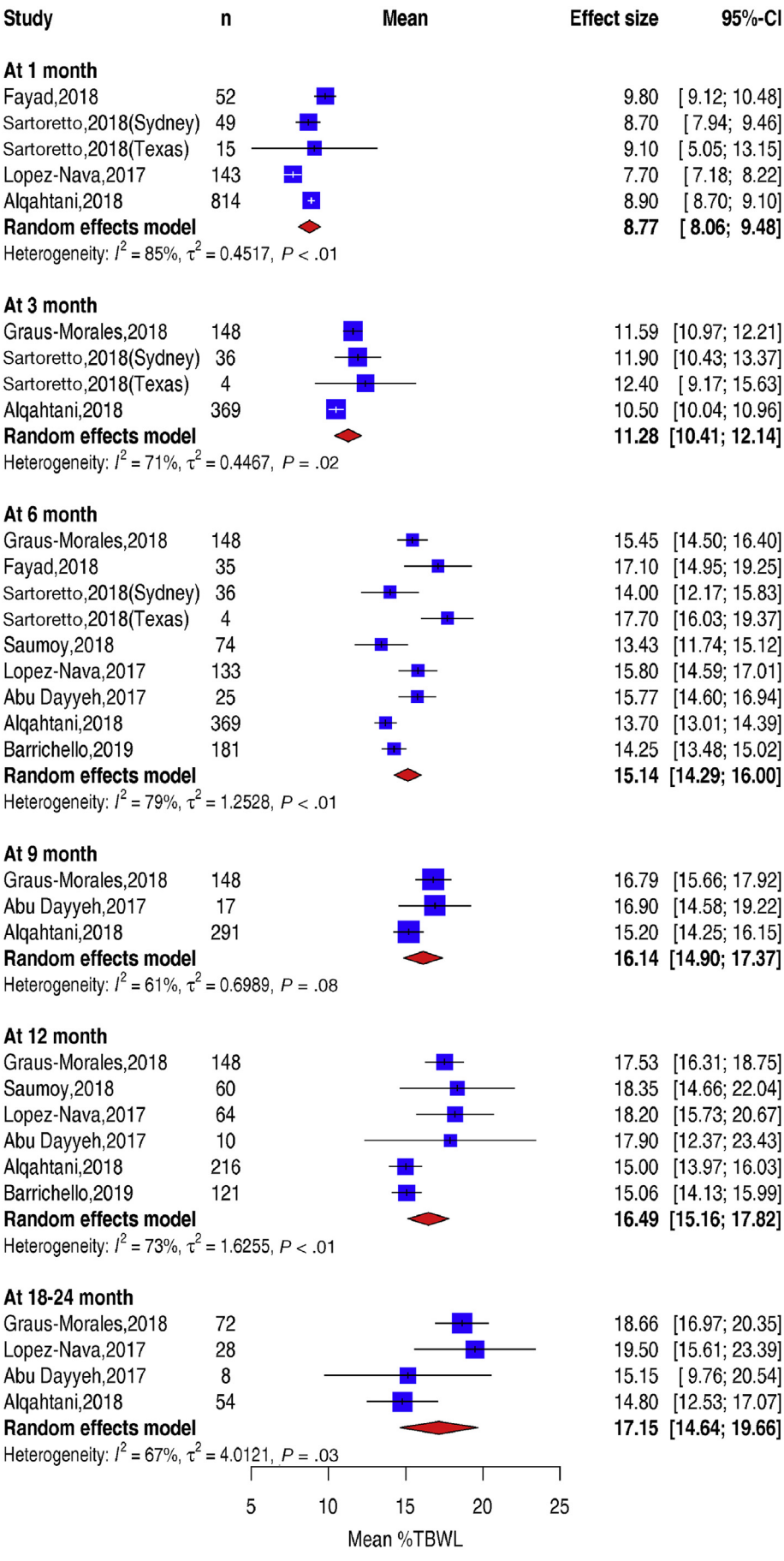

Figure 1. Forest plots of the included studies evaluating TBWL.

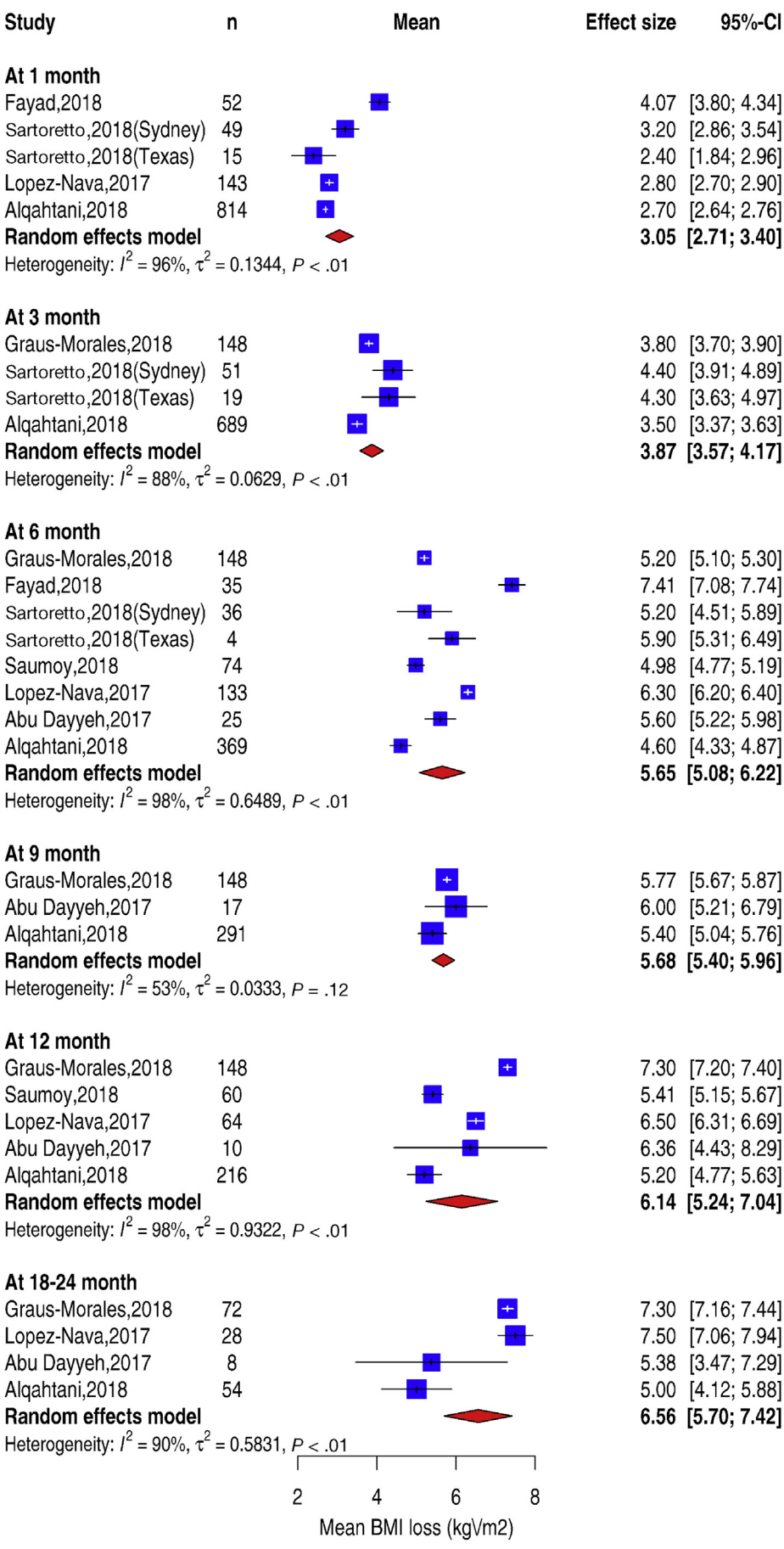

Figure 2. Forest plots of the included studies evaluating patient BMI reduction.

Table 2. Subgroup Analysis at Each Time Point for TWBL, Decrease in BMI, and EWL

Outcomes	Time Point	Number of cohorts	Cochran Q Test	Q Test *P* Value	τ^2	I^2 (%)	Pooled Proportion (95% CI)
Percentage of TBWL	At 1 mo	5	26.24	<.01	0.4517	84.8	8.77 (8.06–9.47)
	At 3 mo	4	10.21	<.01	0.4467	70.6	11.28 (10.41–12.14)
	At 6 mo	9	35.97	<.01	1.25	78.9	15.14 (14.29–16.00)
	At 9 mo	3	5.15	08	0.6989	61.1	16.13 (14.90–17.37)
	At 12 mo	6	18.44	<.01	1.6255	72.9	16.50 (15.19–17.82)
	At 18–24 mo	4	8.99	03	4.0121	66.6	17.15 (14.64–19.67)
BMI reduction	At 1 mo	5	100.90	<.01	0.1344	96.0	3.05 (2.71–3.40)
	At 3 mo	4	24.27	<.01	0.0629	87.6	3.86 (3.58–4.1662)
	At 6 mo	8	458.11	<.01	0.6489	98.5	5.65 (5.07–6.22)
	At 9 mo	3	4.27	.12	0.0333	53.1	5.67 (5.40–5.96)
	At 12 mo	5	266.57	<.01	0.9322	98.5	6.14 (5.24–7.04)
	At 18–24 mo	4	30.50	<.01	0.583	90.2	6.56 (5.70–7.47)
EWL	At 1 mo	4	87.04	<.01	69.1404	96.6	32.42 (23.50–41.34)
	At 3 mo	4	10.89	.01	17.5837	72.5	47.07 (42.10–52.03)
	At 6 mo	7	37.77	<.01	47.5125	84.1	57.71 (52.02–63.41)
	At 9 mo	3	5.25	.07	36.1429	61.9	66.21 (57.54–74.87)
	At 12 mo	5	12.95	<.01	39.1419	69.1	61.83 (54.75–68.93)
	At 18–24 mo	3	6.44	.04	142.7103	69.0	66.92 (50.22–83.61)

BMI, body mass index; CI, confidence interval; EWL, excess weight loss; TBWL, total body weight loss.

Twelve studies had overlapping patients and were therefore excluded. One study[9] pooled results from 2 different countries (United States and Australia) without overlapping patients and were included separately as 2 different cohorts. Finally, 8 studies[9,10,21–25] with 9 different cohorts involving 1772 patients fulfilling all inclusion criteria as described were included in our meta-analysis. Study characteristics are summarized in Table 1: 1110 (62.6%) patients were men, and the mean age was 38.3 ± 10.9 years. All 8 studies were cohort studies: 3 retrospective[9,10,22] and 5 prospective[21,23–26]; none were randomized controlled trials**.** The studies were all published from 2016 to 2019. Sample sizes at baseline ranged from 25 to 1000. BMI at baseline was between 33.3 ± 4.5 kg/m^2 and 43.0 ± 8.9 kg/m^2. All studies except one[25] showed a large female predominance. Results of the quality assessment of all included studies were satisfying and are shown in Supplementary Table 2. Absolute and relative TBWL was reported as a mean ± SD in all studies.

Relative TBWL

TBWL was reported at 1 month in 5 cohorts,[9,10,24,25] at 3 months in 4 cohorts,[9,22,25] at 6 months in 8 cohorts,[9,10,21–25] at 9 months in 3 cohorts,[21,22,25] at 12 months in 5 cohorts,[21,22,25] and at 18–24 months in 4 cohorts (Figure 1).[21,22,24,25] When the random-effects model was used, the pooled mean TBWL was 8.8% (95% CI, 8.1%–9.5%) at 1 month (Cochran's Q test $P \leq .01$, $I^2 = 85\%$), 11.2% (95% CI, 10.4%–12.14%) at 3 months (Cochran's Q test $P \leq .01$, $I^2 = 78.2\%$), 15.1% (95% CI, 14.3%–16.0%) at 6 months (Cochran's Q test $P < .01$, $I^2 = 80\%$), 16.1% (95% CI, 14.9%–17.4%) at 9 months (Cochran's Q test p = .08, $I^2 = 61\%$), 16.5% (95% CI, 15.2%–17.8%) at 12 months (Cochran's Q test $P < .01$, $I^2 = 73\%$), and 17.1% (95% CI, 14.6%–19.7%) at 18–24 months (Cochran's Q test $P = .03$, $I^2 = 67\%$). The funnel plots for TBWL at 6 months shows that there was no obvious publication bias detected for these outcome measures (Supplementary Figure 2). However, in the metaregression, only sex distribution ($P = .02$) was marginally associated with mean TBWL (Supplementary Figure 3). The slope of the line of best fit declines with increasing male predominance, which suggests that TBWL decreases as the proportion of men increases. There was no statistically significant association between baseline BMI, setting (Europe/United States), number of sutures used, cohort size, procedural time, or length of follow-up (Supplementary Table 3).

Absolute Decrease in BMI

Decrease in BMI was reported at 1 month in 5 cohorts,[9,10,24,25] at 3 months in 4 cohorts,[9,22,25] at 6 months in 8 cohorts,[9,10,21–25] at 9 months in 3 cohorts,[21,22,25] at 12 months in 5 cohorts,[21–25] and at 18–24 months in 4 cohorts (Figure 2).[21,22,24,25] When the random-effects model was used, the pooled BMI loss was 3.0 kg/m^2 (95% CI, 2.7–3.4) at 1 month (Cochran Q test $P < .01$, $I^2 = 96\%$), 3.9 kg/m^2 (95% CI, 3.6–4.2) at 3 months (Cochran Q test $P < .01$, $I^2 = 88\%$), 5.6 kg/m^2 (95% CI, 5.1–6.2) at 6 months (Cochran Q test $P < .01$, $I^2 = 98\%$), 5.7 kg/m^2 (95% CI, 5.4–6.0) at 9 months (Cochran Q test $P = .12$, $I^2 = 53\%$), 6.1 kg/m^2 (95% CI, 5.2–7.0) at 12 months (Cochran Q test $P < .01$, $I^2 = 98\%$), and 6.5 kg/m^2 (95%CI 5.7–7.4) at 18–24 months (Cochran Q test $P < .01$, $I^2 = 90\%$; Table 2).

Relative EWL

EWL was reported at 1 month in 4 cohorts,[9,24,25] at 3 months in 4 cohorts,[9,22,25] at 6 months in 7

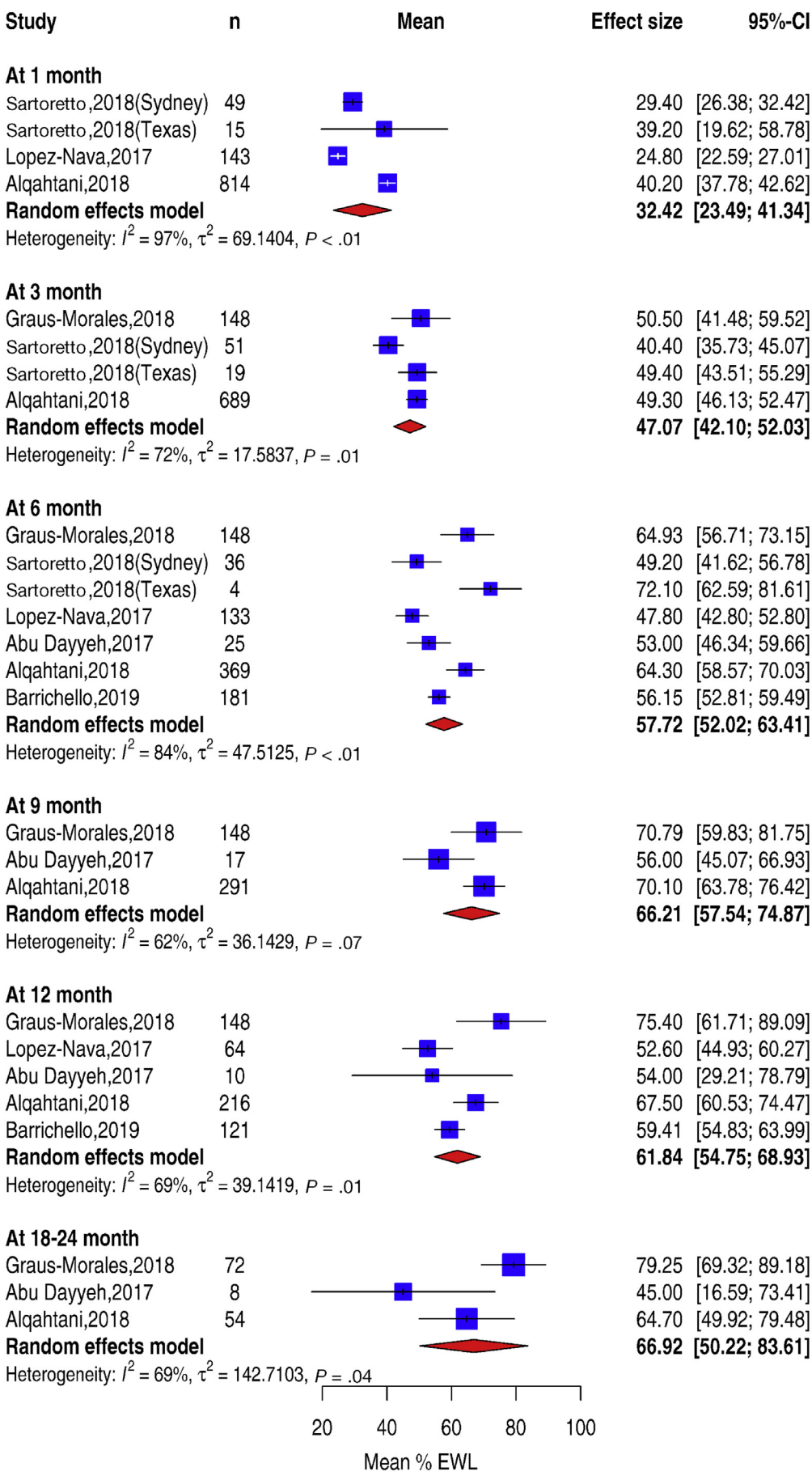

Figure 3. Forest plots of the included studies evaluating patient EWL.

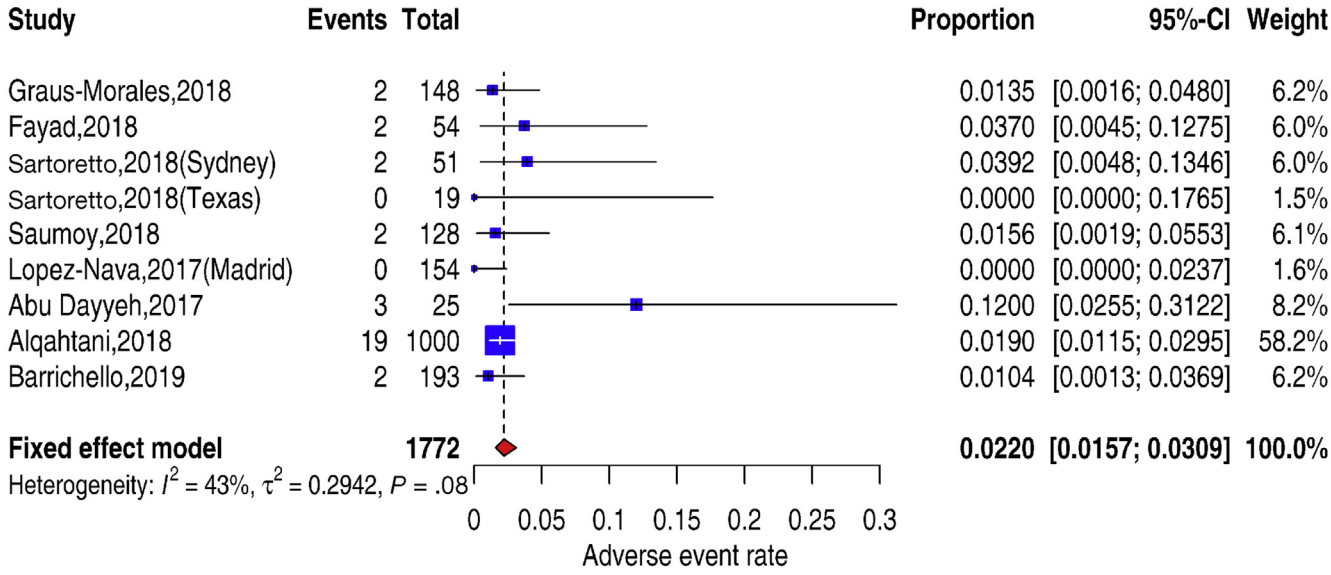

Figure 4. Forest plots of the included studies evaluating severe adverse event rate.

cohorts,[9,21,22,24–26] at 9 months in 3 cohorts,[21,22,25] at 12 months in 5 cohorts,[21,22,24–26] and at 18–24 months in 3 cohorts (Figure 3).[21,22,25] When the random-effects model was used, the pooled EWL was 32.4% (95% CI, 23.5%–41.3%) at 1 month (Cochran Q test $P < .01$, $I^2 = 96\%$), 47.1% (95% CI, 42.1%–52.0%) at 3 months (Cochran Q test $P < .01$, $I^2 = 73\%$), 57.7% (95% CI, 52.0%–63.4%) at 6 months (Cochran Q test $P = .01$, $I^2 = 84\%$), 66.2% (95% CI, 57.5%–74.9%) at 9 months (Cochran Q test $P = .07$, $I^2 = 62\%$), 61.8% (95% CI, 54.7%–68.9%) at 12 months (Cochran Q test $P < .01$, $I^2 = 69.1\%$), and 66.9% (95% CI, 50.2%–83.6%) at 18–24 months (Cochran Q test $P = .04$, $I^2 = 69\%$; Table 2).

Sensitivity Analysis, Subgroup Analysis and Metaregression

We investigated the influence of a single study on the overall percentage of TBWL by omitting 1 study at a time. The omission of any one study showed no clinically significant difference in the results, indicating that the results were statistically reliable. However, after omitting the study of Alqahtani et al,[25] heterogeneity of TBWL decreased to 73% (Supplementary Figure 4). There was no evidence of small study effect graphically based on funnel plot with no gap on the bottom corners of the plot (Supplementary Figure 2). One of the large studies had a smaller treatment effect compared with other large cohorts without clinical significance.[25] Lack of publication bias was further confirmed by Egger's test. Multiple preplanned subgroup analyses were performed to assess for stability of these findings and identify potential sources of heterogeneity (Supplementary Table 3). Sample size, study design, baseline BMI, and sex ratio did not explain study heterogeneity. We performed a metaregression to evaluate whether the number of sutures applied was associated with amount of weight reduction. Metaregression showed no statistical correlation between number of sutures and percentage of TBWL at 6 months.

Severe Adverse Events

Procedural severe adverse events were reported in all studies included in the meta-analysis (Figure 4). The pooled estimate of post-ESG severe adverse event rate was 2.2% (95% CI, 1.57%–3.09%), with a moderate heterogeneity (Cochran Q test $P = .08$, $I^2 = 45$). No patient died from the procedure. Reported severe adverse events were pain or nausea requiring hospitalization (n = 18, 1.08%), upper gastrointestinal bleeding (n= 9, 0.56%), perigastric leak or collection (n = 8, 0.48%), pulmonary embolism (n = 1, 0.06%), and pneumoperitoneum (n = 1, 0.06%).

Discussion

We report the results of a meta-analysis that evaluates the efficacy and safety of ESG. The data presented suggest that ESG confers significant and sustained weight loss with an acceptable safety profile. We report that at 6 months, mean TBWL was 15.1% (95% CI, 14.3%–16.0%), decrease in BMI was 5.6 kg/m^2 (95% CI, 5.1–6.2 kg/m^2), and relative EWL was 57.7% (95% CI, 52.0%–63.4%). Remarkably, these results were sustained at 18–24 months, though the number of patients with this duration of follow-up was limited. The pooled estimate of post-ESG severe adverse event rate was low and estimated at 2.2% (95% CI, 1.6%–3.1%).

Intense diet and lifestyle modification with caloric restriction, exercise and cognitive-behavioral therapy remain the cornerstones of therapy for weight loss in overweight and obese individuals.[27] Though effective, results of several meta-analyses suggest that there is a considerable variability in the magnitude of weight loss achieved.[28,29]

Furthermore, maintenance of weight loss has been a point of concern and contention.[30] A systematic review by Dombrowski et al[31] demonstrated that weight loss maintenance interventions using lifestyle modification and medications were slightly effective. Moreover, weight regain was observed when medications were stopped.[32] Roughly 20% of individuals who were overweight or obese were successful at maintaining weight loss up to 24 months.[33] Interestingly, to date there has been no head-to-head randomized controlled trial comparing ESG with medications or intense diet and lifestyle therapy.

The Preservation and Incorporation of Valuable Endoscopic Innovation thresholds to assess endoscopic bariatric therapy has been set jointly by the American Society of Gastrointestinal Endoscopy and the American Society for Metabolic and Bariatric Surgery. They recommend efficacy targets of greater than 25% EWL at 12 months and a <5% rate of severe adverse events.[34,35] In our meta-analysis, overall pooled results and individual trial results exceed these criteria despite heterogeneity in inclusion criteria, procedure, postprocedure management and length of follow-up. Notably, due to the lack of control groups in the included studies, we were not able to assess efficacy compared with a sham cohort.

Bariatric surgery is currently the most effective intervention for treatment of obesity and obesity-associated diseases.[36] The Roux-en-Y gastric bypass has fallen out of favor, the more contemporary laparoscopic sleeve gastrectomy (LSG) increased in popularity, while the laparoscopic adjustable gastric band is now seldom performed.[37] Bariatric surgery is associated with successful long-term maintenance of weight loss and reduction in obesity-related comorbidities, as well as improvement in quality of life.[5] In a randomized trial comparing Roux-en-Y gastric bypass vs LSG vs intensive medical management in patients with BMI 27–43 kg/m^2, TBWL was 23%, 19%, and 5% at 5 years, respectively.[38] However, despite its efficacy, few eligible patients select bariatric surgery as their treatment of choice due to several factors: fear of "going under the knife," "stigma of altered anatomy," and the perceived risk of adverse events.

Patients and the majority of clinicians treating patients who are obese likely perceive the adverse event rate of bariatric surgery to be disproportionate to what is represented by published data. Furthermore, there is the perception that endoscopic bariatric therapies confer a substantially superior favorable risk-benefit profile when compared with bariatric surgery, particularly in patients with a relatively lower BMI. Therefore, ESG has been considered by many as the preferred approach for early intervention, such as to treat patients with BMI 30–35 kg/m^2 or to prevent the development of obesity associated comorbidities. In the absence of high-quality randomized controlled trial evidence comparing ESG with bariatric surgery, one must be tempered when portraying ESG in this manner. Even in patients with class 1 obesity (BMI 30–35 kg/m^2), bariatric surgery, including LSG, has demonstrated an excellent efficacy and safety profile.[39,40] Not only does it produce weight loss, but also the data illustrate profound improvements in obesity related comorbidities, including type 2 diabetes and its associated micro- and macrovascular complications.[39,40] Thus, what appears to be preventing bariatric surgery from being performed in patients with class 1 obesity are concerns regarding its safety profile. Interestingly, the 30-day severe adverse event rate of bariatric surgery in patients with class 1 obesity has been reported at 3.8%, with a mortality rate of 0.5%.[41] Our meta-analysis revealed a 2.2% (95% CI, 1.6%–3.1%) rate of severe adverse events with ESG. It confirms that the rate of severe adverse events of ESG is low, making it a suitable option for those not willing to undergo bariatric surgery.

There is a paucity of data demonstrating an improvement in obesity related metabolic comorbidities in patients who undergo ESG. Sharaiha et al[42] demonstrated a reduction in markers of diabetes, hypertension, fatty liver, and hypertriglyceridemia at 12 months post-ESG. However, one can extrapolate from robust data demonstrating that an improvement in metabolic parameters is seen with as little as 10% TBWL.[43,44] Does ESG induced TBWL of ~17% then have the potential to treat type 2 diabetes mellitus and reduce the risk of other obesity related comorbidities such as coronary heart disease and stroke? Further data is needed to answer to this crucial question; however, ESG appears to be a novel and promising treatment for obesity and its comorbid conditions. In addition, the cost benefit that one would see with treating obesity and its associated conditions with an outpatient procedure that takes approximately 60 minutes could be substantial.

The evidence from this meta-analysis suggests that ESG can be safely introduced into clinical practice for treatment of obesity and obesity-associated disease. The durability and weight loss results of ESG at 12 months, suggest that this endoscopic technique is effective, resulting in clinically significant weight loss, sustained over at least the intermediate term. As with any procedure, there is a learning curve until proficiency is achieved. By analyzing the first 128 consecutive patients at a tertiary-care academic medical center, Saumoy et al[23] found that efficiency (refining performance to decrease procedure time) for ESG was attained after an average of 38 procedures, and mastery (absence of outliers) after 55. Hill et al[45] found that endoscopists experienced in endoscopic suturing are expected to achieve a reduction in procedure time and number of plications per procedure in successive cases, with progress plateauing at 7 and 9 cases, respectively. Based on these results, ESG has the potential to be rapidly scaled, such that it can be used safely to help tackle the global obesity epidemic.[46]

The strengths of our meta-analysis include a comprehensive and well-defined search and a relatively large number of patients. However, there are also several limitations. First, we did not have access to individual participant data; hence, all analyses were performed at a study level. Like all meta-analyses, the results need to be

interpreted bearing in mind that endoscopic treatment varies based on patient characteristics (eg, age, sex, baseline BMI) although we did control for this in the meta-regression. Second, most of the studies are of retrospective design without controls, which can lead to biases. For most of the studies, the high percentage of "lost to follow-up" is likely to bias toward an overestimation of the treatment effect. Third, the longest follow-up time available was 2 years; hence, long-term effects could not be assessed or evaluated. Future studies with longer follow up are needed. Fourth, most of the studies did not evaluate and report on clinical comorbidities. These data are paramount as improvement in metabolic parameters translates into improved quality of life and decreased health care costs. Fifth, it is noteworthy that in most articles, mild adverse events were considered "expected" and were not reported. Although, these events are less concerning clinically, reporting them may be of utility in optimizing pre and post procedure prophylaxis regimens. Sixth, there were no randomized controlled trials identified. Seventh, a substantial statistical heterogeneity was found. Sensitivity analysis, subgroup analysis, and metaregression were not able to find a population or procedure characteristics explaining it. Omitting the study from Alqahtani et al,[25] differing from other studies by the number of patients recruited and sex repartition, partly reduced overall heterogeneity. Meta-regression, even though underpowered due to the small number, found that male sex could be associated with a lower treatment effect. However, owing to the excessive influence of the study of Alqahtani et al,[25] this result has to be interpreted cautiously. One of the reasons that could explain statistical heterogeneity could be variability in the ESG procedure. Since the first ESG report, variable numbers of sutures, orientation of sutures, spacing and frequency of bites, and tightness of cinching have been reported. An important element of all suture patterns is the distal to proximal movement within each running suture that is placed along the greater curvature, contracting the stomach longitudinally to confer the intended gastric shortening while simultaneously narrowing the lumen. Variation of the procedure has not been extensively evaluated in this meta-analysis and could partially explain heterogeneity.

Future researchers should prioritize assessing health outcomes following ESG, establishing its cost-effectiveness and examining its performance against conventional bariatric interventions, such as intense diet and lifestyle, medications, and LSG, in a randomized fashion. In addition, predictors of procedural success and optimization of aftercare all require further exploration. In summary, the quality of the available literature is limited. However, given the significant weight loss observed, reproducibility of the results among independent centers, and the low prevalence of severe adverse events, ESG is an effective treatment for obesity that deserves to be further explored in comparative studies and randomized controlled trials.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2019.08.022.

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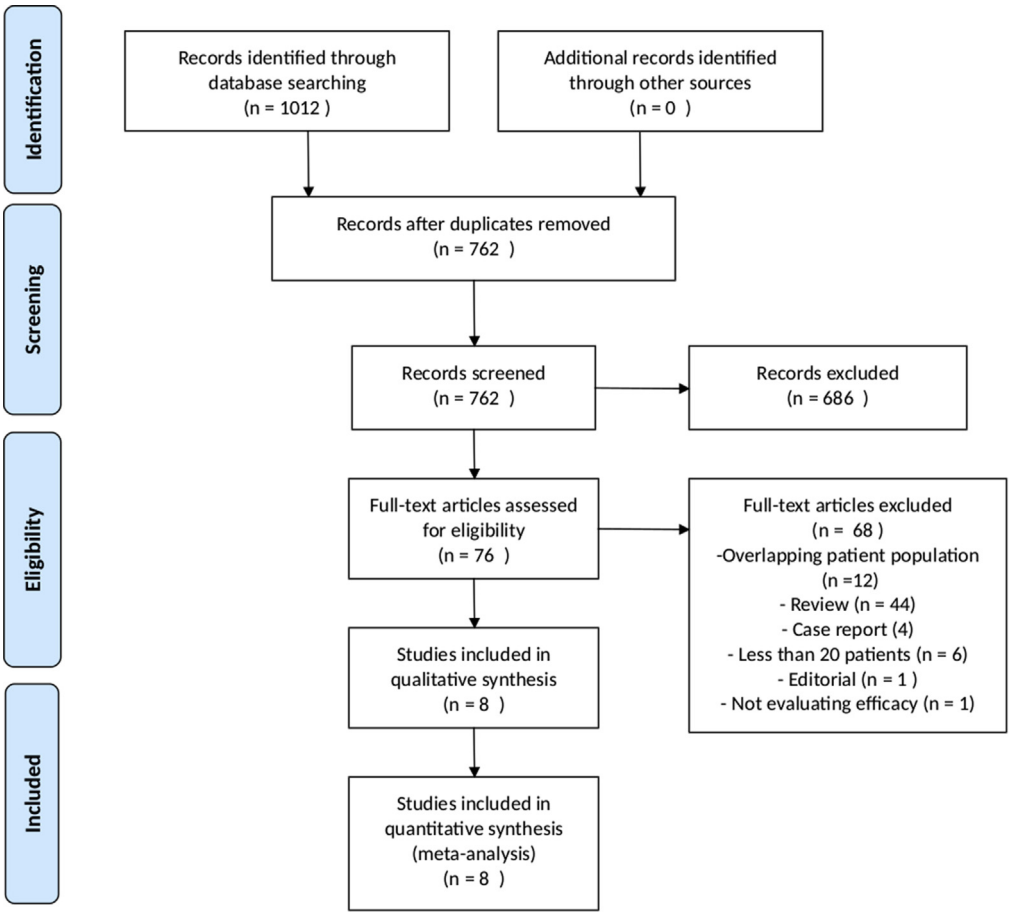
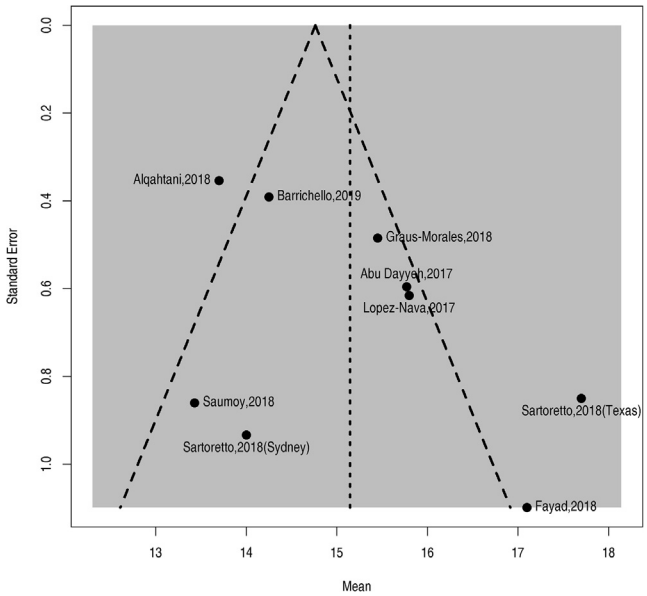
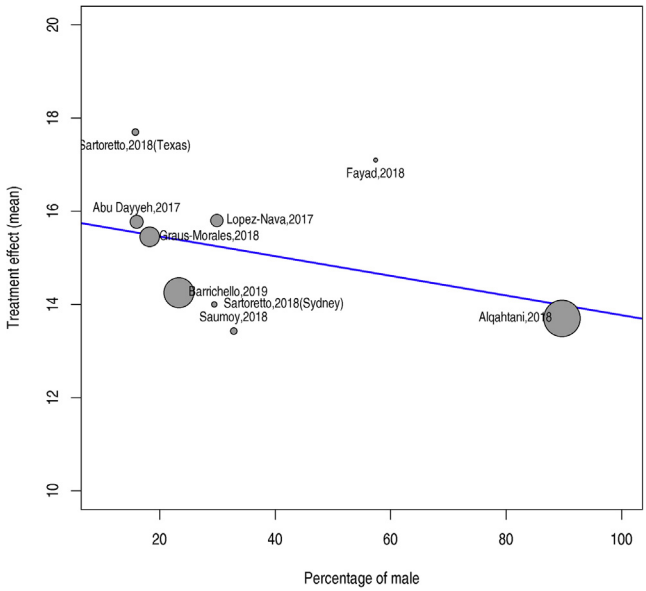
Conflicts of interest
These authors disclose the following: Barham K. Abu Dayyeh has served as a consultant for Boston Scientific, Metamodix, BFKW, USGI; received research support from Aspire Bariatrics, GI Dynamics, Apollo Endosurgery, USGI, Medtronic, Spatz, and Cairns; and served as a speaker for Johnson and Johnson and Olympus. Manoel Galvão Neto has served as a consultant for Fractyl Labs, GI Dynamics,. GI windows, Apollo EndoSurgery, Ethicon Endo-Surgery, Meditronics, and Olympus. Javier Graus Morales has served as a consultant for Apollo Endosurgery, Inc. Adrian Sartoretto has served as a consultant for Apollo Endosurgery, BAROnova, and AMSL (Australian distributors of the Aspire Assist). Gontrand Lopez Nava has served as a consultant for Apollo, Usgi, and Nitinotes. Mouen A Khashab has served as a consultant for Boston scientific, Olympus America, and Medtronic. Aayed R. Alqahtani has served as a consultant for Medtronic, Ethicon, and Apollo. Christopher C Thompson has served as a consultant for Boston Scientific, Medtronic, USGI Medical, Olympus, Apollo Endosurgery, GI Windows, Aspire Bariatrics, Fractyl, Spatz, and GI Dynamics. Vivek Kumbhari has served as a consultant for Medtronic, Reshape Lifesciences, Boston Scientific, and Apollo Endosurgery; and received research Support from ERBE and Apollo Endosurgery. The remaining authors disclose no conflicts.



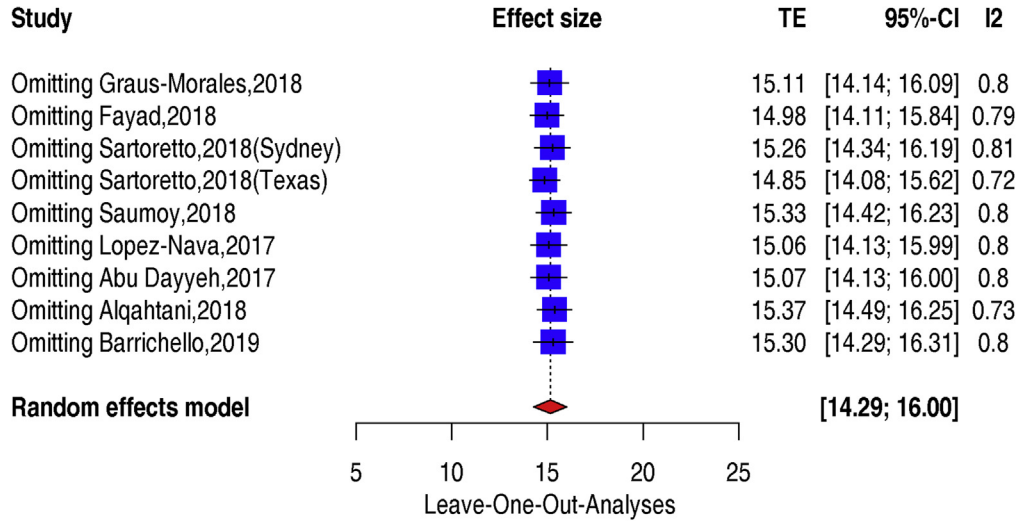
Supplementary Figure 1. PRISMA flow diagram.



Supplementary Figure 2. Funnel plots used to obtain evidence of total body weight loss at 6 months.



Supplementary Figure 3. Random-effects metaregression of total body weight loss according to male sex predominance. The blue line represents a line of best fit from metaregression. The diameter of the circles reflects the weight of the individual studies in the random-effects meta-regression. The slope of the line of best fit declines with increasing male predominance which suggests that total body weight loss decreases as the proportion of male increase.



Supplementary Figure 4. Sensitivity analyses using the leave-one-out analysis. CI, confidence interval; TE, treatment effect.

Supplementary Table 1. MOOSE Checklist

Item No	Recommendation	Reported on §
Reporting of background should include		
1	Problem definition	I **§ 1**
2	Hypothesis statement	I **§ 2**
3	Description of study outcome(s)	I **§ 3**
4	Type of exposure or intervention used	I **§ 2**
5	Type of study designs used	M **§ 1**
6	Study population	M **§ 2**
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	M **§ 1**
8	Search strategy, including time period included in the synthesis and key words	M **§ 1**
9	Effort to include all available studies, including contact with authors	M **§ 3**
10	Databases and registries searched	M **§ 1**
11	Search software used, name and version, including special features used (eg, explosion)	M **§ 5**
12	Use of hand searching (eg, reference lists of obtained articles)	M **§ 1**
13	List of citations located and those excluded, including justification	M **§ 1**
14	Method of addressing articles published in languages other than English	M **§ 2**
15	Method of handling abstracts and unpublished studies	NA
16	Description of any contact with authors	NA
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	R **§ 1**
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	M **§ 4**
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	NA
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	NA
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	NA
22	Assessment of heterogeneity	**R § 5**
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	M **§ 5**
24	Provision of appropriate tables and graphics	Table 2, Supp Table 2, Figures 1–4
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Figures 1–4
26	Table giving descriptive information for each study included	Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	Supp Table 3
28	Indication of statistical uncertainty of findings	Tables 2–3, Figures 1–4
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	**R § 5**
30	Justification for exclusion (eg, exclusion of non-English language citations)	-
31	Assessment of quality of included studies	Supp Table 1
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	NA
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	**D § 8**
34	Guidelines for future research	**D § 8**
35	Disclosure of funding source	-

I, Introduction; M, Method; D, Discussion; R, Results; NA, Not appropriate.

Supplementary Table 2. Study Quality Assessment Based on NIH Scale

Criterion	Graus-Morales, 2018	Fayad, 2018	Sartoretto, 2018	Saumoy, 2017	Lopez-Nava, 2017	Abu Dayyeh, 2016	Alqahtani, 2018	Barrichello 2019
1. Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Were all eligible participants that met the prespecified entry criteria enrolled?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the sample size sufficiently large to provide confidence in the findings?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Were the people assessing the outcomes blinded to the participants' exposures/ interventions?	No	No	No	No	No	No	No	No
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	Yes	No	No	No	Yes	Yes	Yes	Yes
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided *p* values for the pre-to-post changes?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

NIH, National Institutes of Health.

Supplementary Table 3. Subgroup Analysis at Each Time Point for TBWL

Variable	Subgroup	Trials	Cochran Q-test Q	Cochran Q-test *P* value	I^2 (%)	Model	Pooled proportion (95% CI)	Test for subgroup difference Q	*df*	*P* value
Sample size	<105	4	9.73	.02	69.2	RE	16.12 (14.62–17.61)	3.21	1	.073
	≥105	5	15.18	.01	74	RE	14.54 (13.69–15.39)			
Design	Prospective	5	15.78	.01	75	RE	14.58 (13.68–15.49)	2.55	1	.110
	Retrospective	4	10.63	.17	71.8	RE	16.01 (14.51–17.50)			
BMI	<36 kg/m^2	5	27.36	.01	85	RE	15.22 (14.09–16.35)	0.031	1	.858
	≥36 kg/m^2	4	9.76	.02	69.3	RE	15.04 (13.53–16.56)			
Male ratio	<29%	4	9.13	.87	67.2	FE	15.74 (14.56–16.91)	0.78	1	.3776
	≥29%	5	16.43	.01	76	RE	14.69 (113.44–15.95)			

BMI, body mass index; CI, confidence interval; FE, fixed-effects model; RE, random-effects model.