Communication from the ASGE Technology Committee

ASGE TECHNOLOGY COMMITTEE SYSTEMATIC REVIEW AND META-ANALYSIS

ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies

Prepared by: ASGE BARIATRIC ENDOSCOPY TASK FORCE AND ASGE TECHNOLOGY COMMITTEE

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee periodically performs systematic reviews and meta-analyses to evaluate endoscopic technologies in order to determine whether these have met previously established Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) thresholds.

A subcommittee of the ASGE Technology Committee, a newly formed ASGE Bariatric Endoscopy Task Force, comprising experts in the subject area, and the Technology Committee Chair, performed this systematic review and meta-analyses. The systematic review and meta-analyses are ultimately submitted to the ASGE Governing Board for approval. The systematic review and meta-analyses undergo peer review by outside experts in statistics and meta-analysis before receiving final ASGE Governing Board approval.

The PIVI initiative is an ASGE program whose objectives are to identify important clinical questions related to endoscopy and to establish a priori diagnostic and/or therapeutic thresholds for endoscopic technologies designed to resolve these clinical questions. Once endoscopic technologies meet an established PIVI threshold, those technologies are appropriate to incorporate into clinical practice, presuming the appropriate training in that endoscopic technology has been achieved. ASGE encourages and supports the appropriate use of technologies that meet its established PIVI thresholds.

ABSTRACT

The increasing global burden of obesity and its associated comorbidities has created an urgent need for additional treatment options to fight this pandemic. Endoscopic bariatric therapies (EBTs) provide an effective and minimally invasive treatment approach to obesity that would increase treatment options beyond surgery, medications, and lifestyle measures. This systematic review and meta-analysis were performed by the American Society for Gastrointestinal Endoscopy (ASGE) Bariatric Endoscopy Task Force comprising experts in the subject area and the ASGE Technology Committee Chair to specifically assess whether acceptable performance thresholds outlined by an ASGE Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) document for clinical adoption of available EBTs have been met. After conducting a comprehensive search of several English-language databases, we performed direct meta-analyses by using random-effects models to assess whether the Orbera intragastric balloon (IGB) (Apollo Endosurgery, Austin, Tex) and the EndoBarrier duodenal-jejunal bypass sleeve (DJBS) (GI Dynamics, Lexington, Mass) have met the PIVI thresholds. The meta-analyses results indicate that the Orbera IGB meets the PIVI thresholds for both primary and nonprimary bridge obesity therapy. Based on a meta-analysis of 17 studies including 1683 patients, the percentage of excess weight loss (%EWL) with the Orbera IGB at 12 months was 25.44% (95% confidence interval [CI], 21.47%-29.41%) (random model) with a mean difference in % EWL over controls of 26.9% (95% CI, 15.66%-38.24%; $P \leq .01$) in 3 randomized, controlled trials. Furthermore, the pooled percentage of total body weight loss (% TBWL) after Orbera IGB implantation was 12.3% (95% CI, 7.9%–16.73%), 13.16% (95% CI, 12.37%–13.95%), and 11.27% (95% CI, 8.17%–14.36%) at 3, 6, and 12 months after implantation, respectively, thus exceeding the PIVI threshold of 5% TBWL for nonprimary (bridge) obesity therapy. With the data available, the DJBS liner does appear to meet the %EWL PIVI threshold at 12 months, resulting in 35% EWL

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(95% CI, 24%-46%) but does not meet the 15% EWL over control required by the PIVI. We await review of the pivotal trial data on the efficacy and safety of this device. Data are insufficient to evaluate PIVI thresholds for any other EBT at this time. Both evaluated EBTs had ≤5% incidence of serious adverse events as set by the PIVI document to indicate acceptable safety profiles.

Our task force consequently recognizes the Orbera IGB for meeting the PIVI criteria for the management of obesity. As additional data from the other EBTs become available, we will update our recommendations accordingly.

INTRODUCTION

Obesity is a worldwide epidemic associated with multiple comorbidities.[1,2] Lifestyle intervention and pharmacological treatment approaches are only modestly effective and have limited weight loss durability.[3,4] Bariatric surgical procedures are effective but are associated with high costs, adverse events, and low patient acceptance. There is a need for weight loss therapies that are (a) more effective and durable than lifestyle interventions and pharmacological treatment, (b) less invasive and risky than bariatric surgery, and (c) easily performed at a lower expense than that of surgery, thereby allowing improved access and application to a larger segment of the population with moderate obesity.

Emerging endoscopic bariatric therapies (EBTs) potentially meet these criteria and may provide an effective treatment approach to obesity in selected patients and effectively fill the current gap in our management approach to obesity. Many EBTs also offer the potential added advantages of reversibility, repeatability, and cost-effectiveness, depending on the individual therapy. Available EBTs are reviewed in a detailed technology review article on this topic.[5]

Any new EBT should include a defined threshold of efficacy balanced with the risks of the intervention. A joint task force convened by the ASGE and the American Society for Metabolic and Bariatric Surgery defined these thresholds in a Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) document[6,7] as follows:

- EBT intended as a primary* obesity intervention in Class II/III obese individuals (body mass index [BMI] >35 kg/m^2) should achieve a mean minimum threshold of 25% excess weight loss (%EWL) measured at 12 months.
- In addition to the absolute threshold of weight loss, the mean %EWL difference between a "primary" EBT and control groups should be a minimum of 15% EWL and be statistically significant.
- Five percent of the total body weight lost should represent the absolute minimum threshold for any nonprimary† EBT (eg, early intervention, bridging, or metabolic therapy).
- The risk associated with EBT should equate to a ≤5% incidence of serious adverse events.
- If a low-risk EBT proves to have a significant impact on 1 or more obesity-related comorbidities, the threshold for intervention may extend to Class I obese individuals (BMI 30-35 kg/m^2).

An EBT that meets these established PIVI thresholds would be considered appropriate to incorporate into clinical practice, presuming that the appropriate training and credentialing in that EBT has been achieved. This systematic review and meta-analysis was performed by the ASGE Bariatric Endoscopy Task Force in conjunction with the ASGE Technology Committee chair to specifically assess whether existing EBTs have met these PIVI thresholds. Of the EBTs discussed in the referenced technology review, the following had sufficient (3 or more human trials, with at least 1 of them a randomized, controlled trial [RCT]) published data to evaluate in meta-analyses: (1) BioEnterics Intragastric Balloon (Allergan, Irvine, Calif), currently known as Orbera Intragastric Balloon (IGB) (Apollo Endosurgery, Austin, Tex) and (2) EndoBarrier duodenal-jejunal bypass sleeve (DJBS) (GI Dynamics, Lexington, Mass).

METHODS

Data sources and search strategies

A comprehensive search of several English-language databases was conducted for studies published between January 1, 1988 and December 16, 2014. The databases included Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus. The search strategy was designed and conducted by an experienced librarian with input from the study team. Controlled vocabulary supplemented with key words was used to search for studies evaluating the 3 included EBTs. The search strategy is detailed in the Supplemental Material of the paper (Supplements 1 and 2, available online at www.giejournal.org). Relevant studies were also identified from the bibliography of studies obtained through the search and based on input from expert members on the ASGE Bariatric Endoscopy Task Force.

*Primary obesity interventions are stand-alone interventions in combination with lifestyle modification and or behavioral therapy to induce weight loss and improvement in obesity- associated medical comorbidities.

†Bridge obesity intervention is an intervention to promote weight loss specifically to reduce the risk from a subsequent intervention, including bariatric and nonbariatric surgery such as orthopedic, cardiovascular, and organ transplant surgeries. Patients with Class III (BMI >50) or higher obesity present greater technical challenges and surgical risk than less obese, healthier patients; therefore, EBTs used for this indication should perform well in higher BMI groups.

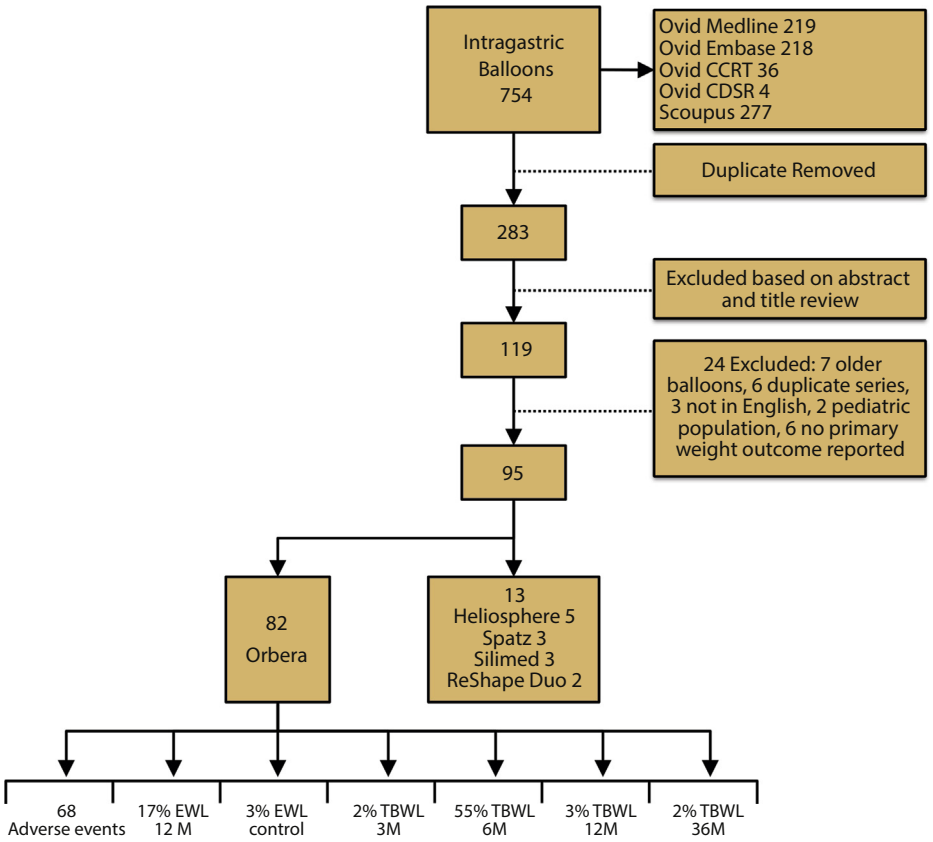

Figure 1. Flow diagram depicting search findings and study selection for inclusion in the intragastric balloon meta-analyses. *CCRT*, Cochrane Central Register of Controlled Trials; *CDSR*, Cochrane Database of Systematic Reviews; *%EWL*, percentage of excess weight loss; *%TBWL*, percentage of total body weight loss.

Study selection

Our collective search strategies returned 754 citations for IGBs and 135 citations for EndoBarrier DJBS. After removing duplicate citations and reviewing titles and abstracts of studies retrieved by our search strategies, we identified 119 potential eligible citations for IGBs and 44 for EndoBarrier DJBS. Full-length manuscript reviews narrowed eligible citations to 82 for Orbera IGBs and 11 for EndoBarrier DJBS, which were included in our meta-analyses (Figs. 1 and 2). Two reviewers (B.K.A.D. and N.K.) selected the included studies; when a disagreement occurred, a third blinded reviewer was consulted to resolve the disagreement. Consensus was reached on the included manuscripts. For inclusion in the meta-analysis, a study had to meet the following inclusion criteria: human trial, published in English (full text) in a peer-reviewed journal, and assessing at least 1 of the thresholds defined in the PIVI EBT document. Abstracts, letters, editorials, expert opinions, reviews without original data, case reports, and studies not directly evaluating the PIVI thresholds were excluded from the meta-analysis. All prospective, randomized trials included in the meta-analysis met the majority of the criteria set forth by the Evidence-Based Gastroenterology Steering Group for methodological quality, indicating studies of reasonable quality, and were scored by using the Jadad scale (Table 1).[8,9] The Jadad scale allocates trials a score of between 0 (very poor) and 5 (rigorous).

Data extraction and statistical analysis

Two independent reviewers performed data extraction (B.K.A.D. and N.K.) from each selected citation. When ambiguity on outcomes determination was present, a third reviewer was consulted, and the outcome was determined by consensus. To best summarize the available evidence, we conducted direct meta-analyses for each evaluated EBT. Given the degree of heterogeneity, a random-effects meta-analysis was used to provide a comprehensive summary of the totality of available evidence. For studies not reporting standard deviations or in which standard deviations could not be calculated from reported confidence intervals, standard errors, t values, *P* values, or f values, the reported mean of the study was used as an estimate of its standard deviation to allow it to be combined in the meta-analysis without overly biasing the results. The estimates of standard deviation were similar to that reported in other studies in the same meta-analysis. Statistical heterogeneity was evaluated by means of I^2 statistics and Q values. An I^2 value greater than 50% was considered to indicate high statistical heterogeneity. A funnel plot and Egger regression

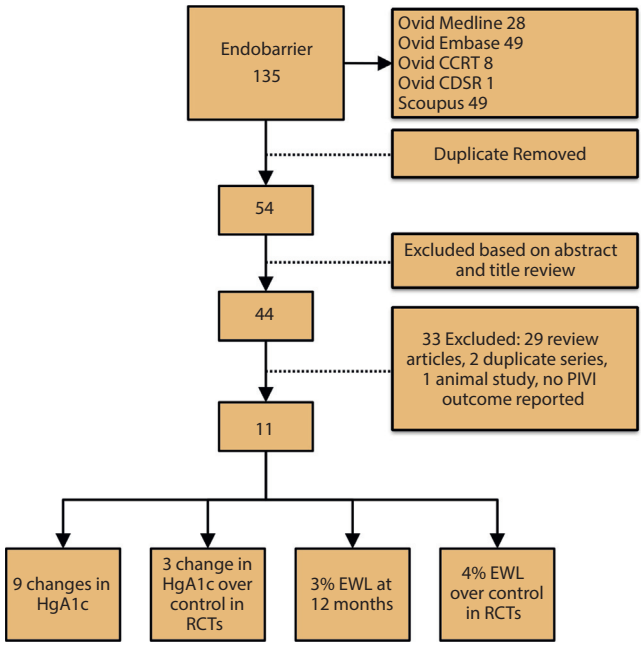

Figure 2. Flow diagram depicting search findings and study selection for inclusion in the EndoBarrier meta-analyses. *CCRT*, Cochrane Central Register of Controlled Trials; *CDSR*, Cochrane Database of Systematic Reviews; *%EWL*, percentage of excess weight loss; *HgA_{1c}*, glycosylated hemoglobin; *RCTs*, randomized, controlled trials.

asymmetry were used to assess potential publication bias. We also performed subgroup analyses and meta-regression when possible. Analyses were performed using the comprehensive Meta-analysis software (Borenstein M, et al. Comprehensive Meta Analysis, Version 2.2, July 2011, Biostat Inc, Englewood, NJ).

RESULTS

Search results

Results of the searches are summarized in Figures 1 and 2. Studies included in the meta-analyses are summarized in Table 1. Eighty-two studies were included in the Orbera IGB systematic review.[10-91] Sixty-eight studies were used to calculate adverse events and early removal rates,[10-19,23-41,43-57,59-63,65,66,68-72,75,78-80,82-85,87,88,90] 17 reported %EWL at 12 months (6 months after balloon removal),[15,25,28,35,41,44,46,50,57,59,60,65,67-69,72,81] 3 RCTs reported the %EWL over a sham or control group at balloon removal,[30,72,87] 55 reported the percentage of total body weight loss (%TBWL) at 6 months,[10,15,17,19-21,26-28,31-34,36-38,41-44,46-51,53-58,60-66,68-71,73,74,79,81-83,86,88-91] 3 reported %TBWL at 12 months,[44,68,81] and 2 reported %TBWL at 36 months.[45,79]

For the EndoBarrier DJBS meta-analyses, 11 studies met inclusion criteria.[92-102] Of these, 9 reported adverse events and early removal rates,[92-97,99-101] 3 reported %EWL at 12 months,[97,100,101] 4 were RCTs that reported %EWL over a sham or control group at device removal,[92,94,95,100] 9 reported changes in glycosylated hemoglobin (HgA_{1c}),[92,93,95-100,102] and 3 reported changes in HgA_{1c} over a sham or control group in RCTs.[93,95,100]

%EWL at 12 months and mean difference in %EWL over a control group for primary EBTs

Orbera IGB. Based on a meta-analysis of 17 studies including 1638 patients, the %EWL with the Orbera IGB at 12 months was 25.44 (95% CI, 21.47-29.4) (Fig. 3). This finding was associated with a high degree of heterogeneity (I^2 = 97.4%). There was no evidence of publication bias based on a visual inspection of the funnel plot. Three RCTs compared %EWL in patients who received the Orbera IGB (n = 131) with a control group (n = 95). The mean difference in %EWL in patients who received the Orbera IGB over controls was 26.9% (95% CI, 15.6–38.2; $P \leq .001$) (Fig. 4). This finding was associated with a high degree of heterogeneity (I^2 = 87.6%). There was no evidence of publication bias based on a visual inspection of the funnel plot.

EndoBarrier DJBS. Three studies enrolling 105 patients indicated that the EndoBarrier DJBS may exceed the PIVI threshold of 25% EWL at 12 months by achieving a %EWL of 35.3% (95% CI, 24.6-46.1) at 12 months (Fig. 5). Four RCTs compared 12 to 24 weeks of treatment with the EndoBarrier DJBS (90 subjects) with a sham or control arm (84 subjects). The mean %EWL difference compared with a control group was significant at 9.4% (95% CI, 8.26–10.65). The pooled %EWL of the EndoBarrier DJBS over control did not meet the 15% PIVI threshold (Fig. 6); however, the duration of these studies (12-24 weeks) was 25% to 50% of the current duration of treatment with the EndoBarrier DJBS (12 months). Both of the above findings were associated with a high degree of heterogeneity, but there was no evidence of publication bias on visual inspection of the funnel plot.

The EndoBarrier DJBS demonstrated an impact on diabetic control after implantation, with improvements in HgA_{1c} from −0.7 (95% CI, −1.76 to 0.2; $P = .16$) at 12 weeks to −1.7 (95% CI, −2.5 to -0.86; $P < .001$) at 24 weeks, and −1.5 (95% CI, −2.2 to −0.78; $P < .001$) after 52 weeks implantation (Fig. 7). This improvement in HgA_{1c} is statistically significant compared with a sham or control diabetic group, where the EndoBarrier DJBS resulted in an additional −1% (95% CI, −1.67 to −0.4; $P = .001$) improvement in HgA_{1c} compared with that seen in controls (Fig. 8).

%TBWL for nonprimary EBTs (bridge therapy). Sufficient data (>5 studies reporting %TBWL at 6 months) were available to evaluate the effectiveness of the Orbera IGB as bridge (nonprimary) obesity therapy. The PIVI sets a threshold of 5% TBWL for nonprimary (bridge) EBTs. The pooled %TBWL after Orbera IGB implantation was 12.3% (95% CI, 7.91–16.73), 13.16% (95% CI, 12.37–13.95), and 11.27% (95% CI, 8.17–14.36) at 3, 6, and 12 months after implantation, respectively (Fig. 9). For an EBT to be used as nonprimary (bridge) obesity

TABLE 1. Studies included in the systematic review and meta-analyses

Name	Country	Study design	Intervention	Age active, y	Weight active, kg HgA_{1c}	BMI active, kg/m^2	Control	Age control, y	Weight control, kg HgA_{1c}	BMI control, kg/m^2	Jadad score RCTs
Orbera IGB											
Loffredo, 2001	Italy	Pros	Orbera + diet	38.2	133.5	46.1					
Sallet, 2004	Brazil	Retro	Orbera + diet	37.5 ± 12.4	110 ± 34.4	38.1 ± 9.4					
Busetto, 2004	Italy	Pros	Orbera + diet	43.3 ± 10.5	171 ± 25.4	58.4 ± 6.6					
Balduyck, 2005	Belgium	Retro	Orbera	36.8 ± 10.2	117.4 ± 22.8	40.8 ± 6.2					
Lordache, 2005	Romania	Retro	Orbera	33.1		32.0 ± 4.5					
Busetto, 2005	Italy	Pros	Orbera + diet		168.1 ± 27.9	55.8 ± 9.9					
Herve, 2005	Belgium	Pros	Orbera + diet	34.8 (range 13.0-64.0)	95.9 (range 67.0-210.0)	34.0 (range 25.3-60.2)					
Mathus-Vliegen, 2005	Netherlands	Pros	Orbera + diet	38.3	124.7	43.8					
Mion, 2005	France	Pros	Orbera + diet	34.9 (range 19.0-57.0)		34.4 ± 0.7					
Angrisani, 2006	Italy	Retro	Orbera + diet	37.1 ± 11.6		54.4 ± 8.1					
Genco, 2006	Italy	RCT	Orbera + diet	36.2 ± 5.2		43.9 ± 1.1	Sham	36.3 ± 5.9		43.6 ± 1.8	5.0
Alfalah, 2006	France	Pros	Orbera + diet	33 ± 11	175 ± 25	64 ± 7					
Kotzampassi, 2006	Greece	Pros	Orbera + diet	44.1 ± 8	127.6 ± 27.6						
Spyropoulos, 2007	Greece	Pros	Orbera + diet	40.8 ± 8.1	193.9 ± 29.2	65.3 ± 9.8					
Puglisi (a), 2007	Italy	Pros	Orbera + diet	38 ± 7.9	122.4 ± 19.1	44.7 ± 5.8					
Puglisi (b), 2007	Italy	Pros	Orbera + diet	39 ± 9.6	136.3 ± 27.1	47.6 ± 7.3					
Ganesh, 2007	Singapore	Retro	Orbera + diet	40 (range 28-52)	79.6 (67.6-103)	31.5 (27.8-8.8)					
Rossi, 2007	Italy	Pros	Orbera + diet	45	116	41.5					
Frutos, 2007	Spain	Pros	Orbera	40.1 ± 11.1	149.3 ± 26.3	55.2 ± 6.9					
de Goederen, 2007	Netherlands	Pros	Orbera	36.6 ± 5.7	142.4 ± 25.5	46.5 ± 5.7					
Genco, 2008	Italy	Retro	Orbera + diet	38 ± 10.9	117 ± 22.6	42.1 ± 6.5					
Ricci, 2008	Italy	Retro	Orbera + diet	41.3		42.1 ± 5.8					
Mohamed, 2008	UK	Pros	Orbera + diet	42 ± 9.3	149.9 ± 36.8	52.8 ± 8.2					
Crea, 2009	Italy	Pros	Orbera + diet	36.2 ± 5.7	98.5 ± 16.3	36.2 ± 9.7					
Dastis, 2009	Switzerland	Pros	Orbera + diet	39.2 ± 11.2	96.5 ± 18.8	35 ± 5.6					
Genco, 2009	Italy	Pros	Orbera + diet	40.9 ± 9.3	156.1 ± 18.6	54.1 ± 2.9					
Gottig (a), 2009	Germany	Retro	Orbera + diet	39.1 ± 8.4	211.0 ± 36.9	68.8 ± 8.9					
Gottig (b), 2009	Germany	Retro	Orbera + diet	39 ± 9.6	168.4 ± 58.9	55.6 ± 17.5					
Konopko-Zubrzycka, 2009	Poland	Pros	Orbera + diet	40.0 ± 11.9	138.5 ± 26.2	47.3 ± 5.7					
Ohta, 2009	Japan	Pros	Orbera + diet	40.0 ± 9.0	111.0 ± 28.0	40.0 ± 9.0					
Donadio, 2009	Italy	Pros	Orbera + diet	36.7 ± 10.6	122.2 ± 25.9	44.9 ± 8.9					
Mazure, 2009	Spain	Retro	Orbera + diet	38.1		41.8					
Forlano, 2010	Italy	Pros	Orbera + diet	38.6 ± 12.0	118.8 ± 23.6	43.1 ± 8.0					
Peker, 2010	Turkey	Pros	Orbera + diet	35.5 ± 9.3	119.3 ± 22.6	41.8 ± 8.3					
Saruc, 2010	Turkey	Pros	Orbera + diet	35.2 ± 13.4		43.5 ± 8.7					
Stimac, 2011	Croatia	Pros	Orbera + diet	39.2 ± 10.5	123.2 ± 2.0	41.6 ± 7.5					
Al Kahtani, 2010	Saudi	Pros	Orbera + diet	34.5 ± 11.6	124 ± 39.6	46.7 ± 14.1					
Coskun, 2010	Turkey	Pros	Obera + diet	36.8 ± 8.6	111.5 ± 18.3	40.6 ± 7.62					
Genco, 2010	Italy	Pros	Orbera + diet	31.4 ± 2.6	106 ± 12.5	42.6 ± 2.7					
Mui, 2010	China	Pros	Orbera + diet	37.8 ± 10.0	103.7 ± 24.1	38.4 ± 8.0					
DeCastro, 2010	Spain	Pros	Orbera + diet	45.4 ± 8.0	121 ± 17.0	44.2 ± 5.0					
Nikolic, 2011	Croatia	Pros	Orbera + diet	35	114	41.4					
Dabrowiecki, 2011	Poland	Retro	Orbera	51.6	115 ± 25.1	43 ± 9.0					

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TABLE 1. Continued

Name	Country	Study design	Intervention	Age active, y	Weight active, kg HgA_{1c}	BMI active, kg/m^2	Control	Age control, y	Weight control, kg HgA_{1c}	BMI control, kg/m^2	Jadad score RCTs
Lopez-Nava, 2011	Spain	Retro	Orbera + diet	38.4 ± 16.1	106.3 ± 21.5	37.6 ± 5.7					
Tayyem, 2011	Saudi	Pros	Orbera + diet	40.9 ± 12.1	172 ± 19.5	61.4 ± 8.3					
Giardiello, 2012	Italy	Pros	Orbera + diet	36.7 ± 10.9	125 ± 20.0	46.5 ± 5.9					
Bozkurt, 2012	Turkey	Retro	Orbera + diet	34.37 ± 9.61	113.2 ± 27.0	39 ± 8.22					
Farina, 2012	Italy	Pros	Orbera + diet	36.6 ± 1.5	115 ± 3.3	42.3 ± 1.0					
Kotzampassi, 2012	Greece	Pros	Orbera + diet	39.0 ± 11.5	126.2 ± 28.3	43.7 ± 8.4					
Papavramidis, 2012	Greece	Retro	Orbera	38.1 ± 12.0	111 ± 17.7	40.0 ± 5.4					
Papavramidis, 2012	Greece	Retro	Orbera	40.7 ± 11.4	113.7 ± 21.1	41.6 ± 8.6					
Benamouzig, 2013	Hong-Kong	Pros	Orbera + diet	38.9 ± 9.7		36.6 ± 3.3					
Fuller, 2013	Australia	RCT	Orbera + behavioral therapy	43.4 ± 9.4	104.6 ± 14.8	36 ± 2.7	Behavioral therapy	48.1 ± 7.3	103.4 ± 13.9	36.7 ± 2.9	3
Deliopoulou, 2013 (nondepressed)	Greece	Pros	Orbera + diet	33.9 ± 11.5	122.3 ± 24.2	41.9 ± 7.4					
Deliopoulou, 2013 (depressed)	Greece	Pros	Orbera + diet	37.5 ± 11.8	124.7 ± 32.3	43.5 ± 9.5					
Abdel, 2013	Egypt	Retro	Orbera + diet	33.2 ± 12.0	124.4 ± 35.8	45.3 ± 11.0					
Genco, 2013	Multi	Retro	Orbera	38.7 ± 3.6	80.5 ± 11.4	28.6 ± 0.4					
Dogan, 2013	Turkey	Pros	Orbera + diet	37.9 ± 10.6	127.6 ± 34.6	44.7 ± 12.4					
Tai, 2013	Taiwan	Pros	Orbera + diet	31.6		32.4 ± 3.7					
Khan, 2013	UK	Pros	Orbera + diet	45.0 ± 1.4		69.1 ± 1.0					
Su, 2013	Taiwan	Pros	Orbera + diet	36.8 ± 9.16	93.9 ± 24	35.9 ± 9.0					
Mathus-Vliegen, 2014	Netherlands	Pros	Orbera + diet	37.7 ± 10.9	124.0 ± 21.1	43.0 ± 5.5					
Mohammed, 2014	Egypt	RCT	Orbera + diet	44.0 (range 29.0-63.0)	136.9 ± 8.0	47.87 ± 1.0	Life-style	41.0 (range 32.0-56.0)	137.8 ± 9.8	47.5 ± 1.8	2
Zafar, 2014	Pakistan	Retro	Orbera + diet	33.0 ± 8.0	125.8 ± 37.5	43.6 ± 3.6					
Kotzampassi, 2014	Greece	Retro	Orbera + diet	39.5 ± 11.2	126.6 ± 27.9	43.9 ± 8.4					
Genco, 2014	Italy	Pros	Orbera	41.4 ± 11.8		44.9 ± 8.4					
Genco, 2014	Italy	Pros	Orbera + diet	37.4		43.7					
EndoBarrier DJBS											
					Weight active, kg HgA_{1c}				Weight control, kg HgA_{1c}		
Tarnoff, 2009	Chile	RCT	EndoBarrier + diet	38.0 ± 10.0	114.0 ± 20.9	42.0 ± 5.1	Life-style	43.0 ± 10.6	108.0 ± 12.0	40.0 ± 3.5	1
Rodriguez, 2009	Chile	RCT	EndoBarrier + diet	45.0 ± 7.0	103.4 ± 21.3 9.2 ± 1.7	38.9 ± 5.9	Sham	51 ± 13	106.2 ± 21.6 9 ± 2	39 ± 7.2	4
Gersin, 2010	USA	RCT	EndoBarrier + diet	45 ± 7	131 ± 21	46 ± 5	Sham	43 ± 10	130 ± 21	46 ± 6	4
Schouten, 2010	Netherlands	RCT	EndoBarrier + diet	40.9 (range 20-59)	142.4 (range 114-189) 8.8 ± 1.7	48.9 (range 39-60)	Life-style	41.2 (range 19-57)	137.5 (range 86-160) 7.3 ± 0.1	49.2 (range 37-60)	3
Escalona, 2012	Chile	Pros	EndoBarrier + diet	35.6 ± 10.4	108.9 ± 17.6 6.3 ± 0.3	43.7 ± 5.9					
De Moura, 2012	Brazil	Pros	EndoBarrier + diet	46.2 ± 10.5	119.2 ± 22.9 8.9 ± 1.7	44.8 ± 7.4					
De Jonge, 2013	Netherlands	Pros	EndoBarrier + diet	51.0 ± 2.0	116.0 ± 5.8 8.4 ± 0.2	37.0 ± 1.3					
Cohen (a), 2013	Brazil	Pros	EndoBarrier + diet	49.8 ± 6.7	82 ± 4.5 8.6 ± 0.2	30 ± 0.9					
Cohen (b), 2013	Brazil	Pros	EndoBarrier + diet	49.8 ± 6.7	84.0 ± 16.6 8.7 ± 0.9	30.0 ± 3.6					

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TABLE 1. Continued

Name	Country	Study design	Intervention	Age active, y	Weight active, kg HgA_{1c}	BMI active, kg/m^2	Control	Age control, y	Weight control, kg HgA_{1c}	BMI control, kg/m^2	Jadad score RCTs
Koehestanie, 2014	Netherlands	RCT	EndoBarrier + diet	49.5 (range 42-58)	105.4 (range 98.2-116.1) 8.3 (range 7.7-9)	34.6 (range 32.4-38.1)	Life-style	49 (range 44-55)	110.8 (range 99.7-129) 8.3 (7.7-8.9)	36.8 (range 32.6-42)	3
Munoz, 2014	Chile	Pros	EndoBarrier + diet	35.4 ± 9.7		43.0 ± 5.6					

BMI, Body mass index; *RCTs*, randomized, controlled trials; *IGB*, intragastric balloon; *Pros*, prospective; *Retro*, retrospective.

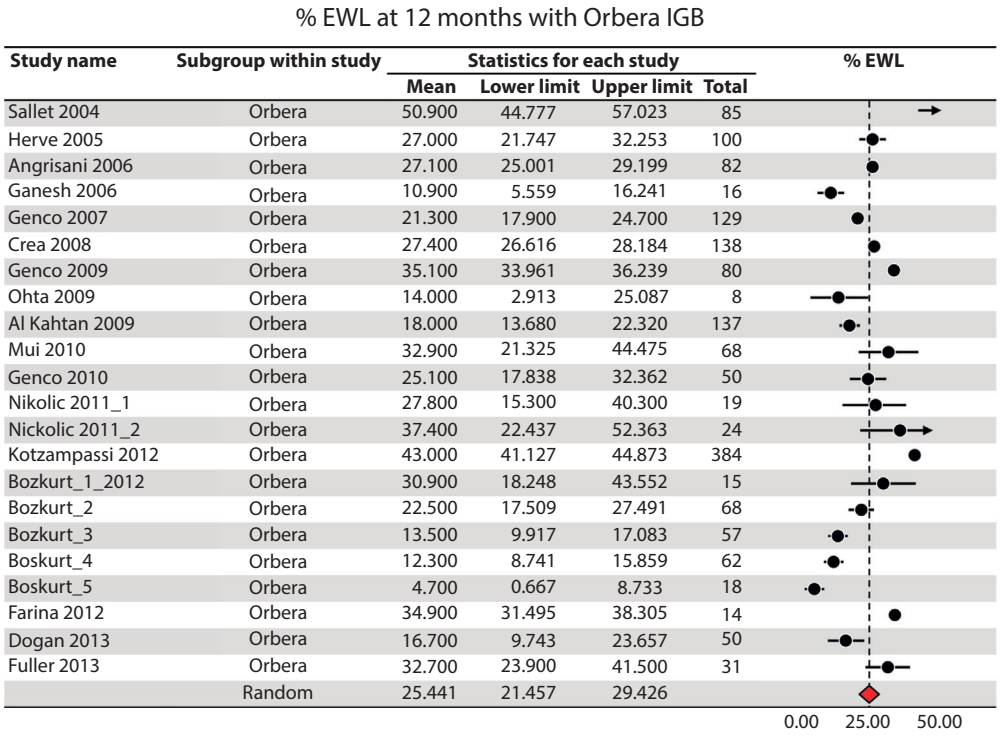

Figure 3. Forest plot of studies evaluating the percentage of excess weight loss (%EWL) at 12 months after intragastric balloon (IGB) implantation.

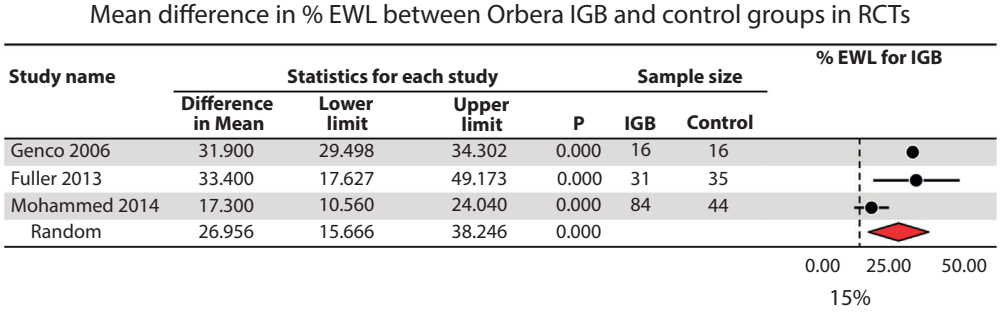

Figure 4. Forest plot of studies evaluating the mean difference in the percentage of excess weight loss (%EWL) compared with sham or control groups after intragastric balloon (IGB) implantation. *RCTs*, randomized, controlled trials.

therapy, it needs to perform sufficiently well in patients with a BMI >40 kg/m^2. We therefore performed a meta-regression to assess the efficacy of the Orbera IGB in patients within a range of BMIs. Figure 10 demonstrates the association between the baseline BMI and the %TBWL achieved at 6 months after Orbera IGB implantation. The regression line shows no statistically significant difference ($P = .09$) in %TBWL over a wide range of BMIs, indicating

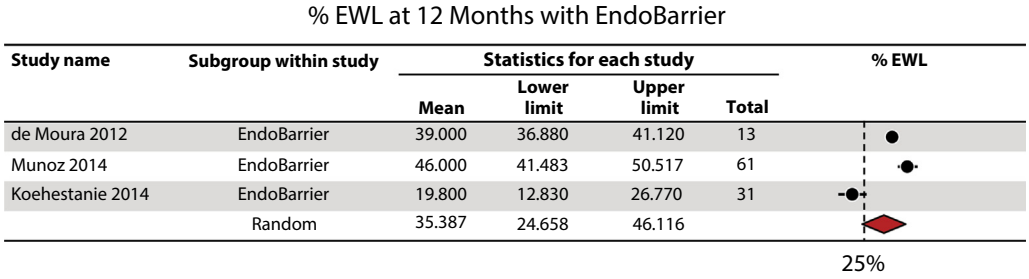

Figure 5. Forest plot of studies evaluating the percentage of excess weight loss (%EWL) at 12 months after EndoBarrier implantation.

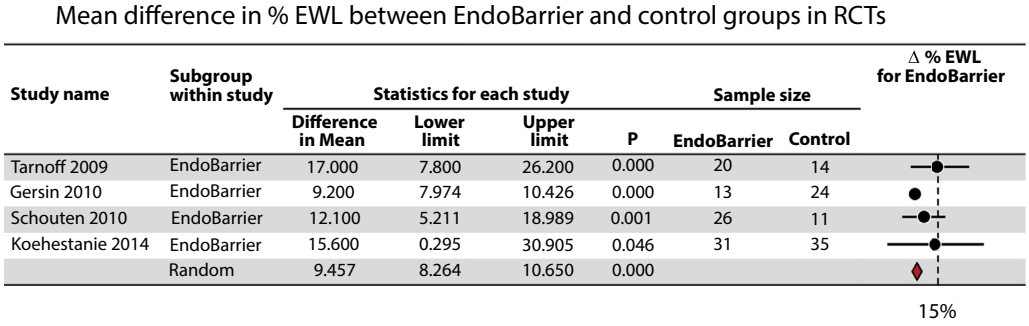

Figure 6. Forest plot of studies evaluating the mean difference in the percentage of excess weight loss (%EWL) compared with the sham or control groups after EndoBarrier implantation. *RCTs*, randomized, controlled trials.

that the Orbera IGB performs as well in higher BMI groups and thus might be effective as a nonprimary (bridge) EBT.

Safety

Intragastric balloons. The rates of adverse events after implantation of the Orbera IGB were pooled from a manual review of 68 studies and are summarized in Figure 11. Pain and nausea were frequent side effects after Orbera IGB implantation, occurring in 33.7% of subjects. The early removal rate for the Orbera IGB was approximately 7%. Serious side effects with the Orbera IGB were rare, with an incidence of migration and gastric perforation of 1.4% and 0.1%, respectively. Fifty percent (4/8) of gastric perforations with the Orbera IGB occurred in patients who had undergone previous gastric surgeries. Four deaths associated with the Orbera IGB are reported in the literature, and these were either related to gastric perforation or an aspiration event.[23,24,31]

EndoBarrier DJBS. The published safety profile of the EndoBarrier DJBS appears favorable based on experience with 271 implantations detailed in the literature. The incidence of early removal and adverse events are detailed in Figure 12. Serious adverse events included migration (4.9%), GI bleeding (3.86%), sleeve obstruction (3.4%), liver abscess (0.126%), cholangitis (0.126%), acute cholecystitis (0.126%), and esophageal perforation (0.126%) secondary to trauma from an uncovered barb at withdrawal. Enrollment in the multicenter U.S. pivotal trial was placed on hold in March 2015 by the U.S. Food and Drug Administration, after reports of 4 cases of hepatic abscess among the 325 patients already enrolled. The U.S. Food and Drug Administration has requested additional information to further analyze the risk/benefit profile of the EndoBarrier DJBS in this study. The analysis will be critical in determining the safety of this device.

DISCUSSION

Combating the obesity epidemic requires a concerted multipronged effort, including societal, behavioral, and therapeutic interventions. Our current therapeutic armamentarium to treat obesity lacks nonsurgical, efficacious, and lower cost interventions. Despite the positive impact of bariatric surgery on individual patients, only approximately 1% of qualified patients receive surgery.[103] As previously discussed, this may be related to multiple factors including access and patient preference, as well as the risks and cost of surgery. Given this low use rate, a significant gap exists between those who get effective obesity treatment and those who do not. Considering the modest effects seen with medications or lifestyle intervention alone in patients with obesity, EBTs appear well suited to bridge the current management gap by offering an effective weight loss intervention with potentially lower risks, lower costs, and higher patient acceptability. These benefits of EBTs will need to be studied and documented as we move forward in the management of obesity.

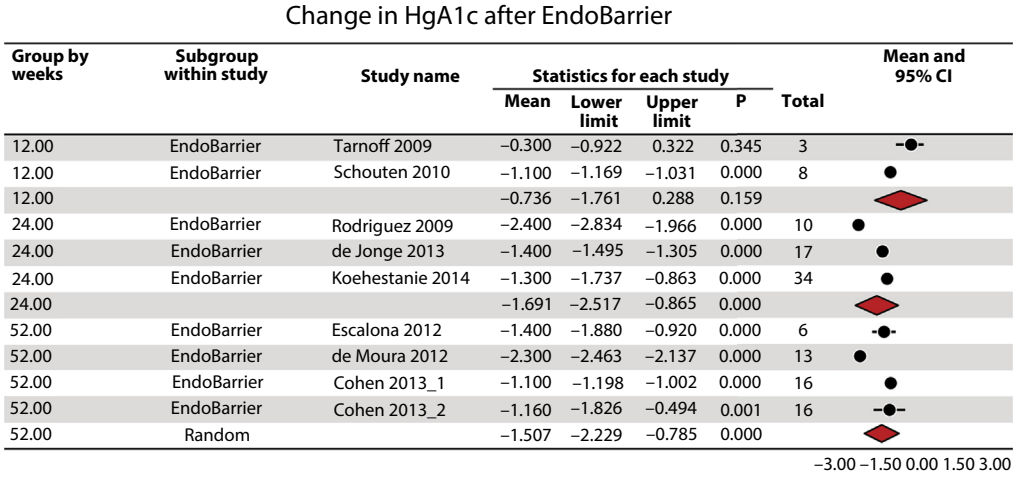

Figure 7. Forest plot depicting changes in glycosylated hemoglobin (HgA_{1c}) after 12, 24, and 52 weeks of EndoBarrier implantation.

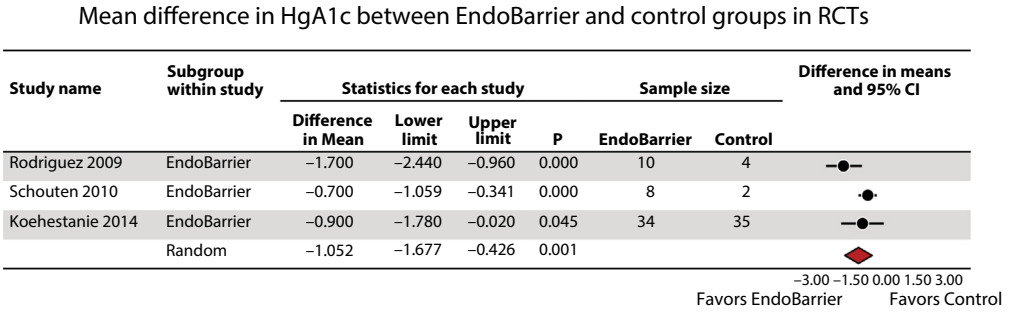

Figure 8. Forest plot of studies reporting mean difference in glycosylated hemoglobin (HgA_{1c}) between EndoBarrier and sham or control groups in randomized, controlled trials (RCTs). *CI*, confidence interval.

A joint task force from the ASGE and American Society for Metabolic and Bariatric Surgery defined thresholds for adopting EBTs in clinical practice in a PIVI document.[6] This systematic review and series of meta-analyses confirm that the Orbera IGB meets these thresholds both as a primary or bridge (nonprimary) EBT and is statistically significantly superior to control. We await review of the pivotal U.S. trial data to determine the efficacy and safety of the EndoBarrier DJBS. Newer IGBs such as the ReShape Duo and Spatz IGB, aspiration therapy, endoscopic gastroplasty techniques, and other EBTs reviewed in detail in a status evaluation report on this topic[5] are also undergoing studies at this time with insufficient data to include in this meta-analysis. These data are required to evaluate their ability to meet PIVI thresholds. Our Task Force concludes that the Orbera IGB has met the PIVI criteria for the management of obesity with a mean %EWL of 25% at 1 year. Clinical implementation should proceed as previously described in the bariatric PIVI document,[6] an excerpt of which is detailed below:

> *Weight loss interventions have been demonstrated to achieve superior outcomes when the intervention is performed as part of a comprehensive, multidisciplinary treatment program. EBT should also be performed in this context in order to achieve maximal benefit. Nutritional support, experienced nursing care, behavioral medicine specialists, and physicians experienced in the management of obese patients, are essential components of such programs. In addition, the ability and availability of physicians and surgeons willing and able to manage potential complications in obese patients is advised. Training and skill acquisition with EBT techniques and technologies are mandatory before clinical application is undertaken, and should include didactic as well as hands-on practical education. Importantly, any practitioner who is interested in performing an EBT should also be educated in the clinical management of obese patients. The duration and type of training is likely to depend on the complexity of a particular EBT. For all EBTs, early studies should assess the learning curve in order to guide subsequent training and credentialing processes.*[6]

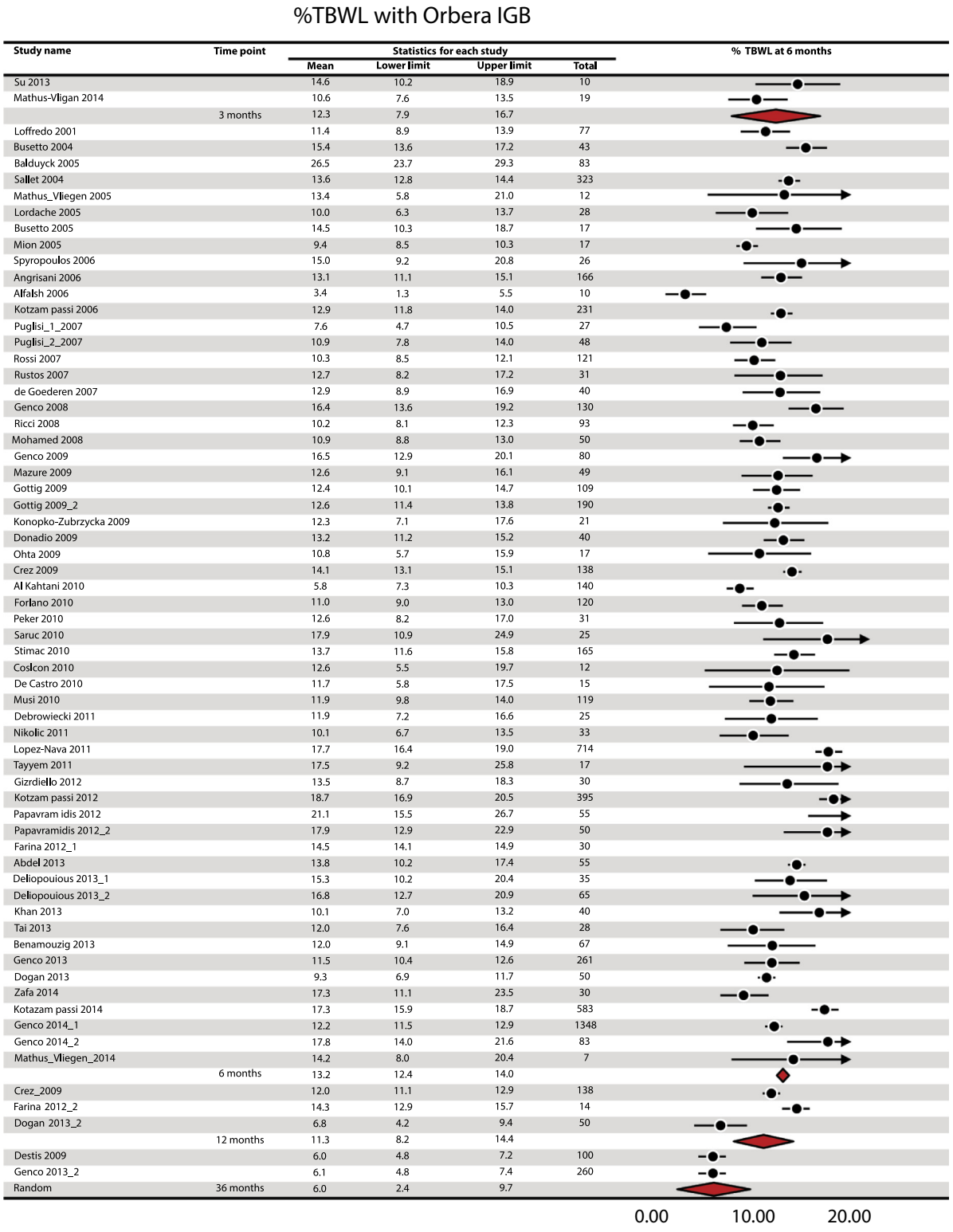

Figure 9. Forest plot of studies reporting the percentage of total body weight loss (%TBWL) after Orbera intragastric balloon implantation.

As stated earlier, these recommendations should not be taken to imply that these devices could be used on their own without appropriate screening, dietary, and lifestyle intervention support, nor should they be used without consideration of surgical therapy. These devices should be used in conjunction with other stakeholders taking care of patients with obesity, such as medical obesity specialists, behavioral therapy professionals, registered

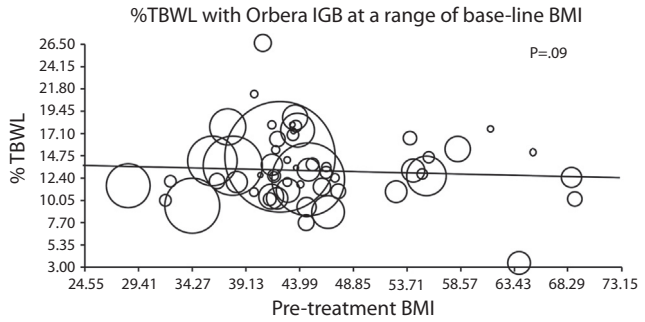

Figure 10. Meta-regression linear plot depicting the best-fit regression line of the association between baseline body mass indexes (BMIs) and percentage of excess weight loss (%EWL) at 6 months after Orbera intragastric balloon (IGB) implantation. The sample size of individual studies is proportional to the diameter of the circle by which it is represented on the graph.

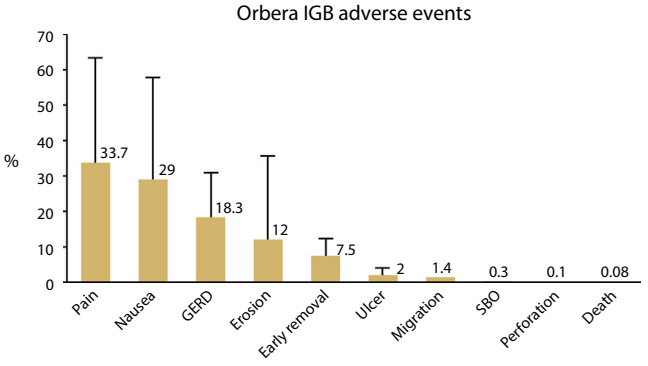

Figure 11. Pooled rates of adverse events observed with the Orbera intragastric balloon (IGB). *SBO*, small bowel obstruction.

dietitians, and bariatric surgeons. EBTs should complement, rather than compete with, current obesity therapy options and should be used as adjunctive therapy as outlined in a previous ASGE publication.[6] Endoscopy expertise should be incorporated within a multidisciplinary team to optimize the care of patients with obesity.

Limitations of our meta-analyses include the high degree of heterogeneity among included studies, risk of bias in non-RCT studies, different methods used among studies to report the %EWL (Metropolitan Life Tables vs BMI 25 method), and lack of sufficient data to evaluate all PIVI-defined thresholds. One of the thresholds requires a comparison of EBT weight loss outcomes with a control (not sham) group. To optimize power, we included studies that compared EBTs with both sham and control groups. Furthermore, there were insufficient data available to evaluate the use of low-risk EBTs with significant impact on 1 or more obesity-related comorbidities in Class I obese patients.

The ASGE will continue to work with ASGE members and other medical societies involved in obesity therapy to promote and facilitate widespread adoption and implementation of safe and effective EBTs in clinical practice.

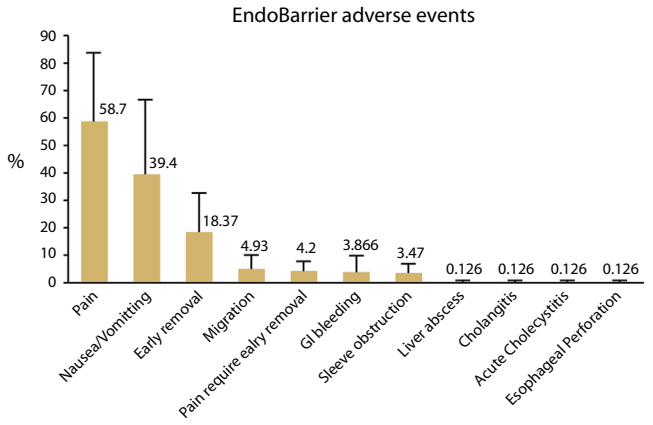

Figure 12. Pooled rates of adverse events observed with the EndoBarrier.

DISCLOSURE

Dr Abu Dayyeh is a consultant for and has received a grant from Apollo Endosurgery; is a consultant for Metamodix; has received grant support from Aspire Bariatric and research support from GI Dynamics. Dr Edmundowicz is a consultant for and serves on the advisory board of Boston Scientific, Olympus, GI Dynamics, and Fractyl; is a stockholder and serves on the advisory board for SynerZ Medical; is a consultant for Beacon Endoscopic; and has received institutional research grants from Aspire Bariatrics, US GI, ReShape Medical, Obalon, and Baranova. Dr Sullivan is a consultant for Obalon and has performed contracted research for ReShape Medical, GI Dynamics, Aspire Bariatrics, and USGI Medical. Dr Jonnalagadda served on the data safety monitoring and clinical events monitoring committee for ReShape Medical. Dr Thompson is a consultant for Boston Scientific, Covidien, Beacon Endoscopic, Apollo Endosurgery; received lab support from Olympus, a research grant from Aspire Bariatrics, and has an ownership interest in GI Windows. All other authors disclosed no financial relationships relevant to this publication.

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Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; BMI, body mass index; CI, confidence interval; DJBS, duodenal-jejunal bypass sleeve; EBT, endoscopic bariatric therapy; %EWL, percentage of excess weight loss; HgA_{1c}, glycosylated hemoglobin; IGB, intragastric balloon; PIVI, Preservation and Incorporation of Valuable endoscopic Innovations; RCT, randomized, controlled trial; %TBWL, percentage of total body weight loss.

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SUPPLEMENTARY MATERIAL A

Ovid

Database(s): Embase 1988 to 2014 Week 21, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials April 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 2014

Search Strategy:

#	Searches	Results
1	exp Gastric Balloon/	584
2	("gastric balloon*" or "gastric bubble*" or "intragastric balloon*" or "intragastric bubble*" or "intra-gastric balloon*" or "intra-gastric bubble*" or "ballobes balloon*" or "ballobes bubble*" or "stomach balloon*" or "stomach bubble*").mp.	1600
3	1 or 2	1600
4	exp Obesity/	412186
5	(obes* or "body mass ind*" or adipos* or overweight or "over weight" or "overload syndrom*" or overeat* or "over eat*" or overfeed* or "over feed*" or overfed or "over fed" or "weight cycling" or ((weight or fat) adj3 (gain* or reduc* or los* or maint* or decreas* or watch* or control*)) or "skinfold thickness" or antiobesity or "anti- obesity" or obesitas or bodyweight or "body weight").mp.	1442103
6	4 or 5	1460739
7	3 and 6	1096
8	exp evidence based medicine/	696265
9	exp meta analysis/	126995
10	exp Meta-Analysis as Topic/	27256
11	exp "systematic review"/	74741
12	exp Guideline/ or exp Practice Guideline/	336614
13	exp controlled study/	4416701
14	exp Randomized Controlled Trial/	701733
15	exp triple blind procedure/	58
16	exp Double-Blind Method/	336920
17	exp Single-Blind Method/	49794
18	exp latin square design/	265
19	exp Placebos/	261084
20	exp Placebo Effect/	6972
21	exp comparative study/	2418707
22	exp Cross-Sectional Studies/	290387
23	exp Cross-Over Studies/	98939
24	exp Cohort Studies/	1621921
25	exp longitudinal study/	1033539
26	exp retrospective study/	829818
27	exp prospective study/	676547
28	exp population research/	66635
29	exp observational study/	57953
30	exp clinical trial/	1686114
31	clinical study/	50508
32	exp Evaluation Studies/	198374
33	exp Evaluation Studies as Topic/	1096825
34	exp quantitative study/	5427
35	exp validation studies/	109152
36	exp experimental study/	13839
37	exp quasi experimental study/	1883
38	exp field study/	1434
39	in vivo study/	182388
40	exp panel study/	357
41	exp Pilot Projects/	164417
42	exp pilot study/	164417
43	exp prevention study/	1988
44	exp replication study/	882
45	exp theoretical study/	1325532
46	exp Feasibility Studies/	95926
47	exp Models, Theoretical/	1344399
48	exp trend study/	10719
49	exp correlational study/	9901
50	exp case-control studies/	752866
51	exp confidence interval/	118252
52	exp regression analysis/	547509
53	exp proportional hazards model/	89713
54	exp multivariate analysis/	329686
55	"limit follow up studies to medline only. embase maps to follow up".ti.	0
56	exp follow up studies/	1294917
57	exp case study/	1704812
58	"limit case study above to embase only. medline maps to case report".ti.	0
59	odds ratio/	357935
60	"limit odds ratio above to embase. medline maps to risk".ti.	0
61	((evidence adj based) or (meta adj analys*) or (systematic* adj3 review*) or guideline* or (control* adj2 study) or (control* adj2 trial) or (randomized adj2 study) or (randomized adj2 trial) or (randomised adj2 study) or (randomised adj2 trial) or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or multivariate or random* or control* or "comparative study" or "comparative survey" or "comparative analysis"	19517783

(*continued on the next page*)

Continued

#	Searches	Results
	or (intervention* adj2 study) or (intervention* adj2 trial) or "cross-sectional study" or "cross-sectional analys*" or "cross-sectional survey*" or "cross-sectional design*" or "prevalence study" or "prevalence analys*" or "prevalence survey*" or "disease frequency study" or "disease frequency analys*" or "disease frequency survey*" or crossover or "cross-over" or "cohort study" or "cohort survey" or "cohort analysis" or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "retrospective study" or "retrospective survey" or "retrospective analysis" or "prospective study" or "prospective survey" or "prospective analysis" or "population study" or "population survey" or "population analysis" or "concurrent study" or "concurrent survey" or "concurrent analysis" or "incidence study" or "incidence survey" or "incidence analysis" or "follow-up study" or "follow-up survey" or "follow-up analysis" or "observational study" or "observational survey" or "observational analysis" or "case study" or "case series" or "clinical series" or "case studies" or "clinical study" or "clinical trial" or "evaluation study" or "evaluation survey" or "evaluation analysis" or "twin study" or "twin survey" or "twin analysis" or "quantitative study" or "quantitative analys*" or "validation study" or "validation survey" or "validation analysis" or "experimental study" or "experimental analysis" or "quasi experimental study" or "quasi experimental analysis" or "quasiexperimental study" or "quasiexperimental analysis" or "field study" or "field survey" or "field analysis" or "in vivo study" or "in vivo analysis" or "panel study" or "panel survey" or "panel analysis" or "pilot study" or "pilot survey" or "pilot analysis" or "prevention study" or "prevention survey" or "prevention analysis" or "replication study" or "replication analysis" or "theoretical study" or "theoretical analysis" or "feasibility study" or "feasibility analysis" or "trend study" or "trend survey" or "trend analysis" or (correlaton* adj study) or (correlaton* adj analys*) or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case compeer study" or "case comparison study" or "odds ratio" or "confidence interval" or study or pilot or trial or cohort* or "regression analysis" or "hazards model*" or "multivariate analysis" or "change analysis").mp.	
62	from 56 keep 758892-1253282	494391
63	from 57 keep 1-23743	23743
64	from 59 keep 1-296215	296215
65	or/8-54	12261471
66	or/61-65	20990546
67	7 and 66	724
68	from 7 keep 602-1049	448

Continued

#	Searches	Results
69	limit 68 to (clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or evaluation studies or guideline or meta analysis or multicenter study or observational study or pragmatic clinical trial or practice guideline or randomized controlled trial or systematic reviews or validation studies) [Limit not valid in Embase,CCTR,CDSR; records were retained]	111
70	67 or 69	725
71	limit 70 to (book or book series or editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR,CDSR; records were retained]	27
72	70 not 71	698
73	72 not (exp animals/ not exp humans/)	680
74	from 7 keep 1093-1096	4
75	73 or 74	684
76	limit 75 to english language [Limit not valid in CDSR; records were retained]	616
77	76 not "conference abstract".pt.	477
78	remove duplicates from 77	274

Scopus

1 TITLE-ABS-KEY("gastric balloon*" or "gastric bubble*" or "intragastric balloon*" or "intragastric bubble*" or "intra-gastric balloon*" or "intra-gastric bubble*" or "ballobes balloon*" or "ballobes bubble*" or "stomach balloon*" or "stomach bubble*")

2 TITLE-ABS-KEY(obes* or "body mass ind*" or adipos* or overweight or "over weight" or "overload syndrom*" or overeat* or "over eat*" or overfeed* or "over feed*" or overfed or "over fed" or "weight cycling" or ((weight or fat) W/3 (gain* or reduc* or los* or maint* or decreas* or watch* or control*)) or "skinfold thickness" or antiobesity or "anti-obesity" or obesitas or bodyweight or "body weight")

3 TITLE-ABS-KEY(((evidence W/1 based) or (meta W/1 analys*) or (systematic* W/3 review*) or guideline* or (control* W/2 study) or (control* W/2 trial) or (randomized W/2 study) or (randomized W/2 trial) or (randomised W/2 study) or (randomised W/2 trial) or (doubl* W/1 blind*)

or (doubl* W/1 mask*) or (singl* W/1 blind*) or (singl* W/1 mask*) or (tripl* W/1 blind*) or (tripl* W/1 mask*) or (trebl* W/1 blind*) or (trebl* W/1 mask*) or "latin square" or placebo* or multivariate or random* or control* or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* W/2 study) or (intervention* W/2 trial) or "cross-sectional study" or "cross-sectional analys*" or "cross-sectional survey*" or "cross-sectional design*" or "prevalence study" or "prevalence analys*" or "prevalence survey*" or "disease frequency study" or "disease frequency analys*" or "disease frequency survey*" or crossover or "cross-over" or "cohort study" or "cohort survey" or "cohort analysis" or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "retrospective study" or "retrospective survey" or "retrospective analysis" or "prospective study" or "prospective survey" or "prospective analysis" or "population study" or "population survey" or "population analysis" or "concurrent study" or "concurrent survey" or "concurrent analysis" or "incidence study" or "incidence survey" or "incidence analysis" or "follow-up study" or "follow-up survey" or "follow-up analysis" or "observational study" or "observational survey" or "observational analysis" or "case study" or "case series" or "clinical series" or "case studies" or "clinical study" or "clinical trial" or "evaluation study" or "evaluation survey" or "evaluation analysis" or "twin study" or "twin survey" or "twin analysis" or "quantitative study" or "quantitative analys*" or "validation study" or "validation survey" or "validation analysis" or "experimental study" or "experimental analysis" or "quasi experimental study" or "quasi experimental analysis" or "quasiexperimental study" or "quasiexperimental analysis" or "field study" or "field survey" or "field analysis" or "in vivo study" or "in vivo analysis" or "panel study" or "panel survey" or "panel analysis" or "pilot study" or "pilot survey" or "pilot analysis" or "prevention study" or "prevention survey" or "prevention analysis" or "replication study" or "replication analysis" or "theoretical study" or "theoretical analysis" or "feasibility study" or "feasibility analysis" or "trend study" or "trend survey" or "trend analysis" or (correlaton* W/1 study) or (correlaton* W/1 analys*) or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case compeer study" or "case comparison study" or "odds ratio" or "confidence interval" or study or pilot or trial or cohort* or "regression analysis" or "hazards model*" or "multivariate analysis" or "change analysis"))

4 Language(English)

5 1 and 2 and 3 and 4

6 DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

7 5 and not 6

8 PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)

9 7 and not 8

SUPPLEMENTARY MATERIAL B

Ovid

Database(s): Embase 1988 to 2015 Week 02, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials December 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to November 2014

Search Strategy:

#	Searches	Results
1	(DJBL or DJBLs or DJBS or DJBSs or "duodenaljejunal bypass liner*" or "duodenal-jejunal bypass liner*" or "duodenaljejunal bypass sleeve*" or "duodenal-jejunal bypass sleeve*" or "duodenojejunal bypass liner*" or "duodeno-jejunal bypass liner*" or "duodenojejunal bypass sleeve*" or "duodeno-jejunal bypass sleeve*" or EndoBarrier or "fluoropolymer liner*" or "fluoro-polymer liner*" or "fluoropolymer sleeve*" or "fluoro-polymer sleeve*").mp.	200
2	exp Obesity/	436924
3	(obes* or "body mass ind*" or adipos* or overweight or "over weight" or "overload syndrom*" or overeat* or "over eat*" or overfeed* or "over feed*" or overfed or "over fed" or "weight cycling" or ((weight or fat) adj3 (gain* or reduc* or los* or maint* or decreas* or watch* or control*)) or "skinfold thickness" or antiobesity or "anti- obesity" or obesitas or bodyweight or "body weight").mp.	1513725
4	2 or 3	1533608
5	1 and 4	195
6	exp evidence based medicine/	741830
7	exp meta analysis/	137765
8	exp Meta-Analysis as Topic/	30742
9	exp "systematic review"/	83264
10	exp Guideline/ or exp Practice Guideline/	350530
11	exp controlled study/	4594667
12	exp Randomized Controlled Trial/	722844
13	exp triple blind procedure/	81
14	exp Double-Blind Method/	341985
15	exp Single-Blind Method/	51449
16	exp latin square design/	282
17	exp Placebos/	271594
18	exp Placebo Effect/	7294
19	exp comparative study/	2451532
20	exp Cross-Sectional Studies/	313291
21	exp Cross-Over Studies/	101799
22	exp Cohort Studies/	1675281
23	exp longitudinal study/	257521
24	exp retrospective study/	877532

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Continued

#	Searches	Results
25	exp prospective study/	706047
26	exp population research/	69253
27	exp observational study/	72048
28	exp clinical trial/	1731802
29	clinical study/	56623
30	exp Evaluation Studies/	208888
31	exp Evaluation Studies as Topic/	1121100
32	exp quantitative study/	6221
33	exp validation studies/	114572
34	exp experimental study/	15402
35	exp quasi experimental study/	2206
36	exp field study/	1630
37	in vivo study/	195632
38	exp panel study/	387
39	exp Pilot Projects/	172914
40	exp pilot study/	172914
41	exp prevention study/	2258
42	exp replication study/	1006
43	exp theoretical study/	1350844
44	exp Feasibility Studies/	101127
45	exp Models, Theoretical/	1371253
46	exp trend study/	11892
47	exp correlational study/	12443
48	exp case-control studies/	785229
49	exp confidence interval/	124585
50	exp regression analysis/	576344
51	exp proportional hazards model/	97026
52	exp multivariate analysis/	352292
53	"limit follow up studies to medline only. embase maps to follow up".ti.	0
54	exp follow up studies/	1373402
55	exp case study/	1731875
56	"limit case study above to embase only. medline maps to case report".ti.	0
57	odds ratio/	405907
58	"limit odds ratio above to embase. medline maps to risk".ti.	0
59	((evidence adj based) or (meta adj analys*) or (systematic* adj3 review*) or guideline* or (control* adj2 study) or (control* adj2 trial) or (randomized adj2 study) or (randomized adj2 trial) or (randomised adj2 study) or (randomised adj2 trial) or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or multivariate or random* or control* or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* adj2 study) or (intervention* adj2 trial) or "cross-sectional	20243232

Continued

#	Searches	Results
	study" or "cross-sectional analys*" or "cross-sectional survey*" or "cross-sectional design*" or "prevalence study" or "prevalence analys*" or "prevalence survey*" or "disease frequency study" or "disease frequency analys*" or "disease frequency survey*" or crossover or "cross-over" or "cohort study" or "cohort survey" or "cohort analysis" or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "retrospective study" or "retrospective survey" or "retrospective analysis" or "prospective study" or "prospective survey" or "prospective analysis" or "population study" or "population survey" or "population analysis" or "concurrent study" or "concurrent survey" or "concurrent analysis" or "incidence study" or "incidence survey" or "incidence analysis" or "follow-up study" or "follow-up survey" or "follow-up analysis" or "observational study" or "observational survey" or "observational analysis" or "case study" or "case series" or "clinical series" or "case studies" or "clinical study" or "clinical trial" or "evaluation study" or "evaluation survey" or "evaluation analysis" or "twin study" or "twin survey" or "twin analysis" or "quantitative study" or "quantitative analys*" or "validation study" or "validation survey" or "validation analysis" or "experimental study" or "experimental analysis" or "quasi experimental study" or "quasi experimental analysis" or "quasiexperimental study" or "quasiexperimental analysis" or "field study" or "field survey" or "field analysis" or "in vivo study" or "in vivo analysis" or "panel study" or "panel survey" or "panel analysis" or "pilot study" or "pilot survey" or "pilot analysis" or "prevention study" or "prevention survey" or "prevention analysis" or "replication study" or "replication analysis" or "theoretical study" or "theoretical analysis" or "feasibility study" or "feasibility analysis" or "trend study" or "trend survey" or "trend analysis" or (correlaton* adj study) or (correlaton* adj analys*) or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case compeer study" or "case comparison study" or "odds ratio" or "confidence interval" or study or pilot or trial or cohort* or "regression analysis" or "hazards model*" or "multivariate analysis" or "change analysis").mp.	
60	from 54 keep 827584-1331286	503703
61	from 55 keep 1-27454	27454
62	from 57 keep 1-342547	342547
63	or/6-52	12682433
64	or/59-63	21745995
65	5 and 64	159
66	from 5 keep 144-186	43
67	limit 66 to (clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or evaluation	16

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Continued

#	Searches	Results
	studies or guideline or meta analysis or multicenter study or observational study or pragmatic clinical trial or practice guideline or randomized controlled trial or systematic reviews or validation studies) [Limit not valid in Embase,CCTR,CDSR; records were retained]	
68	65 or 67	159
69	limit 68 to (book or book series or editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR,CDSR; records were retained]	5
70	68 not 69	154
71	70 not (exp animals/ not exp humans/)	151
72	from 5 keep 187-195	9
73	71 or 72	152
74	limit 73 to english language [Limit not valid in CDSR; records were retained]	147
75	limit 74 to yr="2000 -Current"	147
76	75 not "conference abstract".pt.	86
77	remove duplicates from 76	52

Scopus

1 TITLE-ABS-KEY(DJBL OR DJBLs OR DJBS OR DJBSs OR "duodenaljejunal bypass liner*" OR "duodenal-jejunal bypass liner*" OR "duodenaljejunal bypass sleeve*" OR "duodenal-jejunal bypass sleeve*" OR "duodenojejunal bypass liner*" OR "duodeno-jejunal bypass liner*" OR "duodenojejunal bypass sleeve*" OR "duodeno-jejunal bypass sleeve*" OR EndoBarrier OR "fluoropolymer liner*" OR "fluoro-polymer liner*" OR "fluoropolymer sleeve*" OR "fluoro-polymer sleeve*")

2 TITLE-ABS-KEY(obes* or "body mass ind*" or adipos* or overweight or "over weight" or "overload syndrom*" or overeat* or "over eat*" or overfeed* or "over feed*" or overfed or "over fed" or "weight cycling" or ((weight or fat) W/3 (gain* or reduc* or los* or maint* or decreas* or watch* or control*)) or "skinfold thickness" or antiobesity or "anti-obesity" or obesitas or bodyweight or "body weight")

3 TITLE-ABS-KEY(((evidence W/1 based) or (meta W/1 analys*) or (systematic* W/3 review*) or guideline* or (control* W/2 study) or (control* W/2 trial) or (randomized W/2 study) or (randomized W/2 trial) or (randomised W/2 study) or (randomised W/2 trial) or (doubl* W/1 blind*) or (doubl* W/1 mask*) or (singl* W/1 blind*) or (singl* W/1 mask*) or (tripl* W/1 blind*) or (tripl* W/1 mask*) or (trebl* W/1 blind*) or (trebl* W/1 mask*) or "latin square" or placebo* or multivariate or random* or control* or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* W/2 study) or (intervention* W/2 trial) or "cross-sectional study" or "cross-sectional analys*" or "cross-sectional survey*" or "cross-sectional design*" or "prevalence study" or "prevalence analys*" or "prevalence survey*" or "disease frequency study" or "disease frequency analys*" or "disease frequency survey*" or crossover or "cross-over" or "cohort study" or "cohort survey" or "cohort analysis" or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "retrospective study" or "retrospective survey" or "retrospective analysis" or "prospective study" or "prospective survey" or "prospective analysis" or "population study" or "population survey" or "population analysis" or "concurrent study" or "concurrent survey" or "concurrent analysis" or "incidence study" or "incidence survey" or "incidence analysis" or "follow-up study" or "follow-up survey" or "follow-up analysis" or "observational study" or "observational survey" or "observational analysis" or "case study" or "case series" or "clinical series" or "case studies" or "clinical study" or "clinical trial" or "evaluation study" or "evaluation survey" or "evaluation analysis" or "twin study" or "twin survey" or "twin analysis" or "quantitative study" or "quantitative analys*" or "validation study" or "validation survey" or "validation analysis" or "experimental study" or "experimental analysis" or "quasi experimental study" or "quasi experimental analysis" or "quasiexperimental study" or "quasiexperimental analysis" or "field study" or "field survey" or "field analysis" or "in vivo study" or "in vivo analysis" or "panel study" or "panel survey" or "panel analysis" or "pilot study" or "pilot survey" or "pilot analysis" or "prevention study" or "prevention survey" or "prevention analysis" or "replication study" or "replication analysis" or "theoretical study" or "theoretical analysis" or "feasibility study" or "feasibility analysis" or "trend study" or "trend survey" or "trend analysis" or (correlaton* W/1 study) or (correlaton* W/1 analys*) or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case compeer study" or "case comparison study" or "odds ratio" or "confidence interval" or study or pilot or trial or cohort* or "regression analysis" or "hazards model*" or "multivariate analysis" or "change analysis"))

4 PUBYEAR AFT 1999 AND LANGUAGE(english)

5 1 and 2 and 3 and 4

6 DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

7 5 and not 6

8 PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)

9 7 and not 8