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Bariatric surgery: an updated systematic review and meta-analysis, 2003–2012

Su-Hsin Chang, PhD[1], **Carolyn R.T. Stoll, MPH, MSW**[1], **Jihyun Song, PhD**[2], **J. Esteban Varela, MD, MPH, FACS**[3], **Christopher J. Eagon, MD**[3], and **Graham A. Colditz, MD, DrPH**[1]

[1]Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine

[2]Department of Statistics, Seoul National University

[3]Minimally Invasive and Bariatric Surgery, Department of Surgery, Washington University School of Medicine

Abstract

Importance—The prevalence of obesity and outcomes of bariatric surgery are well established. However, analyses of the surgery impact have not been updated and comprehensively investigated since 2003.

Objective—Up-to-date, comprehensive data and appropriate meta-analytic techniques were used to examine effectiveness and risks of bariatric surgery.

Data Sources—Literature searches of Medline, Embase, Scopus, Current Contents, Cochrane Library, and Clinicaltrials.gov between 2003 and 2012 were performed.

Study Selection—Exclusion criteria included publication of abstracts only, case reports, letters, comments, or reviews; animal studies; languages other than English; duplicate studies; no surgical intervention; and no population of interest. Inclusion criteria were at least one outcome of interest resulting from the studied surgery was reported – comorbidities, mortality, complications, reoperations, or weight loss. Of the 25,060 initially identified articles, 24,023 studies met the exclusion criteria, and 259 met the inclusion criteria.

Corresponding Author: Su-Hsin Chang, PhD, Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, 660 S. Euclid Avenue, Campus Box 8100, St. Louis, MO 63110, changsh@wudosis.wustl.edu, Phone: (314) 362-8623, Fax: (314) 454-7941.

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Supplemental material: Appendix

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Study concept and design: Chang, Colditz
Analysis and interpretation of data: Chang, Stoll, Song, Varela, Eagon, Colditz
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Data Extraction—A review protocol was followed throughout. Three reviewers independently reviewed studies, abstracted data, and resolved disagreements by consensus. Studies were evaluated for quality.

Results—A total of 164 studies were included (37 randomized controlled trials (RCTs) and 127 observational studies). Analyses included 161,756 patients with mean age 45 years and body mass index (BMI) 46 kg/m^2. We conducted random-effects and fixed-effect meta-analyses and meta-regression. In RCTs, ≤30 days mortality rate was 0.08% [95%CI, 0.01%–0.24%]; >30 days mortality rate was 0.31% [95%CI, 0.01%–0.75%]. BMI loss at the post-surgery five years was 12–17 kg/m^2. The complication rate was 17% [95%CI, 11%–23%], and the reoperation rate was 7% [95%CI, 3%–12%]. Gastric bypass (GB) was more effective in weight loss but associated with more complications. Adjustable gastric banding (AGB) had lower mortality and complication rates; yet, the reoperation rate was higher and weight loss was less substantial than GB. Sleeve gastrectomy appeared to be more effective in weight loss than AGB and comparable to GB.

Conclusions—Bariatric surgery provides substantial and sustained effects on weight loss and ameliorates obesity-attributable comorbidities in the majority of bariatric patients, although risks of complication, reoperation, and death exist. Death rates were lower than those reported in previous meta-analyses.

1. INTRODUCTION

The prevalence of overweight and obesity is increasing globally.[1] Among high-income countries, the United States has the highest mean body mass index[a] (BMI) for men and women,[2] and over two-thirds of U.S. adults aged 20 or older are overweight or obese.[3] Overweight and obesity are associated with increased risk of morbidity[4–9] and mortality.[10–13] Approximately 112,000 deaths per year are associated with obesity in the United States.[14]

Treatments of obesity, except surgery, are generally ineffective in long-term weight control.[15–20] In addition to sustained weight loss, surgical treatment provides additional benefits to people with obesity-related comorbidities and reduces relative risk of death due to significant weight loss.[20–24] Consequently, the demand for bariatric surgery has risen dramatically in recent years. The total number of operations performed in the United States and Canada reached 220,000 in 2008 to 2009.[25,26]

Clinical trials have provided data for targeted surgical procedure(s) on different sets of patients, but general questions regarding effectiveness of surgical treatment of obesity and which surgical procedure is the most efficacious remain unanswered. Previous reviews, e.g., Buchwald et al.[27] and Maggard et al.,[28] provided comprehensive analyses, but included data from clinical trials and studies published before 2003. A recent systematic review and meta-analysis conducted by Padwal and colleagues[29] focused only on randomized controlled trials (RCTs). Their data included recently published trials, but did not exclude early publications. Due to advances in technology of bariatric surgery[b] and accumulation of surgeons' experience, information provided in previous reviews is outdated. Therefore, it is necessary to reassess surgical treatments using more up-to-date data.

The goal of the study is to quantify risks and benefits of various bariatric surgery procedures focusing on adult patients. Specifically, we report the risks (defined as peri- and post-operative mortality, complications, and reoperations) and the effectiveness (defined as weight loss and remission of obesity-related diseases). We conducted a systematic review

[a]BMI is defined by weight in kilograms (kg) divided by the square of height in meters (m).
[b]For example, new procedures, such as sleeve gastrectomy, were developed.

and meta-analysis on relevant studies selected from recent publications, including both RCTs and observational studies (OBSs). For each study design,[30] random-effects (RE) or/and fixed-effect (FE) models[31] were considered, and appropriate meta-analytic techniques were used to analyze the data.

2. METHODS

This systematic review and meta-analysis was conducted and reported according to the established guidelines.[32,33] A review protocol[c] was followed throughout.

2.1 Data Sources and Searches

A search strategy was created by an MLIS qualified librarian. Comprehensive searches of the literature were performed on MEDLINE, EMBASE, SCOPUS, COCHRANE, and CLINICALTRIALS.GOV with the timeframe of January 1st, 2003 to March 31st, 2012. Searches were performed using the Firefox browser, and results were imported to EndNote X5. Search terms are detailed in the Appendix (Section 1).

2.2 Study Selection and Criteria

Search results were screened by scanning abstracts for the following exclusion criteria: publication of abstracts only, case reports, letters, comments, reviews, or meta-analyses; animal studies; languages other than English; duplicate studies; no surgical intervention; lack of outcomes of interest (weight change, surgical mortality and complications, and disease impacts); and not population of interest (adults aged>18 years). After removing excluded abstracts, full articles were obtained and studies were screened again more thoroughly using the same exclusion criteria.

2.3 Data Extraction

Studies were included in data extraction if they reported surgical procedure performed and at least one outcome of interest resulting from that surgery. Data needed to be presented separately by surgical procedure if more than one procedure was performed. Initial study population size and sample size at all data collection points was recorded. Characteristics of the starting study sample, such as age, race, sex, and weight information were collected when available. Pre- and post-surgery data regarding comorbid conditions, body composition, and any other pertinent category were extracted. The target obesity-related comorbidities included type-2 diabetes mellitus, cardiovascular disease, hypertension, dyslipidemia, and sleep apnea. Conversion of units to keep data consistent was performed when necessary. Extracted studies included RCTs and OBSs. Three reviewers independently reviewed the studies, abstracted data, and resolved disagreements by consensus.

2.4 Quality Assessment

All studies were evaluated for quality using a six-category scoring system (range 0–6).[34] The categories were (1) clear definition of surgeries; (2) clear time points given for outcomes; (3) adjustment for potential confounders in analysis (for OBSs only) and adequate randomization (for RCTs only); (4) defined a priori sample size calculations; (5) loss to follow up less than 20%; (6) reports of funding sources/conflicts of interest.[29,34–37] For categories 1–4, studies received a score of 1 if the study fulfilled the criteria, and 0 otherwise. For categories 5 and 6, studies could receive a score of 0, 0.5, or 1. For category 5, a score of 0 indicated that no information regarding loss to follow up was given, a score of 0.5 indicated that loss to follow up information was given, but loss to follow up was

[c]The review protocol is available on the website: http://www.publichealthsciences.wustl.edu/en/Faculty/ChangSu-Hsin.

>20%, and a score of 1 indicated that loss to follow up was <20%. For category 6, a score of 0 indicated that the article gave no information regarding funding sources or conflicts of interest, a score of 0.5 indicated that the article was funded by surgical-related industry, and a score of 1 indicated that funding and conflicts of interest were declared, and there was no link to industry. A higher score indicated a higher quality study. Categories 3–6 were designed to assess the risk of study bias.

2.5 Statistical Analysis

Analyses were performed using only the data from studies in the data extraction subset. Study and individual-level data were summarized using descriptive statistics. Different surgical procedures were grouped into five categories: (i) gastric bypass (GB); (ii) adjustable gastric banding (AGB); (iii) vertical banded gastroplasty (VBG); (iv) sleeve gastrectomy (SG); and (v) non-surgical interventions (Control). Surgical outcomes in terms of percent excess weight loss[d] (%EWL), BMI change (ΔBMI), peri- and post-operative mortality, complication and reoperation rate, and percentage of remission of the obesity-attributable comorbidities were synthesized by meta-analysis. Meta-analyses were done separately for RCTs and OBSs.

2.5.1 Operative mortality, complication rate, and percentage of remission of the obesity-attributable comorbidities—We recorded the incidence of these outcomes in each study. For operative mortality, we ran separate analyses on studies which identified the deaths occurring within 30 days of the surgery and studies which identified the deaths occurring after 30 days of the surgery. Unclear timing of death was treated as if deaths were observed at the latest time of follow-up.[e] Surgical complications included all adverse events associated with surgery reported in the studies, such as bleeding, stomal stenosis, leak, vomiting, reflux, gastrointestinal symptoms, and nutritional and electrolyte abnormalities.[f] Reoperation rate was analyzed separately. Percentage of remission of comorbidities was defined as the proportion of the surgery patients who reported the target comorbid condition being either resolved or improved after surgery.[g]

Mortality, complication, and comorbidity remission rates were estimated by Bayesian random-effects meta-analysis method[40,41] to avoid statistical problems caused by zero or rare events in each study.[42–44] In addition, simple averaging method proposed by Bhaumik et al.[44] was conducted as an alternative to the Bayesian RE meta-analysis. Both methods are detailed in the Appendix (Section 2).

2.5.2 Weight loss outcomes—All yearly post-surgery weight outcomes were compared to the pre-surgery weight. FE and RE models were constructed, and the Frequentist approach was used. The I^2 index was computed to quantify the degree of study heterogeneity.[45,46] Publication bias was evaluated using funnel plots and Egger's test.[47,48] We report post-surgery ΔBMI and %EWL for both study designs. Meta-regression of ΔBMI was conducted to account for patient characteristics (e.g., pre-surgery BMI, gender composition, and age), study design and quality, surgical procedure, and geographic location. We performed a preliminary meta-regression, using overall quality scores to

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[d]Percent excess weight loss = [(operative weight-follow-up weight)/operative excess weight]×100, where excess weight = actual weight-ideal weight,[38] and ideal weight is derived from the 1983 Metropolitan insurance height and weight tables.[39]

[e]Deaths of unspecified causes were not excluded in any mortality analyses.

[f]Specific surgical complications were variably reported and difficult to catalog. Therefore, only overall complication rate was analyzed.

[g]Due to the heterogeneity in the reporting of comorbidity outcomes, we provided a table recording the definitions of the target comorbidity and surgical outcomes associated with the target comorbidity in eTable 9 in the Appendix.

determine if analyses of ΔBMI should be limited to studies with higher scores, followed by a main meta-regression analysis controlling for each quality category.

To make use of the information on repeated measurements of ΔBMI at different study time points in the trials and to compare and contrast the findings in Padwal et al.,[29] we conducted mixed treatment comparison (MTC) meta-analysis using a Bayesian approach,[49] targeting all RCTs from which we extracted data. This method allows us to statistically combine information on multiple pairwise comparisons to make inferences about relative effects between multiple surgical procedures.[50] We categorized into 11 surgical procedures/ interventions, and further grouped those procedures into 5 larger surgery categories (Appendix, Section 3 and eTable 3).[h] Four MTC models were considered (Appendix, Section 3). We estimated post-surgery ΔBMI compared to the reference[i] (relative surgery effect) in these models, taking advantage of the direct and indirect comparisons within study arms of RCTs. Here, we only present the first two models.

We computed the standard deviations of ΔBMI whenever possible[j] if they were not reported in the original articles. Otherwise, we imputed the missing values by conducting a separate meta-analysis to estimate the distribution of standard deviations and then using the estimated distribution to predict the missing values.[49]

FE and RE meta-analyses using the Frequentist approach were performed using STATA (SE/11.2, Stata Corp, College Station, TX). Bayesian RE meta-analysis was conducted by R (2.14.0, R Development Core Team, Vienna, Austria) and JAGS, "runjags" package (0.9.9-2). Bhaumik estimates and the numerical solutions of the standard errors were obtained using MATLAB (7.11, R2012a, MathWorks Inc, Natick, MA). MTC meta-analyses were conducted using WinBUGS 1.4.3 (The BUGS Project, Cambridge, UK). For weight outcomes, we report the means for RE, the relative surgery effect for MTC, and the estimates for meta-regression; for the other outcomes, we report the means for Bayesian RE models, while the rest is presented in Appendix. 95% confidence/credible intervals (CIs) associated with the Frequentist/Bayesian estimates are reported in brackets.

3. RESULTS

3.1 Data Retrieval

A flow diagram outlining the systematic review process is provided in Figure 1. The initial searches resulted in 25,060 articles. After reviewing abstracts for exclusion criteria, 1,037 abstracts remained. Full articles were retrieved, and after screening for exclusion and inclusion criteria, data were extracted from 259 articles. Of these, 164 articles (37 RCTs and

[h]The 5 categories were the same as the aforementioned 5 categories. 11 surgical procedures/interventions included (1) laparoscopic Roux-en-Y Gastric Bypass (LRYGB); (2) open RYGB (ORYGB); (3) LRYGB with presurgery weight loss; (4) laparoscopic biliopancreatic diversion with duodenal switch (LBD-DS); (5) biliopancreatic diversion with RYGB (BPD-RYGB); (6) laparoscopic adjustable gastric banding (LAGB) – Lapband; (7) LAGB – Swedish; (8) laparoscopic vertical banded gastroplasty (VBG); (9) open VBG; (10) laparoscopic sleeve gastrectomy (SG); and (11) nonsurgical interventions. Among them, (1)–(5) belong to procedure 1, GB; (6)–(7) are procedure 2, AGB; (8) and (9) belong to procedure 3, VBG; (10) is procedure 4, SG, and (11) belongs to procedure 5, Control.

[i]Among those procedures, the laparoscopic Roux-en-Y Gastric Bypass (LRYGB) was the mostly commonly compared procedure (Appendix, Section 3 and eFigure 1), and, therefore, LRYGB procedure was the reference in Model 1. In Model 2, GB category was the reference.

[j]We computed standard deviation from the reported 95% confidence intervals or exact p-values when a statistical test was conducted in the original study to compare the pre- and post- surgery BMI.

127 OBSs) were included in meta-analyses.[k] Studies could contribute to more than one analysis.

3.2 Study and Patient Characteristics

Sixty-two of the included articles were published between 2003 and 2007, and 102 were published between 2008 and 2012 (Table 1). Ninety-one studies had follow-up periods of at least 2 years. Fifty-four studies were conducted in North America, 72 in Europe, 13 in Asia, and 25 in other locations (Australia, New Zealand, South America, and multinational studies). One hundred and forty studies reported patients' mean age, and 142 contained their pre-surgery BMI information.

A total of 161,756 patients were included in our analyses. Among studies reporting participants' information, mean age of the participants was 44.6 years, 79% were female, and 75% were white. Pre-surgery BMI was 45.6 kg/m^2 and pre-surgery weight was 124.5 kg. Among the studies that provided information about obesity-related comorbidities, 26% of the patients had type-2 diabetes, 47% had hypertension, 28% had dyslipidemia, 7% had cardiovascular diseases, and 25% had sleep apnea.

3.3 Meta-analysis Results

3.3.1 Operative mortality, post-operative complication, and reoperation rates—Table 2 shows the meta-analytic results of surgical risks. Operative mortality was relatively low. Sixty-three studies (109 study arms) reported peri-operative (≤30 days) mortality data; and 47 studies (81 study arms) reported post-operative (>30 days) mortality data. For RCTs, peri-operative mortality rate was 0.08% [0.01%–0.24%], and post-operative mortality rate was 0.31% [0.01%–0.75%]. For OBSs, both peri- and post-operative mortality rates were higher – 0.22% [0.14%–0.31%] and 0.35% [0.20%–0.52%]. In OBSs, AGB had the lowest peri- and post-operative mortality rates (0.07% [0.02%–0.12%] and 0.21% [0.08%–0.37%]), followed by SG (0.29% [0.11%–0.63%] and 0.34% [0.14%–0.60%]) and then GB (0.38% [0.22%–0.59%] and 0.72% [0.28%–1.30%]).

Sixty-four studies (16 RCTs and 48 OBSs) contributed to meta-analyses of complications. The complication rate was 17% [11%–23%] for RCTs, but lower for OBSs (10% [7%–13%]). This pattern persisted across all surgical procedures. For RCTs, complications rates were relatively low for SG (13% [1%–44%]) and AGB (13% [5%–26%]) compared to GB (21% [12%–33%]).

Reoperation rates were not as high as complication rates: 7% [3%–12%] for RCTs and 6% [4%–8%] for OBSs. In RCTs, GB appeared to have the lowest reoperation rate (3% [1%–5%]), followed by SG (9% [1%–35%]), while in OBSs, SG has the lowest reoperation rate (3% [2%–5%]), followed by GB (5% [4%–6%]). AGB appeared to have the highest reoperation rate (12% [4%–24%] for RCTs and 7% [4%–11%] for OBSs).

3.3.2 Weight loss—Table 3 presents results of the post-surgery BMI loss and %EWL analysis. Only studies that reported yearly ΔBMI and %EWL were incorporated into our meta-analysis. Sixty-nine studies (109 study arms) provided information on ΔBMI at one year after surgery, but only 11 studies (17 study arms) reported ΔBMI at five years after surgery. BMI loss within five years after surgery was persistent in the range of 12 to 17 kg/

[k]The extracted studies were excluded in the analyses if they reported outcomes inconsistent with our stratification or missed reporting at least one key element to be included in our analyses, e.g., time points, clear definition of the outcome, aggregately reported outcomes. A list of the included articles is available on the website: http://www.publichealthsciences.wustl.edu/en/Faculty/ChangSu-Hsin.

m^2 for OBSs (Figure 2A).[l] There was no evidence of publication bias in any analysis, except for post-surgery years 1 and 3 ΔBMI for OBSs (Appendix, eFigure 2).

The preliminary meta-regression showed that quality scores were not associated with post-surgery BMI changes.[m] Therefore, analyses including only studies with higher quality scores were not performed. The main meta-regression results showed that pre-surgery BMI and younger age were positively associated with post-surgery BMI loss (Appendix, Section 4.3 and eTable 4). RCT design, whether an RCT had adequate randomization, and whether a study provided a priori sample size calculations were associated with more BMI loss in the first year post-surgery. Having loss to follow up >20% was associated with more significant weight loss in the second year after surgery. BMI loss was significantly less for AGB, SG, and non-surgical interventions compared to GB in the first year after surgery. Proportion of female patients, geographical location, and the unmentioned categories of study quality did not have a significant association with BMI loss.

Forty-eight studies (9 RCTs and 39 OBSs) reported %EWL at one year post-surgery, and 18 studies (2 RCTs and 16 OBSs) reported %EWL three years after surgery (lower panel of Table 3). For RCTs, year 1 %EWL was 60% [50%–70%], I^2=85%; year 2 %EWL was 71% [63%–79%], I^2=63%; and year 3 %EWL was 57% [52%–62%], I^2=0%. For OBSs, %EWL in the first three years were 46% [44%–48%], I^2=90%; 64% [55%–73%], I^2=90%; and 67% [65%–69%], I^2=0%.

BMI loss was larger for GB than AGB. Both VBG (Appendix, eTable 2) and SG (Table 3) appeared to have significant effects on BMI loss, although data was limited for these surgical procedures. The one OBS that had 5-year follow-up data on ΔBMI after SG reported sustained BMI loss (~16 kg/m^2) in year 5[n]54 To make more meaningful comparison between surgical procedures, MTC meta-analysis was used.

Figure 2B demonstrates the MTC meta-analysis results of ΔBMI from 17 RCTs. Relative surgery effects compared to the LRYGB procedure are presented in a forest plot. Relative category effects compared to the GB category are presented in the shape of rhombuses. Non-surgical intervention had the least BMI loss, 14 [6–22] kg/m^2 less than LRYGB (Appendix, eTable 5). Among the 5 categories, AGB and VBG resulted in less BMI loss than GB, while SG had similar effect. Within the GB category, the combined methods[o] led to higher BMI loss than LRYGB alone, while ORYGB did not result in as much BMI loss as LRYGB. The AGB procedures did not help patients lose as much BMI as LRYGB, nor did open or laparoscopic VBG. LAGB using Lapband or unspecified brand of band appeared to be slightly more effective than LAGB using Swedish band, and LVBG led to more weight loss than OVBG.

3.3.3 Comorbidity outcomes—Fifty-three articles were included in our meta-analysis of comorbidity outcomes. Comorbid conditions were significantly improved after surgery as shown in our meta-analysis (Table 2). Eight RCTs (206 patients) and 43 OBSs (9,037 patients) provided diabetes information. The percentage of diabetes remission after surgery was 92% [85%–97%] for RCTs and 86% [79%–92%] for OBSs. The remission rates of hypertension were somewhat lower – 75% [62%–86%] for RCTs and 74% [67%–81%] for

[l]Very few studies reported weight loss information beyond five years after surgery. However, two articles[51,52] based on the Swedish Obese Subjects study reporting BMI change 10+ years after surgery reported the mean BMI reduction 10 years and 15 years after surgery was still approximately 6.5 and 7.1 kg/m^2.

[m]p-value = 0.153 for year 1, and p-value = 0.962 for year 2.

[n]In addition, the one OBS that had 5 year follow-up data on ΔBMI after VBG was performed reported sustained BMI change – approximately −16 kg/m^2 for years 4 and 5.[53]

[o]The combined methods included LBD-DS, BPD-RYGB, and LRYGB with pre-surgery weight loss.

OBSs. Fewer studies (5 RCTs and 20 OBSs) investigated dyslipidemia; however, a large number of patients were included (279 patients in RCTs and 1,477 patients in OBSs). Data from RCTs showed 76% [56%–91%] remission of dyslipidemia after surgery. In OBSs, the remission rate was 68% [58%–77%]. Only 3 OBSs (27 patients) studied post-surgery conditions of cardiovascular disease, and the remission rate was 58% [0%–100%]. Five RCTs with 44 patients and 27 OBSs with 9,845 patients were included in the sleep apnea analysis. The remission rates were high: 96% [87%–100%] for RCTs and 90% [81%–95%] for OBSs.

4. COMMENT

We conducted an up-to-date and comprehensive systematic review and meta-analysis of bariatric surgery based on literature published after 2003. We evaluated risks and benefits associated with bariatric surgery.

In accordance with previous systematic reviews and meta-analyses,[27–29] we found significant weight reduction and low mortality outcomes associated with surgery. However, the estimated mortality rates in our study were lower than those in previous meta-analyses,[27,28] Buchwald et al. and Maggard et al.[p]. We also found significant improvement in comorbidities, which is consistent with findings in Buchwald et al.[q],[27] while Padwal et al.[29] did not find this relationship. Consistent with Padwal et al. and others, our study found that GB is more effective than AGB and much more effective than non-surgical intervention in weight loss. A detailed comparison of findings across previous and our meta-analyses are summarized in eTable 10 in the Appendix.

Our findings are consistent with previous literature that AGB has lower mortality and complication rates than GB,[36,37] but not a decreased reoperation rate. SG was positioned between AGB and GB[56] in terms of mortality and complication rates in OBSs (but not in RCTs) and post-surgery BMI change in MTC meta-analysis of RCTs (but not in RE meta-analyses). The inconsistency is possibly due to the smaller numbers of studies included in the analyses. Overall, SG appeared to be more effective in weight loss than AGB and seemed to be comparable to GB even at five years. However, this conclusion cannot be made without noting that 7 studies were included in the analysis for GB, while only 1 study was included in the analysis for SG. Within the GB category, ORYGB had the least BMI loss, and LBD-DS had the most BMI loss among all procedures. We also found that LBD-DS and BPD-RYGB had better short- (<1 year) and mid-term (≥1 and <3 years) effects on BMI loss (Appendix, eTable 8).

We observed systematic differences in outcomes between RCTs and OBSs in the magnitude of the effects.[57,58] We observed higher mortality in OBSs than in RCTs, which could be attributed to longer follow-up time in OBSs or a higher chance that mortality recorded in OBSs was not associated with surgery. We also found higher complication, reoperation, and comorbidity remission rates in RCTs.[r] This could be explained by more detailed monitoring and reporting of outcomes in RCTs due to smaller sample sizes and shorter follow-up times. Despite these differences, the direction of the effects is the same in all aspects. Agreeing with the findings in Benson et al.,[59] we did not find larger effects in OBSs than in RCTs; on the contrary, estimates of the first-year BMI loss for RCTs are higher than those in OBSs.

[p]Even though zeros were imputed for missing data and grouped into the early death outcome in Maggard et al., lower early mortality rates for RCTs were still found in our study.

[q]In another review article, Buchwald and colleagues found that type-2 diabetes were resolved or improved in the greater majority of bariatric patients.[55]

[r]This holds true for all surgical procedures, except VBG for complication and comorbidity remission rates; and GB for reoperation rates.

Our study is restrained b the following limitations. First, like all other meta-analyses, the results need to be interpreted acknowledging that surgery effects vary based on characteristics of individual patient, e.g., age, gender, pre-surgery BMI, although we controlled for these in the meta-regression. Second, the number of studies included in the analyses was not balanced because (i) some procedures were not as popular as others;[60] (ii) fewer studies reported post-surgery year 3–5 weight loss outcomes. Third, although the employment of MTC of repeated measurement circumvents the need to approximate the observed outcomes at various follow-up times to the closest study times and takes advantage of all information reported at different time points, the limited number of RCTs in our study restricts the estimation capability. Fourth, deaths of unspecified causes were not excluded in mortality analyses, and only overall complication rates were analyzed, which weakened the usefulness of the analyses. Last, although the data synthesis was carefully conducted in this study, the results needs to be interpreted with caution due to the heterogeneous outcome reporting of each included study, e.g., no standardized criteria of comorbidity improvement across studies.[s]

In conclusion, our study suggests that bariatric surgery has substantial and sustained effects on weight and significantly ameliorates obesity-attributable comorbidities in the majority of bariatric surgery patients. However, complication rates associated with bariatric surgery range from 10% to 17% and reoperation rates approximately 7%; nonetheless, mortality associated with surgery is generally low (0.08–0.35%). Among different surgical procedures, GB is more effective in weight change outcomes, but generates more adverse events. AGB is considered safer[61,62] in terms of lower mortality and complication rates. However, the reoperation rate of AGB is higher than that of GB and SG, and the weight loss outcomes of AGB are less substantial than GB and SG.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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[s]Analyses might be weakened by heterogeneous criteria of comorbidity improvements, and the lack of consistent details in the individual studies prevented further subgroup analyses. A table (eTable 9 in the Appendix) comparing criteria across studies was provided to allow interpretation of results in context.

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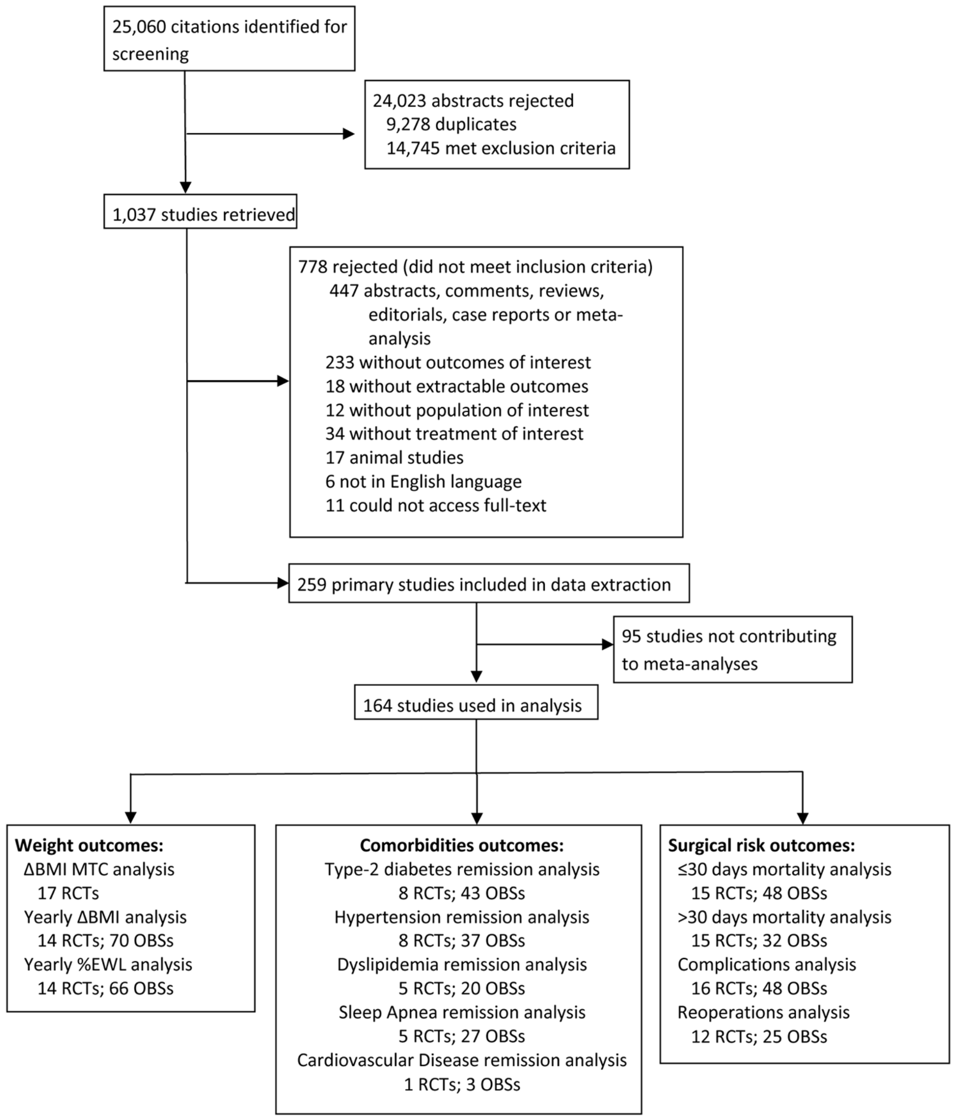

Figure 1. Study attrition diagram

BMI: body mass index; ΔBMI: BMI change; %EWL: percent excess weight loss; RCT: randomized controlled trial; OBS: observational studies. Remission is defined as the target comorbid condition being either resolved or improved after surgery.

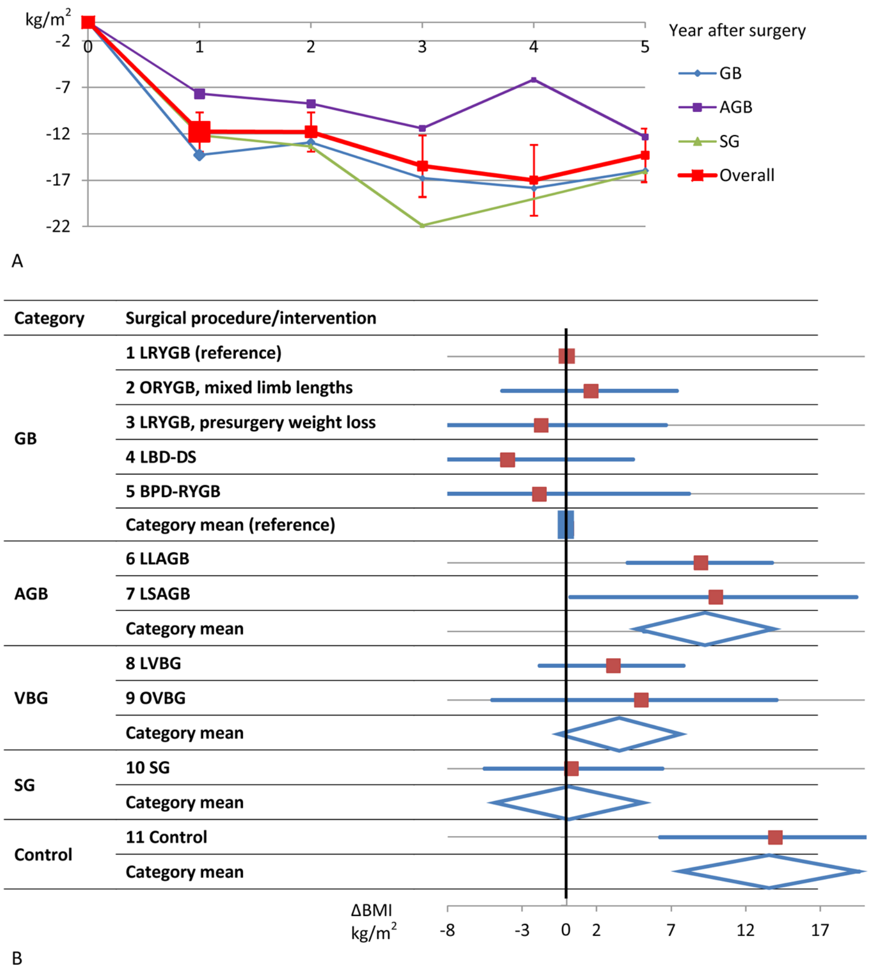

Figure 2. Meta-analysis of BMI change after surgery

Table 1

Study and patient characteristics

Study characteristics	No. of studies	No. of patients	Patient characteristics	No./Total (mean or %)
Publication year			**Age (years)**	(44.56)
2003–2007	62	41,382	**BMI (kg/m^2)**	(45.62)
2008–2012	102	120,374	**Weight (kg)**	(124.53)
Study design			**Sex**	
RCT	37	3,385	**Male**	32,384/153,267 (21.13)
OBS	127	158,371	**Female**	120,883/153,267 (78.87)
Follow-up years			**Race**	
>=2 years	91	28,671	**White**	87,653/117,430 (74.64)
<2 years	73	133,085	**Non-white**	29,777/117,430 (25.36)
Study location			**Comorbidities**	
North America	54	130,045	**Type 2 diabetes**	19,258/73,378 (26.24)
Europe	72	22,703	**Hypertension**	34,092/71,938 (47.39)
Asia	13	3,099	**Cardiovascular disease**	1,913/26,752 (7.15)
Multinational	1	18	**Dyslipidemia**	11,533/41,235 (27.97)
Other	24	5,891	**Sleep Apnea**	11,794/46,609 (25.30)
Age	140	100,094		
BMI	142	90,587		
Weight	68	16,790		

RCT: randomized controlled trial; OBS: observational studies; BMI: body mass index; kg: kilogram; m: meter.

Table 2

Meta-analyses of surgery risk and comorbidities remission outcomes: means and 95% credible intervals are in brackets

		GB	AGB	SG	Control	Overall
Mortality ≤ 30 days						
RCT	**Estimates (%)**	0.08 [0.01, 0.30]	0.11 [0.01, 0.50]	0.50 [0.01, 3.88]	-- [--, --]	0.08 [0.01, 0.24]
	Study/arm/patient #	11/18/934	5/8/743	1/2/40	0/0/0	15/30/1,803
OBS	**Estimates (%)**	0.38 [0.22, 0.59]	0.07 [0.02, 0.12]	0.29 [0.11, 0.63]	-- [--, --]	0.22 [0.14, 0.31]
	Study/arm/patient #	19/30/90,090	26/29/40,538	10/11/3,647	1/1/9	48/79/136,903
Mortality > 30 days						
RCT	**Estimates (%)**	0.39 [0.01,0.86]	0.14 [0.00, 0.55]	6.00 [0.00, 100.00]	-- [--, --]	0.31 [0.01, 0.75]
	Study/arm/patient #	11/19/954	5/7/613	2/2/40	0/0/0	15/30/1,703
OBS	**Estimates (%)**	0.72 [0.28, 1.30]	0.21 [0.08, 0.37]	0.34 [0.14, 0.60]	-- [--, --]	0.35 [0.20, 0.52]
	Study/arm/patient #	13/18/29,256	18/22/33,950	8/9/3,099	0/0/0	32/51/66,897
Complication rates						
RCT	**Estimates (%)**	21.00 [12.00, 33.00]	13.00 [5.20, 26.00]	13.00 [0.70, 44.00]	-- [--, --]	17.00 [11.00, 23.00]
	Study/arm/patient #	10/14/649	7/11/855	2/2/137	2/2/59	16/30/1,778
OBS	**Estimates (%)**	12.00 [7.30, 17.00]	7.80 [3.90, 13.00]	8.90 [5.60, 13.00]	-- [--, --]	9.80 [7.40, 13.00]
	Study/arm/patient #	19/28/71,020	22/24/36,778	8/20/4,987	0/0/0	48/74/113,002
Reoperation rates						
RCT	**Estimates (%)**	2.56 [0.61, 5.36]	12.23 [4.46, 24.46]	9.05 [0.77, 34.56]	-- [--, --]	6.95 [3.27, 12.04]
	Study/arm/patient #	6/8/512	8/10/502	2/2/161	0/0/0	12/23/1,322
OBS	**Estimates (%)**	5.34 [4.48, 6.48]	7.01 [3.99, 11.24]	2.96 [1.70, 4.71]	-- [--, --]	5.75 [4.05, 7.83]
	Study/arm/patient #	6/8/23,688	18/21/30,314	7/7/2,912	0/0/0	25/39/57,171
Diabetes remission rates						
RCT	**Estimates (%)**	95.15 [88.38, 98.80]	73.88 [36.06, 96.18]	-- [--, --]	17.64 [0.98, 69.27]	91.99 [84.68, 97.18]
	Study/arm/patient #	6/10/152	2/2/35	0/0/0	1/1/30	8/14/206
OBS	**Estimates (%)**	92.83 [85.29, 97.21]	67.58 [49.51, 82.83]	85.53 [72.69, 94.07]	-- [--, --]	86.05 [78.74, 91.62]
	Study/arm/patient #	16/22/5,924	18/19/2,509	14/15/597	0/0/0	43/57/9,037
Hypertension remission rates						
RCT	**Estimates (%)**	80.98 [68.21, 91.52]	53.55 [12.52, 89.63]	-- [--, --]	49.00 [0.00, 99.00]	75.18 [61.52, 86.35]

		GB	AGB	SG	Control	Overall
	Study/arm/patient #	6/11/183	2/2/27	0/0/0	1/1/27	8/15/243
OBS	Estimates (%)	78.13 [63.67, 88.76]	63.73 [51.74, 75.43]	82.23 [68.19, 92.01]	15.00 [1.40, 53.00]	74.36 [66.53, 81.19]
	Study/arm/patient #	11/15/9,586	18/19/6,214	11/12/1,152	2/2/82	37/47/16,962
Dyslipidemia remission rates						
RCT	Estimates (%)	80.16 [61.68, 94.19]	39.95 [4.69, 87.05]	-- [--, --]	-- [--, --]	75.77 [55.63, 91.49]
	Study/arm/patient #	5/8/147	1/1/132	0/0/0	0/0/0	5/9/279
OBS	Estimates (%)	63.22 [40.86, 82.34]	60.91 [49.45, 72.36]	82.86 [62.67, 94.55]	5.42 [0.12, 30.41]	67.93 [58.08, 77.01]
	Study/arm/patient #	5/7/556	11/11/351	5/5/570	1/1/63	20/23/1,477
Cardiovascular disease remission rates						
RCT	Estimates (%)	-- [--, --]	-- [--, --]	-- [--, --]	-- [--, --]	65.81 [6.21, 99.46]
	Study/arm/patient #	0/0/0	0/0/0	0/0/0	0/0/0	1/1/3
OBS	Estimates (%)	22.00 [0.00, 100.00]	78.00 [0.00, 100.00]	-- [--, --]	-- [--, --]	58.00 [0.00, 100.00]
	Study/arm/patient #	1/1/17	2/2/10	0/0/0	0/0/0	3/3/27
Sleep apnea remission rates						
RCT	Estimates (%)	95.41 [84.49, 99.79]	94.26 [49.43, 100.00]	-- [--, --]	-- [--, --]	96.16 [86.66, 99.80]
	Study/arm/patient #	3/6/41	2/2/2	0/0/0	0/0/0	5/9/44
OBS	Estimates (%)	94.68 [86.36, 98.72]	71.14 [48.29, 89.16]	90.77 [80.06, 97.39]	-- [--, --]	89.53 [81.33, 95.08]
	Study/arm/patient #	8/11/5,748	13/14/3,598	8/9/498	0/0/0	27/35/9,845

Estimates were computed using Bayesian random-effects meta-analysis. Arms refer to subgroups within studies receiving different surgical procedures. GB: gastric bypass; AGB: adjustable gastric banding; SG: sleeve gastrectomy; Control: non-surgical interventions (non-surgical interventions were included in the analyses only when they were compared with surgical interventions); Overall: all surgery except for Control; RCT: randomized controlled trials; OBS: observational studies; --: estimates are not available when 0/0/0 (no data were included in the analysis) are presented or not relevant. Remission rate is defined as the proportion of the surgery patients who reported the target comorbid condition being either resolved or improved after surgery.

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Table 3

Meta-analyses of weight change outcomes: means and 95% confidence intervals are in brackets

ΔBMI		GB	AGB	SG	Control	Overall
Year 1						
RCT	**Estimates (kg/m^2)**	−14.53 [−16.82, −12.25]	−10.48 [−13.70, −7.25]	−16.20 [−24.45, −7.95]	-- [--, --]	−13.53 [−15.51, −11.55]
	# of studies/arms	9/15	3/3	1/1	0/0	12/22
OBS	**Estimates (kg/m^2)**	−14.32 [−19.02, −9.62]	−7.70 [−9.37, −6.03]	−12.14 [−14.02, −10.26]	−1.01 [−5.26, 3.23]	−11.79 [−13.89, −9.69]
	# of studies/arms	27/37	24/27	17/18	3/4	57/87
Year 2						
RCT	**Estimates (kg/m^2)**	−14.47 [−16.98, −11.97]	−11.35 [−14.24, −8.46]	-- [--, --]	-- [--, --]	−13.23 [−15.36, −11.11]
	# of studies/arms	6/10	2/2	0/0	0/0	8/15
OBS	**Estimates (kg/m^2)**	−12.93 [−17.39, −8.47]	−8.75 [−10.37, −7.13]	−13.39 [−19.52, −7.26]	0.10 [−7.39, 7.60]	−11.80 [−13.92, −9.69]
	# of studies/arms	12/16	14/16	5/5	1/2	29/40
Year 3						
RCT	**Estimates (kg/m^2)**	-- [--, --]	−9.20 [−15.85, −2.54]	-- [--, --]	-- [--, --]	−9.20 [−15.85, −2.54]
	# of studies/arms	0/0	1/2	0/0	0/0	1/2
OBS	**Estimates (kg/m^2)**	−16.78 [−20.57, −12.99]	−11.43 [−18.14, −4.72]	−21.88 [−27.96, −15.79]	-- [--, --]	−15.48 [−18.79, −12.18]
	# of studies/arms	6/9	7/8	2/2	0/0	17/21
Year 4						
RCT	**Estimates (kg/m^2)**	-- [--, --]	-- [--, --]	-- [--, --]	-- [--, --]	-- [--, --]
	# of studies/arms	0/0	0/0	0/0	0/0	0/0
OBS	**Estimates (kg/m^2)**	−17.86 [−22.20, −13.53]	−6.20 [−18.62, 6.22]	-- [--, --]	-- [--, --]	−17.00 [−20.80, −13.19]
	# of studies/arms	5/8	1/1	0/0	0/0	8/11
Year 5						
RCT	**Estimates (kg/m^2)**	-- [--, --]	−11.40 [−28.08, 5.28]	-- [--, --]	-- [--, --]	−11.40 [−28.08, 5.28]
	# of studies/arms	0/0	1/1	0/0	0/0	1/1
OBS	**Estimates (kg/m^2)**	−15.96 [−20.52, −11.40]	−12.36 [−16.92, −7.79]	−16.10 [−28.22, −3.98]	-- [--, --]	−14.32 [−17.19, −11.45]
	# of studies/arms	4/7	4/7	1/1	0/0	10/16

%EWL		GB	AGB	SG	Control	Overall
Year 1						
RCT	**Estimates (%)**	72.32 [64.60, 80.04]	33.39 [22.57, 44.21]	69.70 [41.09, 98.32]	-- [--, --]	59.82 [50.46, 69.17]
	# of studies/arms	5/7	4/4	1/1	0/0	9/15
OBS	**Estimates (%)**	63.31 [54.20, 72.43]	34.26 [33.98, 34.54]	51.49 [44.41, 58.56]	20.00 [−25.08,65.08]	46.16 [43.89, 48.43]
	# of studies/arms	17/25	14/15	11/11	1/1	39/55
Year 2						
RCT	**Estimates (%)**	74.39 [66.22, 82.55]	53.58 [32.80, 74.87]	-- [--, --]	-- [--, --]	70.58 [62.67, 78.50]
	# of studies/arms	4/6	3/3	0/0	0/0	7/12
OBS	**Estimates (%)**	80.09 [65.74, 94.43]	52.29 [48.67, 55.92]	46.72 [42.89, 50.55]	-- [--, --]	63.98 [55.21, 72.74]
	# of studies/arms	7/9	11/11	3/3	0/0	22/27
Year 3						
RCT	**Estimates (%)**	-- [--, --]	56.72 [51.59, 61.85]	-- [--, --]	-- [--, --]	56.72 [51.59, 61.85]
	# of studies/arms	0/0	2/2	0/0	0/0	2/2
OBS	**Estimates (%)**	76.35 [65.21, 87.50]	58.30 [42.12, 74.49]	59.42 [48.05, 70.78]	-- [--, --]	66.93 [65.05, 68.82]
	# of studies/arms	6/8	6/6	2/2	0/0	16/19
Year 4						
RCT	**Estimates (%)**	-- [--, --]	-- [--, --]	-- [--, --]	-- [--, --]	-- [--, --]
	# of studies/arms	0/0	0/0	0/0	0/0	0/0
OBS	**Estimates (%)**	76.36 [59.02, 93.70]	74.91 [58.54, 91.29]	-- [--, --]	-- [--, --]	74.82 [65.85, 83.80]
	# of studies/arms	3/5	3/3	0/0	0/0	8/10
Year 5						
RCT	**Estimates (%)**	-- [--, --]	41.60 [−9.75, 92.95]	-- [--, --]	-- [--, --]	41.60 [−9.75, 92.95]
	# of studies/arms	0/0	1/1	0/0	0/0	1/1
OBS	**Estimates (%)**	64.92 [44.27, 85.58]	57.23 [47.23, 67.23]	-- [--, --]	-- [--, --]	62.24 [58.71, 65.78]
	# of studies/arms	3/5	5/8	0/0	0/0	10/15

Estimates were obtained from random-effects models using the Frequentist approach. Arms refer to subgroups within studies receiving different surgical procedures. GB: gastric bypass; AGB: adjustable gastric banding; SG: sleeve gastrectomy; Control: non-surgical interventions (non-surgical interventions were included in the analyses only when they were compared with surgical interventions); Overall: all surgery except for Control; RCT: randomized controlled trials; OBS: observational studies; BMI: body mass index; ΔBMI: BMI change; %EWL: percent excess weight loss; --: estimates are not available when 0/0 (no data were included in the analysis) are presented.