

Original Investigation

The Effectiveness and Risks of Bariatric Surgery

An Updated Systematic Review and Meta-analysis, 2003-2012

Su-Hsin Chang, PhD; Carolyn R. T. Stoll, MPH, MSW; Jihyun Song, PhD; J. Esteban Varela, MD, MPH; Christopher J. Eagon, MD; Graham A. Colditz, MD, DrPH

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 To examine the effectiveness and risks of bariatric surgery using up-to-date, comprehensive data and appropriate meta-analytic techniques.

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 a report of surgical procedure performed and at least 1 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.

DATA EXTRACTION AND SYNTHESIS A review protocol was followed throughout. Three reviewers independently reviewed studies, abstracted data, and resolved disagreements by consensus. Studies were evaluated for quality.

MAIN OUTCOMES AND MEASURES Mortality, complications, reoperations, weight loss, and remission of obesity-related diseases.

RESULTS A total of 164 studies were included (37 randomized clinical trials and 127 observational studies). Analyses included 161 756 patients with a mean age of 44.56 years and body mass index of 45.62. We conducted random-effects and fixed-effect meta-analyses and meta-regression. In randomized clinical trials, the mortality rate within 30 days was 0.08% (95% CI, 0.01%-0.24%); the mortality rate after 30 days was 0.31% (95% CI, 0.01%-0.75%). Body mass index loss at 5 years postsurgery was 12 to 17. The complication rate was 17% (95% CI, 11%-23%), and the reoperation rate was 7% (95% CI, 3%-12%). Gastric bypass was more effective in weight loss but associated with more complications. Adjustable gastric banding had lower mortality and complication rates; yet, the reoperation rate was higher and weight loss was less substantial than gastric bypass. Sleeve gastrectomy appeared to be more effective in weight loss than adjustable gastric banding and comparable with gastric bypass.

CONCLUSIONS AND RELEVANCE 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.

JAMA Surg. 2014;149(3):275-287. doi:10.1001/jamasurg.2013.3654
Published online December 18, 2013.

 Supplemental content at
jamasurgery.com

Author Affiliations: Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St Louis, Missouri (Chang, Stoll, Colditz); Department of Statistics, Seoul National University, Seoul, South Korea (Song); Minimally Invasive and Bariatric Surgery, Department of Surgery, Washington University School of Medicine, St Louis, Missouri (Varela, Eagon); currently with ASAN Medical Center, Seoul, South Korea (Song).

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

The prevalence of overweight and obesity is increasing globally.¹ Among high-income countries, the United States has the highest mean body mass index (BMI) for men and women,² and more than two-thirds of US adults 20 years or older are overweight or obese.³ Overweight and obesity are associated with increased risk of morbidity⁴⁻¹¹ and mortality.¹²⁻¹⁵ Approximately 112 000 deaths per year are associated with obesity in the United States.¹⁶

Treatments of obesity, except surgery, are generally ineffective in long-term weight control.¹⁷⁻²² 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.²²⁻²⁶ 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.^{27,28}

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, eg, Buchwald et al²⁹ and Maggard et al,³⁰ 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 colleagues³¹ focused only on randomized clinical trials (RCTs). Their data included recently published trials but did not exclude early publications. Because of advances in technology of bariatric surgery (eg, new procedures, such as sleeve gastrectomy [SG], were developed) 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 was to quantify risks and benefits of various bariatric surgery procedures focusing on adult patients. Specifically, we report the risks (defined as perioperative and postoperative mortality, complications, and reoperations) and the effectiveness (defined as weight loss and remission of obesity-related diseases). We conducted a systematic review and meta-analysis on relevant studies selected from recent publications, including both RCTs and observational studies (OBSs). For each study design,³² random-effects (RE) or/and fixed-effect (FE) models³³ were considered, and appropriate meta-analytic techniques were used to analyze the data.

Methods

This systematic review and meta-analysis was conducted and reported according to the established guidelines.^{34,35} A review protocol (available at <http://www.publichealthsciences.wustl.edu/en/Faculty/ChangSu-Hsin>) was followed throughout.

Data Sources and Searches

A search strategy was created by a Master of Library and Information Science-qualified librarian. Comprehensive searches of the literature were performed on Medline,

Embase, Scopus, Cochrane Library, and Clinicaltrials.gov with the time frame of January 1, 2003, to March 31, 2012. Searches were performed using the Firefox browser (Mozilla), and results were imported to EndNote X5 (Thomson Reuters). Search terms are detailed in the eAppendix (section 1) in the Supplement.

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 >18 years). After removing excluded abstracts, full articles were obtained and studies were screened again more thoroughly using the same exclusion criteria.

Data Extraction

Studies were included in data extraction if they reported surgical procedure performed and at least 1 outcome of interest resulting from that surgery. Data needed to be presented separately by surgical procedure if more than 1 procedure was performed. Initial study population size and sample size at all data collection points were recorded. Characteristics of the starting study sample, such as age, race, sex, and weight information, were collected when available. Presurgery and postsurgery 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.

Quality Assessment

All studies were evaluated for quality using a 6-category scoring system (range, 0-6).³⁶ The categories were (1) clear definition of surgeries; (2) clear times 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%; and (6) reports of funding sources/conflicts of interest.^{31,36-39} For categories 1 to 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 greater than 20%; and a score of 1 indicated that loss to follow-up was less than 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 to 6 were designed to assess the risk of study bias.

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 5 categories: (1) gastric bypass (GB); (2) adjustable gastric banding (AGB); (3) vertical banded gastroplasty (VBG); (4) SG; and (5) nonsurgical interventions (control). Surgical outcomes in terms of percentage of excess weight loss (%EWL) ($\%EWL = [(\text{operative weight} - \text{follow-up weight}) / \text{operative excess weight}] \times 100$, where excess weight = actual weight – ideal weight,⁴⁰ and ideal weight is derived from the 1983 Metropolitan insurance height and weight tables⁴¹), BMI change (Δ BMI), perioperative and postoperative 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.

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 that identified the deaths occurring within 30 days of the surgery and studies that 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 (deaths of unspecified causes were not excluded in any mortality analyses). 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. (Specific surgical complications were variably reported and difficult to catalog. Therefore, only overall complication rate was analyzed.) 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. (Because of 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 1 in the Supplement).

Mortality, complication, and comorbidity remission rates were estimated by the Bayesian RE meta-analysis method^{42,43} to avoid statistical problems caused by zero or rare events in each study.^{44–46} In addition, a simple averaging method proposed by Bhaumik et al⁴⁶ was conducted as an alternative to the Bayesian RE meta-analysis. Both methods are detailed in the eAppendix (section 2) in the Supplement.

Weight Loss Outcomes

All yearly postsurgery weight outcomes were compared with the presurgery weight. The 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.^{47,48} Publication bias was evaluated using funnel plots and the Egger test.^{49,50} We report postsurgery Δ BMI

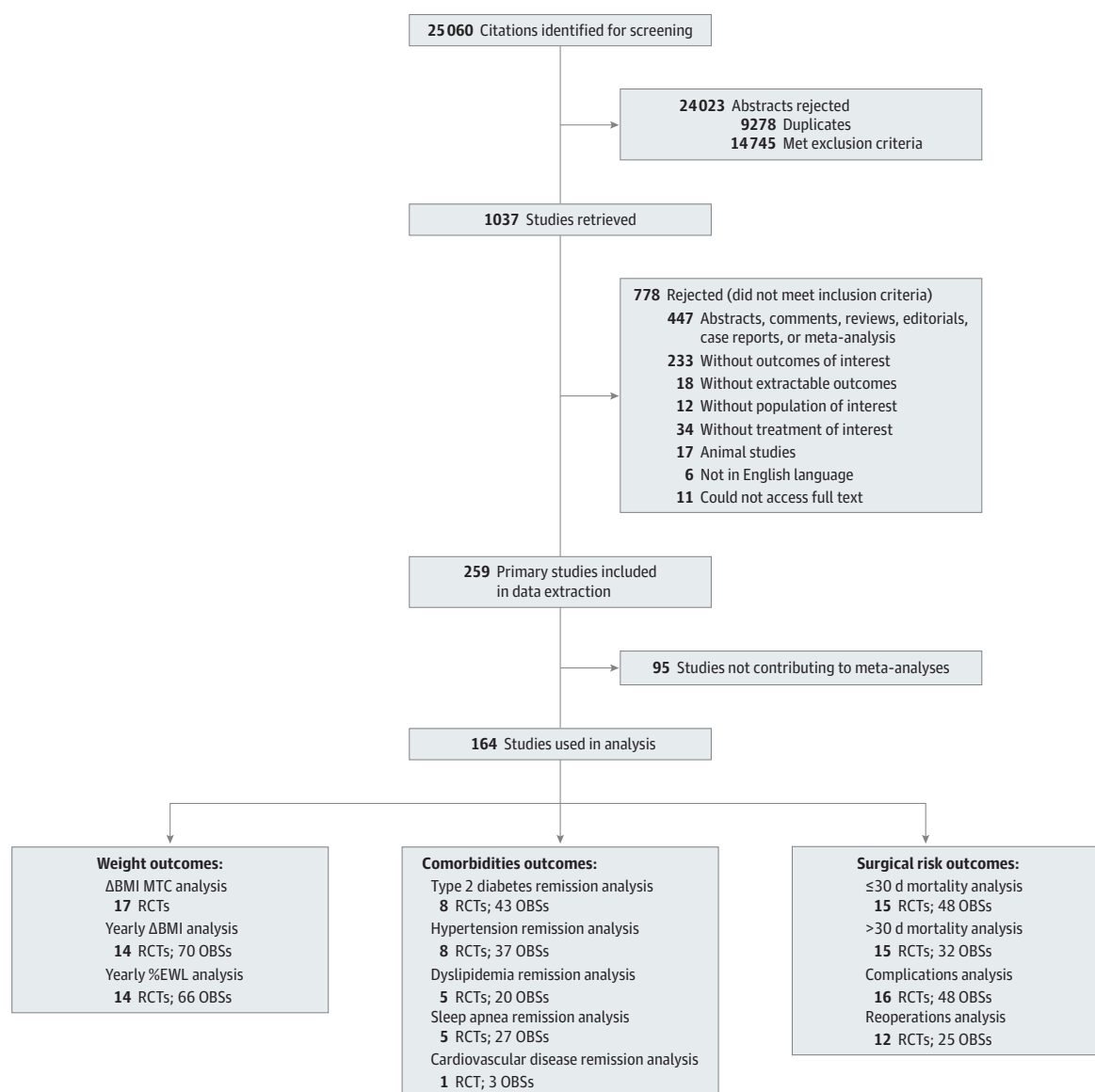
and %EWL for both study designs. Meta-regression of Δ BMI was conducted to account for patient characteristics (eg, presurgery BMI, sex composition, and age), study design and quality, surgical procedure, and geographic location. We performed a preliminary meta-regression, using overall quality scores to determine if analyses of Δ BMI 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 Δ BMI at different study points in the trials and to compare and contrast the findings in Padwal et al,³¹ we conducted mixed treatment comparison (MTC) meta-analysis that allows for repeated measurements using a Bayesian approach,⁵¹ targeting all RCTs from which we extracted data. This method allowed us to statistically combine time-varying information on multiple pairwise comparisons to make inferences about relative effects between multiple surgical procedures.⁵² We categorized into 11 surgical procedures/interventions and further grouped those procedures into 5 larger surgery categories (eAppendix [section 3] and eTable 2 in the Supplement). (The 5 categories were the same as the aforementioned 5 categories. Eleven surgical procedures/interventions included [1] laparoscopic Roux-en-Y GB [LRYGB]; [2] open Roux-en-Y GB [RYGB]; [3] LRYGB with presurgery weight loss; [4] laparoscopic biliopancreatic diversion with duodenal switch [BPD-DS]; [5] BPD with RYGB [BPD-RYGB]; [6] laparoscopic AGB [LAP-BAND (Allergan)]; [7] laparoscopic AGB [Swedish band]; [8] laparoscopic VBG; [9] open VBG; [10] laparoscopic 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.) Four MTC models were considered (eAppendix [section 3] in the Supplement). We estimated postsurgery Δ BMI compared with the reference (relative surgery effect) in these models, taking advantage of the direct and indirect comparisons within study arms of RCTs. (Among those procedures, LRYGB was the most commonly compared procedure [eAppendix (section 3) and eFigure 1 in the Supplement], and therefore, LRYGB was the reference in model 1. In model 2, the GB category was the reference.) Herein, we only present the first 2 models.

We computed the standard deviations of Δ BMI whenever possible if they were not reported in the original articles. (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 presurgery and postsurgery BMI.) 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.⁵¹

The FE and RE meta-analyses using the frequentist approach were performed using Stata (SE/11.2; StataCorp). Bayesian RE meta-analysis was conducted by R (2.14.0; R Development Core Team) and JAGS (“runjags” package version 0.9.9-2; <http://mcmc-jags.sourceforge.net/>). Bhaumik estimates and the numerical solutions of the standard errors were obtained using MATLAB (7.11, R2012a; MathWorks). The MTC meta-analyses were conducted using WinBUGS (1.4.3; The BUGS Project). For weight outcomes, we report the means for RE, the relative sur-

Figure 1. Study Attrition Diagram



Remission is defined as the target comorbid condition being either resolved or improved after surgery. BMI indicates body mass index; %EWL, percentage of

excess weight loss; MTC, mixed treatment comparison; OBS, observational study; RCT, randomized clinical trial; and ΔBMI, BMI change.

gery effect for MTC, and the estimates for meta-regression; for the other outcomes, we report the means for Bayesian RE models, while the rest are presented in the eAppendix, eTable 3, and eTable 4 in the Supplement. The 95% confidence/credible intervals (CIs) associated with the frequentist/Bayesian estimates are also reported.

Results

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, 1037 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 127 OBSs) were included in meta-analyses. (The extracted studies were excluded from the analyses if they reported outcomes inconsistent with our stratification or missed reporting at least 1 key element to be included in our analyses, eg, times, clear definition of the outcome, and aggregately reported outcomes. A list of the included articles is available at <http://www.publichealthsciences.wustl.edu/en/Faculty/ChangSu-Hsin>.) Studies could contribute to more than 1 analysis.

Table 1. Study Characteristics

Study Characteristic	No. of Studies	No. of Patients
Publication year		
2003-2007	62	41 382
2008-2012	102	120 374
Study design		
RCT	37	3385
OBS	127	158 371
Follow-up, y		
≥2	91	28 671
<2	73	133 085
Study location		
North America	54	130 045
Europe	72	22 703
Asia	13	3099
Multinational	1	18
Other	24	5891
Age	140	100 094
BMI	142	90 587
Weight	68	16 790

Abbreviations: BMI, body mass index; OBS, observational study; RCT, randomized clinical trial.

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 forty studies reported patients' mean age, and 142 contained their presurgery BMI information.

A total of 161 756 patients were included in our analyses. Among studies reporting participants' information, mean age of the participants was 44.56 years, 78.87% were female, and 74.64% were white (Table 2). Presurgery BMI was 45.62 and presurgery weight was 124.53 kg. Among the studies that provided information about obesity-related comorbidities, 26.24% of the patients had type 2 diabetes, 47.39% had hypertension, 27.97% had dyslipidemia, 7.15% had cardiovascular diseases, and 25.30% had sleep apnea.

Meta-analysis Results

Operative Mortality, Postoperative Complication, and Reoperation Rates

Table 3 shows the meta-analytic results of surgical risks. Operative mortality was relatively low. Sixty-three studies (109 study arms) reported perioperative (≤30 days) mortality data, and 47 studies (81 study arms) reported postoperative (>30 days) mortality data. For RCTs, perioperative mortality rate was 0.08% (95% CI, 0.01%-0.24%), and postoperative mortality rate was 0.31% (95% CI, 0.01%-0.75%). For OBSs, both perioperative and postoperative mortality rates were higher: 0.22% (95% CI, 0.14%-0.31%) and 0.35% (95% CI, 0.20%-0.52%). In OBSs, AGB had the lowest perioperative and postoperative mortality rates (0.07% [95% CI, 0.02%-0.12%] and 0.21% [95% CI,

Table 2. Patient Characteristics

Patient Characteristic	No./Total No. (%)
Age, y, mean	44.56
BMI, mean	45.62
Weight, kg, mean	124.53
Sex	
M	32 384/153 267 (21.13)
F	120 883/153 267 (78.87)
Race	
White	87 653/117 430 (74.64)
Nonwhite	29 777/117 430 (25.36)
Comorbidities	
Type 2 diabetes	19 258/73 378 (26.24)
Hypertension	34 092/71 938 (47.39)
Cardiovascular disease	1913/26 752 (7.15)
Dyslipidemia	11 533/41 235 (27.97)
Sleep apnea	11 794/46 609 (25.30)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

0.08%-0.37%]), followed by SG (0.29% [95% CI, 0.11%-0.63%] and 0.34% [95% CI, 0.14%-0.60%]) and then GB (0.38% [95% CI, 0.22%-0.59%] and 0.72% [95% CI, 0.28%-1.30%]).

Sixty-four studies (16 RCTs and 48 OBSs) contributed to meta-analyses of complications. The complication rate was 17% (95% CI, 11%-23%) for RCTs but lower for OBSs (10% [95% CI, 7%-13%]). This pattern persisted across all surgical procedures. For RCTs, complications rates were relatively low for SG (13% [95% CI, 1%-44%]) and AGB (13% [95% CI, 5%-26%]) compared with GB (21% [95% CI, 12%-33%]).

Reoperation rates were not as high as complication rates: 7% (95% CI, 3%-12%) for RCTs and 6% (95% CI, 4%-8%) for OBSs. In RCTs, GB appeared to have the lowest reoperation rate (3% [95% CI, 1%-5%]), followed by SG (9% [95% CI, 1%-35%]), while in OBSs, SG had the lowest reoperation rate (3% [95% CI, 2%-5%]), followed by GB (5% [95% CI, 4%-6%]). Adjustable GB appeared to have the highest reoperation rate (12% [95% CI, 4%-24%] for RCTs and 7% [95% CI, 4%-11%] for OBSs).

Weight Loss

Table 4 presents results of the postsurgery 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 1 year after surgery, but only 11 studies (17 study arms) reported ΔBMI at 5 years after surgery. Body mass index loss within 5 years after surgery was persistent in the range of 12 to 17 for OBSs (Figure 2A). (Very few studies reported weight loss information beyond 5 years after surgery. However, 2 articles^{53,54} based on the Swedish Obese Subjects Study reporting ΔBMI≥10 years after surgery reported that the mean BMI reduction 10 years and 15 years after surgery was still approximately 6.5 and 7.1.) There was no evidence of publication bias in any analysis, except for ΔBMI at postsurgery years 1 and 3 for OBSs (eFigure 2 in the Supplement).

Table 3. Meta-analyses of Surgery Risk and Comorbidities Remission Outcomes^a

	Mean (95% CI)				
	GB	AGB	SG	Control	Overall
Mortality ≤30 d					
RCT					
Estimates, %	0.08 (0.01-0.30)	0.11 (0.01-0.50)	0.50 (0.01-3.88)	^b	0.08 (0.01-0.24)
Study/arm/No. of patients	11/18/934	5/8/743	1/2/40	0/0/0	15/30/1803
OBS					
Estimates, %	0.38 (0.22-0.59)	0.07 (0.02-0.12)	0.29 (0.11-0.63)	^b	0.22 (0.14-0.31)
Study/arm/No. of patients	19/30/90 090	26/29/40 538	10/11/3647	1/1/9	48/79/136 903
Mortality >30 d					
RCT					
Estimates, %	0.39 (0.01-0.86)	0.14 (0.00-0.55)	6.00 (0.00-100.00)	^b	0.31 (0.01-0.75)
Study/arm/No. of patients	11/19/954	5/7/613	2/2/40	0/0/0	15/30/1703
OBS					
Estimates, %	0.72 (0.28-1.30)	0.21 (0.08-0.37)	0.34 (0.14-0.60)	^b	0.35 (0.20-0.52)
Study/arm/No. of patients	13/18/29 256	18/22/33 950	8/9/3099	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)	^b	17.00 (11.00-23.00)
Study/arm/No. of patients	10/14/649	7/11/855	2/2/137	2/2/59	16/30/1778
OBS					
Estimates, %	12.00 (7.30-17.00)	7.80 (3.90-13.00)	8.90 (5.60-13.00)	^b	9.80 (7.40-13.00)
Study/arm/No. of patients	19/28/71 020	22/24/36 778	8/20/4987	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)	^b	6.95 (3.27-12.04)
Study/arm/No. of patients	6/8/512	8/10/502	2/2/161	0/0/0	12/23/1322
OBS					
Estimates, %	5.34 (4.48-6.48)	7.01 (3.99-11.24)	2.96 (1.70-4.71)	^b	5.75 (4.05-7.83)
Study/arm/No. of patients	6/8/23 688	18/21/30 314	7/7/2912	0/0/0	25/39/57 171
Diabetes remission rates					
RCT					
Estimates, %	95.15 (88.38-98.80)	73.88 (36.06-96.18)	^b	17.64 (0.98-69.27)	91.99 (84.68-97.18)
Study/arm/No. of patients	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)	^b	86.05 (78.74-91.62)
Study/arm/No. of patients	16/22/5924	18/19/2509	14/15/597	0/0/0	43/57/9037
Hypertension remission rates					
RCT					
Estimates, %	80.98 (68.21-91.52)	53.55 (12.52-89.63)	^b	49.00 (0.00-99.00)	75.18 (61.52-86.35)
Study/arm/No. of patients	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/No. of patients	11/15/9586	18/19/6214	11/12/1152	2/2/82	37/47/16 962
Dyslipidemia remission rates					
RCT					
Estimates, %	80.16 (61.68-94.19)	39.95 (4.69-87.05)	^b	^b	75.77 (55.63-91.49)
Study/arm/No. of patients	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/No. of patients	5/7/556	11/11/351	5/5/570	1/1/63	20/23/1477

(continued)

Table 3. Meta-analyses of Surgery Risk and Comorbidities Remission Outcomes^a (continued)

	Mean (95% CI)				
	GB	AGB	SG	Control	Overall
Cardiovascular disease remission rates					
RCT					
Estimates, %	^b	^b	^b	^b	65.81 (6.21-99.46)
Study/arm/No. of patients	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)	^b	^b	58.00 (0.00-100.00)
Study/arm/No. of patients	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)	^b	^b	96.16 (86.66-99.80)
Study/arm/No. of patients	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)	^b	89.53 (81.33-95.08)
Study/arm/No. of patients	8/11/5748	13/14/3598	8/9/498	0/0/0	27/35/9845

Abbreviations: AGB, adjustable gastric banding; Control, nonsurgical interventions (nonsurgical interventions were included in the analyses only when they were compared with surgical interventions); GB, gastric bypass; OBS, observational study; Overall, all surgery except for Control; RCT, randomized clinical trial; SG, sleeve gastrectomy.

^a Estimates were computed using Bayesian random-effects meta-analysis.

Arms refer to subgroups within studies receiving different surgical procedures. Remission rate is defined as the proportion of the surgery patients who reported the target comorbid condition being either resolved or improved after surgery.

^b Estimates are not available when 0/0/0 (no data were included in the analysis) is presented or not relevant.

The preliminary meta-regression showed that quality scores were not associated with postsurgery Δ BMI ($P = .15$ for year 1 and $P = .96$ for year 2). Therefore, analyses including only studies with higher-quality scores were not performed. The main meta-regression results showed that presurgery BMI and younger age were positively associated with postsurgery BMI loss (eAppendix [section 4.3] and eTable 5 in the Supplement). Randomized clinical trial 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 postsurgery. Having loss to follow-up greater than 20% was associated with more significant weight loss in the second year after surgery. Body mass index loss was significantly less for AGB, SG, and nonsurgical interventions compared with 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 1 year postsurgery, and 18 studies (2 RCTs and 16 OBSs) reported %EWL 3 years after surgery (lower half of Table 4). For RCTs, year 1 %EWL was 60% (95% CI, 50%-70%), $I^2 = 85\%$; year 2 %EWL was 71% (95% CI, 63%-79%), $I^2 = 63\%$; and year 3 %EWL was 57% (95% CI, 52%-62%), $I^2 = 0\%$. For OBSs, %EWL in the first 3 years were 46% (95% CI, 44%-48%), $I^2 = 90\%$; 64% (95% CI, 55%-73%), $I^2 = 90\%$; and 67% (95% CI, 65%-69%), $I^2 = 0\%$.

Body mass index loss was larger for GB than AGB. Both VBG (eTable 4 in the Supplement) and SG (Table 4) appeared to have significant effects on BMI loss, although data were limited for these surgical procedures. The 1 OBS that had 5-year follow-up data on Δ BMI after SG reported sustained BMI loss (approx-

mately 16) in year 5.⁵⁵ (In addition, the 1 OBS that had 5-year follow-up data on Δ BMI after VBG was performed reported sustained Δ BMI of approximately -16 for years 4 and 5.⁵⁶)

To make more meaningful comparison between surgical procedures, MTC meta-analysis was used. Figure 2B demonstrates the MTC meta-analysis results of Δ BMI from 17 RCTs. Relative surgery effects compared with the LRYGB procedure are presented in a forest plot (estimates are shown in eTables 6, 7, 8, and 9 in the Supplement). Relative category effects compared with the GB category are presented in the shape of rhombuses (estimates are shown in eTable 7 in the Supplement). Nonsurgical intervention had the least BMI loss, 14 (95% CI, 6-22) less than LRYGB (eTable 6 in the Supplement). Among the 5 categories, AGB and VBG resulted in less BMI loss than GB, while SG had a similar effect. Within the GB category, the combined methods (laparoscopic BPD-DS, BPD-RYGB, and LRYGB with presurgery weight loss) led to higher BMI loss than LRYGB alone, while open RYGB 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. Laparoscopic AGB using LAP-BAND or an unspecified brand of band appeared to be slightly more effective than laparoscopic AGB using a Swedish band, and laparoscopic VBG led to more weight loss than open VBG.

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 3). Eight RCTs (206 patients) and 43 OBSs (9037 patients) provided diabetes information. The percentage of diabetes remission after surgery was 92% (95% CI, 85%-97%) for

Table 4. Meta-analyses of Weight Change Outcomes^a

	Mean (95% CI)				
	GB	AGB	SG	Control	Overall
ΔBMI					
Year 1					
RCT					
Estimates	-14.53 (-16.82 to -12.25)	-10.48 (-13.70 to -7.25)	-16.20 (-24.45 to -7.95)	^b	-13.53 (-15.51 to -11.55)
No. of studies/arms	9/15	3/3	1/1	0/0	12/22
OBS					
Estimates	-14.32 (-19.02 to -9.62)	-7.70 (-9.37 to -6.03)	-12.14 (-14.02 to -10.26)	-1.01 (-5.26 to 3.23)	-11.79 (-13.89 to -9.69)
No. of studies/arms	27/37	24/27	17/18	3/4	57/87
Year 2					
RCT					
Estimates	-14.47 (-16.98 to -11.97)	-11.35 (-14.24 to -8.46)	^b	^b	-13.23 (-15.36 to -11.11)
No. of studies/arms	6/10	2/2	0/0	0/0	8/15
OBS					
Estimates	-12.93 (-17.39 to -8.47)	-8.75 (-10.37 to -7.13)	-13.39 (-19.52 to -7.26)	0.10 (-7.39 to 7.60)	-11.80 (-13.92 to -9.69)
No. of studies/arms	12/16	14/16	5/5	1/2	29/40
Year 3					
RCT					
Estimates	^b	-9.20 (-15.85 to -2.54)	^b	^b	-9.20 (-15.85 to -2.54)
No. of studies/arms	0/0	1/2	0/0	0/0	1/2
OBS					
Estimates	-16.78 (-20.57 to -12.99)	-11.43 (-18.14 to -4.72)	-21.88 (-27.96 to -15.79)	^b	-15.48 (-18.79 to -12.18)
No. of studies/arms	6/9	7/8	2/2	0/0	17/21
Year 4					
RCT					
Estimates	^b	^b	^b	^b	^b
No. of studies/arms	0/0	0/0	0/0	0/0	0/0
OBS					
Estimates	-17.86 (-22.20 to -13.53)	-6.20 (-18.62 to 6.22)	^b	^b	-17.00 (-20.80 to -13.19)
No. of studies/arms	5/8	1/1	0/0	0/0	8/11
Year 5					
RCT					
Estimates	^b	-11.40 (-28.08 to 5.28)	^b	^b	-11.40 (-28.08 to 5.28)
No. of studies/arms	0/0	1/1	0/0	0/0	1/1
OBS					
Estimates	-15.96 (-20.52 to -11.40)	-12.36 (-16.92 to -7.79)	-16.10 (-28.22 to -3.98)	^b	-14.32 (-17.19 to -11.45)
No. of studies/arms	4/7	4/7	1/1	0/0	10/16

(continued)

RCTs and 86% (95% CI, 79%-92%) for OBSs. The remission rates of hypertension were somewhat lower: 75% (95% CI, 62%-86%) for RCTs and 74% (95% CI, 67%-81%) for OBSs. Fewer studies (5 RCTs and 20 OBSs) investigated dyslipidemia; how-

ever, a large number of patients were included (279 patients in RCTs and 1477 patients in OBSs). Data from RCTs showed 76% (95% CI, 56%-91%) remission of dyslipidemia after surgery. In OBSs, the remission rate was 68% (95% CI, 58%-77%).

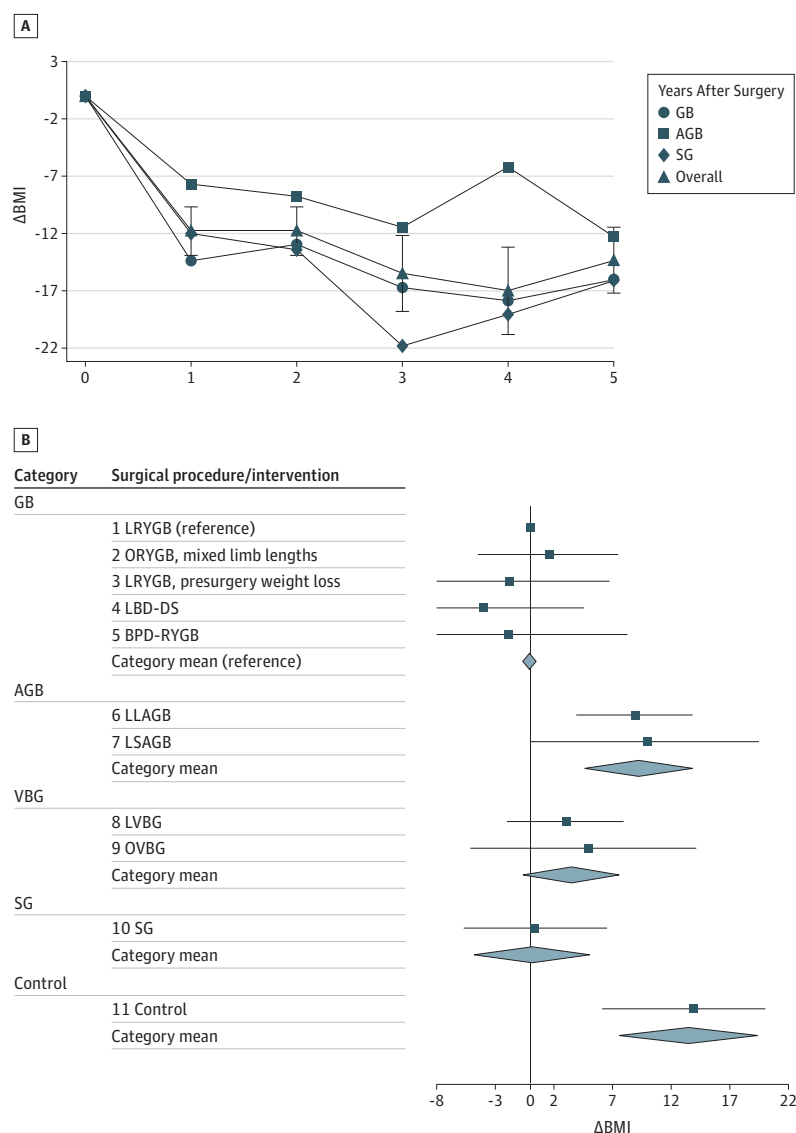
Table 4. Meta-analyses of Weight Change Outcomes^a (continued)

	Mean (95% CI)				
	GB	AGB	SG	Control	Overall
%EWL					
Year 1					
RCT					
Estimates, %	72.32 (64.60 to 80.04)	33.39 (22.57 to 44.21)	69.70 (41.09 to 98.32)	^b	59.82 (50.46 to 69.17)
No. of studies/arms	5/7	4/4	1/1	0/0	9/15
OBS					
Estimates, %	63.31 (54.20 to 72.43)	34.26 (33.98 to 34.54)	51.49 (44.41 to 58.56)	20.00 (−25.08 to 65.08)	46.16 (43.89 to 48.43)
No. of studies/arms	17/25	14/15	11/11	1/1	39/55
Year 2					
RCT					
Estimates, %	74.39 (66.22 to 82.55)	53.58 (32.80 to 74.87)	^b	^b	70.58 (62.67 to 78.50)
No. of studies/arms	4-6	3/3	0/0	0/0	7/12
OBS					
Estimates, %	80.09 (65.74 to 94.43)	52.29 (48.67 to 55.92)	46.72 (42.89 to 50.55)	^b	63.98 (55.21 to 72.74)
No. of studies/arms	7/9	11/11	3/3	0/0	22/27
Year 3					
RCT					
Estimates, %	^b	56.72 (51.59 to 61.85)	^b	^b	56.72 (51.59 to 61.85)
No. of studies/arms	0/0	2/2	0/0	0/0	2/2
OBS					
Estimates, %	76.35 (65.21 to 87.50)	58.30 (42.12 to 74.49)	59.42 (48.05 to 70.78)	^b	66.93 (65.05 to 68.82)
No. of studies/arms	6/8	6/6	2/2	0/0	16/19
Year 4					
RCT					
Estimates, %	^b	^b	^b	^b	^b
No. of studies/arms	0/0	0/0	0/0	0/0	0/0
OBS					
Estimates, %	76.36 (59.02 to 93.70)	74.91 (58.54 to 91.29)	^b	^b	74.82 (65.85 to 83.80)
No. of studies/arms	3/5	3/3	0/0	0/0	8/10
Year 5					
RCT					
Estimates, %	^b	41.60 (−9.75 to 92.95)	^b	^b	41.60 (−9.75 to 92.95)
No. of studies/arms	0/0	1/1	0/0	0/0	1/1
OBS					
Estimates, %	64.92 (44.27 to 85.58)	57.23 (47.23 to 67.23)	^b	^b	62.24 (58.71 to 65.78)
No. of studies/arms	3/5	5/8	0/0	0/0	10/15

Abbreviations: AGB, adjustable gastric banding; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); Control, nonsurgical interventions (nonsurgical interventions were included in the analyses only when they were compared with surgical interventions); GB, gastric bypass; OBS, observational study; Overall, all surgery except for Control; RCT, randomized clinical trial; SG, sleeve gastrectomy; ΔBMI, BMI change; %EWL, percentage of excess weight loss.

^a Estimates were obtained from random-effects models using the frequentist approach. Arms refer to subgroups within studies receiving different surgical procedures.

^b Estimates are not available when 0/0 (no data were included in the analysis) is presented.

Figure 2. Meta-analysis of Body Mass Index Change (Δ BMI) After Surgery

A, Results of random-effects meta-analysis using the frequentist approach for Δ BMI for observational studies. Marker size is proportional to the number of study arms included in each analysis. B, Mixed treatment comparison meta-analysis results for Δ BMI (models 1 and 2) for randomized clinical trials. Estimates of model 1 are presented in the format of a forest plot; each estimate is the relative surgery effect compared with laparoscopic Roux-en-Y gastric bypass (LRYGB). Estimates of model 2 are presented in rhombuses; each estimate of model 2 is the relative category effect compared with gastric bypass (GB). A negative value means that the referent procedure/intervention (category) resulted in a lower Δ BMI, and vice versa. AGB indicates adjustable gastric banding; BPD-RYGB, biliopancreatic diversion with Roux-en-Y gastric bypass; Control, nonsurgical interventions; LBD-DS, laparoscopic biliopancreatic diversion with duodenal switch; LLAGB, laparoscopic adjustable gastric banding with LAP-BAND; LSAGB, laparoscopic adjustable gastric banding with Swedish band; LVGB, laparoscopic vertical banded gastroplasty; ORYGB, open Roux-en-Y gastric bypass; OVGB, open vertical banded gastroplasty; Overall, all surgery except for control; SG, sleeve gastrectomy; and VBG, vertical banded gastroplasty.

Only 3 OBSs (27 patients) studied postsurgery conditions of cardiovascular disease, and the remission rate was 58% (95% CI, 0%-100%). Five RCTs with 44 patients and 27 OBSs with 9845 patients were included in the sleep apnea analysis. The remission rates were high: 96% (95% CI, 87%-100%) for RCTs and 90% (95% CI, 81%-95%) for OBSs.

Discussion

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,²⁹⁻³¹ 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 by Buchwald et al²⁹ and Maggard et al.³⁰ (Even though zeros were imputed for missing data and grouped into the early death outcome in Maggard et al,³⁰ lower early mortality rates for RCTs were still found in our study.) We also found significant improvement in comorbidities, which is consistent with findings in Buchwald et al²⁹ (in another review article, Buchwald and colleagues⁵⁷ found that type 2 diabetes was resolved or improved in the greater majority of bariatric patients), while Padwal et al³¹ 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 nonsurgical intervention in weight loss. A detailed comparison of findings across previous and our meta-analyses are summarized in eTable 10 in the Supplement.

Our findings are consistent with previous literature that AGB has lower mortality and complication rates than GB,^{38,39}

but not a decreased reoperation rate. Sleeve gastrectomy was positioned between AGB and GB⁵⁸ in terms of mortality and complication rates in OBSs (but not in RCTs) and postsurgery Δ BMI in MTC meta-analysis of RCTs (but not in RE meta-analyses). The inconsistency is possibly because of 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 with GB even at 5 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, open RYGB had the least BMI loss, and laparoscopic BPD-DS had the most BMI loss among all procedures. We also found that laparoscopic BPD-DS and BPD-RYGB had better short-term (<1 year) and mid-term (≥ 1 and <3 years) effects on BMI loss (eTable 9 in the Supplement).

We observed systematic differences in outcomes between RCTs and OBSs in the magnitude of the effects.^{59,60} 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. (This holds true for all surgical procedures, except VBG for complication and comorbidity remission rates and GB for reoperation rates.) This could be explained by more detailed monitoring and reporting of outcomes in RCTs because of 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 and Hartz,⁶¹ 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.

Our study is restrained by the following limitations. First, like all other meta-analyses, the results need to be interpreted acknowledging that surgery effects vary based on characteristics of the individual patient, eg, age, sex, and 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 (1) some procedures were not as popular as others⁶² and (2) fewer studies reported post-surgery years 3 to 5 weight loss outcomes. Third, although the use 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 times, 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 need to be interpreted with caution because of the heterogeneous outcome reporting of each included study, eg, no standardized criteria of comorbidity improvement across studies. (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 1 in the Supplement] comparing definitions across studies was provided to allow interpretation of results in context.)

Conclusions

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. Adjustable GB is considered safer^{63,64} 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.

ARTICLE INFORMATION

Accepted for Publication: June 17, 2013.

Published Online: December 18, 2013.
doi:10.1001/jamasurg.2013.3654.

Author Contributions: Dr Chang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Chang, Varela, Eagon, Colditz.

Acquisition of data: Chang, Stoll.

Analysis and interpretation of data: Chang, Stoll, Song, Varela, Colditz.

Drafting of the manuscript: Chang, Stoll, Varela.

Critical revision of the manuscript for important intellectual content: Chang, Stoll, Song, Eagon, Colditz.

Statistical analysis: Chang, Stoll, Song, Varela, Colditz.

Obtained funding: Chang, Colditz.

Administrative, technical, or material support: Chang, Stoll, Colditz.

Study supervision: Chang, Eagon, Colditz.

Conflict of Interest Disclosures: None reported.

Funding/Support: This publication was made possible by grants KMICA156708-01 and U54 CA 155496 through the National Cancer Institute at the National Institutes of Health and grant K01 HSO22330 through the Agency for Healthcare Research and Quality. Funding from the Foundation for Barnes-Jewish Hospital also supported this research. Dr Colditz is supported by an American Cancer Society Clinical Research Professorship.

Role of the Sponsor: The sponsors had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The conclusions and opinions presented herein are solely the responsibility of the authors and do not necessarily represent the official views the National Institutes of Health or the Barnes-Jewish Hospital Foundation.

Additional Contributions: We thank Carol Murray, MLIS, Bernard Becker Medical Library at the Washington University in St Louis, Missouri, who helped develop search strategies and performed computerized searches. We also thank Helen Dakin, PhD, at the Health Economics Research Centre, University of Oxford, for providing computer codes to help understand using WinBUGS to perform MTC meta-analysis. We acknowledge Jennifer Rowley, Ellen Murray, BA, Misty Lewis, MSW, Amanda Calhoun, BA, and Nikki Freeman, MA, for performing substantive data extraction and table editing. Finally, we thank Jean Wang, MD, in the Division of Gastroenterology and Michael Awad, MD, PhD, in the Department of Surgery, Washington University School of Medicine, for helpful conversation regarding complications associated with bariatric surgery.

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