Bariatric Surgery: A Systematic Review of the Clinical and Economic Evidence

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CONTEXT: Use of bariatric surgery for severe obesity has increased dramatically.

OBJECTIVE: To systematically review 1. the clinical efficacy and safety, 2. cost-effectiveness of bariatric surgery, and 3. the association between number of surgeries performed (surgical volume) and outcomes.

DATA SOURCES: MEDLINE (from 1950), EMBASE (from 1980), CENTRAL, EconLit, EURON EED, Harvard Center for Risk Analysis, trial registries and HTA websites were searched to January 2011.

STUDY SELECTION: 1. Randomized controlled trials (RCTs) and 2. cost-utility and cost-minimisation studies comparing a contemporary bariatric surgery (i.e., adjustable gastric banding, Roux-en-Y gastric bypass, sleeve gastrectomy) to another contemporary surgical comparator or a non-surgical treatment or 3. Any study reporting the association between surgical volume and outcome.

DATA EXTRACTION: Outcomes included changes in weight and obesity-related comorbidity, quality of life and mortality, surgical complications, resource utilization, and incremental cost-utility.

RESULTS: RCT data evaluating mortality and obesity-related comorbidity endpoints were lacking. A small RCT of 16 patients reported that adjustable gastric banding reduced weight by 27% ($p < 0.01$) compared to diet-treated controls over 40 weeks. Six small RCTs reported comparisons of commonly used, contemporary procedures. Gastric banding reduced weight to a lower extent than gastric bypass and sleeve gastrectomy and resulted in shorter operating times, fewer serious complications, lower weight loss efficacy, and more frequent reoperations compared to gastric bypass. Sleeve gastrectomy and gastric bypass reduced weight to a similar extent. A 2-year RCT in 50 adolescents reported that gastric banding substantially reduced weight compared to lifestyle modification (35 kg vs. 3 kg; $p < 0.001$). Based on findings of 14 observational studies, higher volume centers and surgeons had lower mortality and complication rates. Surgery resulted in long-term incremental cost-utility ratios of \$ <1,000–

\$40,000 (2009 USD) per quality-adjusted-life-year compared with non-surgical treatment.

CONCLUSIONS: Contemporary bariatric surgery appears to result in sustained weight reduction with acceptable costs but rigorous, longer-term (≥ 5 year) data are needed and a paucity of RCT data on mortality and obesity related comorbidity is evident. Procedure-specific variations in efficacy and risks exist and require further study to clarify the specific indications for and advantages of different procedures.

KEY WORDS: randomized controlled trials; clinical evidence; economic evidence; systematic review.

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BACKGROUND

Over the past two decades, use of bariatric surgery to treat morbid obesity has increased dramatically. An estimated 350,000 bariatric procedures were performed globally (63% in US/Canada) in 2008 compared to fewer than 5,000 procedures between 1987–1989^{1,2}. Currently, 90% of procedures are performed laparoscopically². The most common operations are adjustable gastric banding (AGB; 42%), Roux-en-Y gastric bypass (RYGB; 40%) and sleeve gastrectomy (SG; 5%) (Table 1)².

According to current guidelines, patients who fail non-surgical intervention and who have Class III obesity (body mass index [BMI] ≥ 40 kg/m²) or medically complicated Class II obesity (BMI ≥ 35 –39.9 kg/m² with a major obesity-related comorbidity) are potentially eligible for surgery^{3,4}. Approximately 5.7% of US adults have a BMI ≥ 40 kg/m², 8.6% have BMI levels between 35–39.9 kg/m², and about 60% of this latter group have a major obesity-related complication^{5,6}. Therefore, about 10.9% of US adults are potentially eligible for bariatric surgery. Although indications for bariatric surgery in adolescents are less well established, 12% of children and adolescents have BMI levels above the 97th percentile, and are at greater risk for obesity-related complications and premature mortality in adulthood^{7,8}.

In reality, the mean or median BMI levels of patients undergoing surgery exceeds 45 kg/m² and so the majority of patients undergoing surgery are severely obese^{9,10}. The clinical

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Table 1. Summary of Bariatric Surgical Interventions (reprinted with permission from reference 13)

Procedure	Type	Description	Illustration
Adjustable Gastric Band ^{77, 78} (AGB)	Restrictive	A band encircling the proximal stomach and connected to a subcutaneous port/reservoir is inserted. The band remains initially deflated and is then progressively inflated via the subcutaneous port during subsequent postoperative outpatient visits to achieve gastric restriction and weight loss.
Sleeve Gastrectomy ⁷⁸ (SG)	Restrictive/endocrine or metabolic	The greater curvature and fundus of the stomach are resected, leaving the remaining stomach fashioned into an elongated tube. Fundal removal decreases the levels of ghrelin, a major hunger-inducing hormone.
Roux-en-Y Gastric Bypass ^{77, 78} (RYGB)	Restrictive and diversionary/malabsorptive	The proximal stomach is separated from the distal stomach to form a small, restrictive gastric pouch (20 to 30 mL capacity). The gastric pouch is connected to mid-jejunum (thus forming the alimentary or roux limb) which has been diverted away from the biliopancreatic secretions in the biliary or biliopancreatic limb. The length of small intestine distal to site at which the roux limb and the biliary limb join is termed the 'common limb' and represents the intestinal area where biliopancreatic secretions mix with ingested food and most absorption occurs. The alimentary limb is typically 100 cm in length and the biliopancreatic limb 30 to 50 cm in length. Some surgeons increase the length of the small bowel bypass in patients with severe obesity.

and economic burden of severe obesity alone is substantial, as it doubles the risk of mortality; increases the risk of type 2 diabetes by up to 18-fold; markedly reduces health-related quality of life (QoL); and accounts for 21% of medical expenditures attributable to obesity¹¹. Severe obesity is also the fastest growing obesity subgroup, since its prevalence is increasing twice as quickly as lesser degrees of obesity¹².

We performed a systematic review to qualitatively summarize the highest quality evidence examining bariatric surgery, 1. focusing on clinical efficacy in adults and adolescents, adverse effects, and 2. cost-utility. We also sought to examine 3. the associations between physician- or facility-level surgical volume (i.e., experience in performing bariatric surgery) and clinical outcomes. This project was part of a larger Health Technology Assessment (HTA) for the Canadian Agency for Drugs and Technologies in Health (CADTH) reviewing bariatric surgery, which was conducted according to recommended guidelines¹³. Herein, we summarize results for outcomes deemed to be of greatest clinical relevance and involving the most commonly employed procedures (AGB, RYGB and SG).

METHODS

Data Sources

Search strategies created by a Masters in Library and Information Science qualified librarian and devoid of language restrictions were used to examine MEDLINE (1950 to January 14, 2011), EMBASE (1980 to January 14, 2011), and CENTRAL (January 14, 2011). Trial registries, HTA websites,

additional economic databases (EconLit, EURON EED, Harvard Center for Risk Analysis) and reference lists were also searched¹³.

Study Selection

We selectively yet systematically summarized a subset of studies from our larger HTA project. These criteria are more restrictive than the larger review in terms of type of bariatric surgery, study design and outcomes. Randomized, quasi-randomized (e.g., alternating assignment, assignment based on patient hospital number) controlled trials (RCTs) examining the efficacy/safety of a common contemporary bariatric surgery (i.e., adjustable gastric banding, Roux-en-Y gastric bypass, sleeve gastrectomy) versus another common contemporary surgical comparator or a non-surgical treatment were prioritized for inclusion. Both laparoscopic and open procedures were included. Studies enrolling adult or adolescent (11 to 17 years) populations meeting guideline-concordant eligibility for surgery (Class III obesity or medically complicated Class II obesity) and reporting relevant outcomes (see Data Extraction below) were included in the clinical review. Similarly cost-utility or cost-minimization studies and studies examining bariatric surgery volume-outcome relationships were included in the economic and volume-outcome reviews, respectively.

Two sets of reviewers independently screened citations; each record was reviewed by an internist and an epidemiologist or biostatistician. Citations deemed potentially relevant were retrieved as full-text articles and independent, duplicate review was performed using standardized forms. Disagree-

ments were discussed with a third reviewer and resolved through consensus.

Data Extraction

Changes in weight, obesity-related comorbidity, QoL, mortality, and resource utilization (i.e., length of stay, re-operations) were included as outcomes in the clinical review. Excess weight or BMI were reported if absolute change in weight was not available. To calculate percent excess weight, an ideal weight of 25 kg/m² was subtracted from total weight and the result was divided by ideal weight and multiplied by 100. Mortality and aggregate surgical complications, and incremental cost-utility were included as outcomes in the volume-outcome and economic reviews, respectively. Study characteristics and outcome data were extracted by one reviewer and checked independently by a second. Study quality was assessed using Jadad scores¹⁴ for clinical studies (2 points for an adequate randomization method, 2 points for an adequate double-blinding method, 1 point for adequately describing withdrawals, for a maximum of 5 points) and a checklist adapted from Neumann et al.¹⁵ for economic studies. Full details regarding individual study quality and quantitative meta-analysis can be found in the full CADTH report¹³. This article focuses on qualitative synthesis and summary of the highest quality available data, reported according to the framework recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (www.prisma-statement.org).

RESULTS

I. Clinical Efficacy and Adverse Effects in Adults

A. Description of Included Studies (Table 2). Of 2,494 citations, eight adult RCTs comparing contemporary bariatric surgeries (AGB, RYGB and SG) to standard care (lifestyle modification) or comparing between different types of surgery were identified (Fig. 1). Two RCTs^{16,17} compared surgery to lifestyle modification^{16,17}. Six RCTs compared common contemporary procedures: two compared RYGB to AGB^{18,19}, one compared SG to AGB²⁰, and three compared SG to RYGB^{21–23}.

Studies were generally of poor-to-moderate quality (median Jadad score 1.75). Most studies were unblinded and did not adequately describe methods of randomization or attrition rates¹³. Since very little comorbidity or QoL data were available, we report these results in text and not in Table 2.

B. Surgery vs. Non-surgical Treatments. A small RCT of 16 patients (BMI range 40–56 kg/m²) reported in abstract form only found that AGB reduced weight by 26% compared to a weight gain of 1% in diet-treated controls over 40 weeks ($P < 0.01$)¹⁶. A short 14-day RCT with 22 patients (mean BMI 48 kg/m²) did not find a significant difference in weight loss between surgery and standard care¹⁷.

C. Comparisons Between Surgeries. In a RCT of 197 patients (250 randomized but 53 did not undergo surgery; mean BMI 47 kg/m²) comparing laparoscopic RYGB to laparoscopic AGB. Excess weight loss at 4 years was 68% in the RYGB group and 45% in the AGB group ($P < 0.05$) (mean weight losses not reported).

The results from all eight SF-36 domains were similar (P 's = NS) in both groups after 1 year. Additional results were: 1-year mortality 0.9% vs. 0%, mean operative time 137 for RYGB vs. 68 minutes for AGB, and length-of-stay 3.1 vs. 1.5 days (P 's < 0.01 for all complications except mortality where $P = \text{NS}$)¹⁸. Major perioperative complications (hemorrhage, obstruction, internal herniation, or renal insufficiency) occurred in seven (6.3%) RYGB patients compared to 2 (2.3%) patients in the AGB group ($P = \text{NS}$) and late (> 30 days postoperatively) major complications occurred in 29 (26.1%) RYGB patients (predominantly strictures) vs. 10 (11.6%) AGB patients (predominantly band erosions or migration) ($P = 0.01$).

Similarly, a 43-patient, 5-year RCT (51 randomized but eight withdrew; mean BMI 44 kg/m²) comparing laparoscopic AGB with laparoscopic RYGB reported weight reductions favoring RYGB (36.0 kg versus 22.1 kg; $P < 0.001$)¹⁹. One case of diabetes and two cases of dyslipidemia resolved in RYGB patients. One case of apnea resolved in AGB patients. None of the four cases of hypertension (three in AGB patients and one in RYGB patients) resolved. Reoperations were required in two (11%) of the RYGB patients compared with four (17%) of AGB patients. Reoperations in the RYGB group were primarily performed for more serious complications (perforation, pouch leak, hernia), whereas the AGB group required reoperation for pouch dilation and/or unsatisfactory weight loss.

A 1-year RCT of 32 patients (mean BMI 46 kg/m²) reported equivalent weight reductions with laparoscopic SG and laparoscopic RYGB (43.6 kg vs. 40.0 kg; $P = 0.3$)²¹. Two cases of diabetes resolved in RYGB patients. A 6-month, 20-patient RCT (mean BMI 48 kg/m²) comparing laparoscopic SG to laparoscopic AGB reported greater excess weight loss with SG (61% vs. 29%; $P = 0.001$)²⁰.

Interim results were reported in abstract form for a 32-patient RCT²² (mean BMI 46 kg/m²). At 2 years with only eight patients remaining in follow-up they reported 68% excess weight loss in patients undergoing RYGB surgery vs. 89% in patients undergoing SG surgery, a difference that was not statistically significant. In another SG vs. RYGB trial²³ enrolling 27 patients, the 3-month between group difference in weight loss was not significant (21.6 vs. 25.6 kg).

II. Clinical Efficacy and Adverse Effects in Adolescents

The frequency of bariatric operations in adolescents is increasing, with approximately 200 bariatric procedures performed in 2003²⁴. However, of 2,494 citations (Fig. 1), only one RCT examining surgery in adolescents was identified. A 2-year RCT in 50 adolescents (age 14–18; mean BMI 41 kg/m²) reported a 35 kg (28%) reduction after gastric banding compared to a 3 kg (3%) reduction with lifestyle modification ($p < 0.001$) with significant ($p < 0.05$) improvements in metabolic syndrome prevalence, waist circumference and insulin sensitivity (Table 2)²⁵. However, eight revisional operations were required in seven (28%) banding patients for proximal pouch dilation or tubing injury.

III. Association Between Facility-level or Surgeon-level Surgical Volume and Clinical Outcomes

A. Description of Included Studies. Of 973 citations, 14 articles met inclusion criteria and examined the relationship between

Table 2. Description and Outcomes of Clinical Studies

Author, Year, Country	Follow-up in years (% complete**)	Jadad score	Baseline			Interventions (Sample size)	Outcomes*			
			Mean BMI, kg/m ²	Mean age, y	% female		Mean change in weight	No. of deaths	Mean length of stay, d	No. with reoperations
Adult RCTs										
Campos ¹⁷ 2010 USA	14d (nr)	0	48	44	68	RYGB (12)	-9.9 kg	nr	nr	nr
						Standard care (10)	-8.2 kg			
Nguyen ¹⁸ 2009 US	4 (69)	1	47	43	82	AGB (86)	-45% EWL	0	1.5	11
						RYGB (111)	-68% EWL	1	3.1	14
Peterli ²² 2009 (A) Switzerland	1.58 (nr)	1	46	41	78	SG (17)	89% EWL	nr	nr	nr
						RYGB (15)	68% EWL			
Peterli ²³ 2009 (B) Switzerland	0.25 (100)	3	46	40	nr	SG (14)	-21.6 kg	nr	nr	nr
						RYGB (13)	-25.6 kg			
Karamanakos ²¹ 2008 Greece	1 (100)	5	46	34	84	SG (16)	-43.6 kg	0	nr	nr
						RGYB (16)	-40.0 kg	0		
Angrisani ¹⁹ 2007 Italy	5 (98)	2	44	34	82	AGB (24)	-22.1 kg	0	2	4
						RYGB (19)	-36.0 kg	0	4	2
Langer ²⁰ 2005 Australia	0.5 (nr)	1	48	39	90	SG (10)	-61.4% EWL	0	nr	nr
						AGB (10)	-28.7% EWL	0		
Heindorf ¹⁶ 1997 Denmark	0.83 (nr)	1	range 40–56	range 21–43	44	AGB (8)	-26 kg	nr	nr	nr
						Standard care (8)	+1 kg			
Adolescent RCT										
O'Brien ²⁵ 2010 Australia	2 (84)	3	41	17	68	AGB (25)	-34.6 kg	0	1.1	7
						Standard care (25)	-3.0 kg	0	na	na

RCT randomized controlled trial, PC prospective cohort, US United States of America, AGB adjustable gastric banding, RYGB Roux-en-Y gastric bypass, SG sleeve gastrectomy, BMI body mass index, EWL excess weight loss, nr not reported, na not applicable

*bolded results are significantly different at P<0.05

hospital volume (10 studies)^{26–35}, surgeon volume (eight studies)^{27,28,30,34,36–39}, and outcomes; four studies^{27,28,30,34} examined two of these relationships. Study sample sizes ranged from 150 to 102,069 patients. Mortality, surgical sequelae, resource utilization and costs were the outcomes considered. Herein, we detail mortality and non-specific surgical sequelae; complete information on all volume–outcome relationships can be found elsewhere¹³.

B. Hospital Volume. All seven studies^{26,27,30–32,34,35} examining mortality found a significant inverse association between surgical volume and mortality (Table 3). Four^{26,30,34,35} of five³² studies employing multivariable models to control for other clinical factors which might impact outcomes found that this inverse relationship remained significant after adjustment. The second largest study²⁶ (n=51,842) reported that hospitals with <125 cases per year had increased mortality compared to higher volume hospitals (Adj OR 2.22, 95% CI, 1.43–3.45). However, absolute mortality rates were very low at 0.22%; therefore the incremental increase in risk was small.

All eight studies^{27–33,35} examining surgical complications reported an increased unadjusted odds or risk in lower volume (as compared to higher volume) hospitals, which persisted after statistical adjustment in five^{27,28,30,33,35} of six studies³² (Table 3).

C. Surgeon Volume. Five^{27,30,34,37,39} of six studies³⁸ found significant increases in the odds or risk of death in cases done by surgeons who performed fewer bariatric surgeries (Table 3). One study²⁷ (n = 19,174) reported significantly higher mortality for surgeons who performed < 99 cases versus ≥ 500 cases over five years (RR 2.85, 95% CI, 1.32–6.16).

All six studies^{27,28,30,36,38,39} examining surgical sequelae demonstrated increases in complications with lower surgeon volumes, including the three studies that reported adjusted results (Table 3).

IV. Economic Analyses

Of 1,904 citations, 13 economic analyses met inclusion criteria (Fig. 1; Table 4)^{40–52}. From the payer perspective, the long-term (10 years to lifetime) cost-utility of surgery compared with non-surgical management appears attractive, with incremental cost-utility ratios (ICURs) ranging from \$1,000 to \$40,000 per quality-adjusted life-year (QALY; 2009 USD) (Table 4)^{40–42,44,45,47}. While cost-effectiveness studies comparing between alternate surgical approaches were identified, the current evidence base did not allow for definitive conclusions regarding the relative cost-effectiveness between different procedures.

The cost-effectiveness of bariatric surgery compared with non-surgical management appears to be particularly favorable in patients with type 2 diabetes. Cost-utility studies using RCT data to inform the efficacy of bariatric surgery in patients with diabetes reported AGB led to increased QALYs and cost savings (dominant) compared to non-surgical management⁴⁶ when a 2-year RCT was extrapolated to lifetime in a population with Class I/II obesity (mean BMI 37 kg/m²). Another model using data from a meta-analysis in patients with diabetes reported ICURs of \$7–10,000 over a 10-year time horizon⁵⁰. Analyses of bariatric surgery in several European countries also reported that bariatric surgery was either dominant

Figure 1. Search results and study inclusion.

or associated with cost-utility ratios that are likely to be considered attractive compared with standard care^{41,48}.

COMMENT

In summary, the available RCT data suggest that 1) contemporary bariatric surgery is efficacious in reducing weight compared to non-surgical treatment in adults and adolescents with severe obesity but data are limited to a few small studies; 2) important differences exist between surgeries in terms of weight loss, types of complications, reoperation rates and serious adverse effects; 3) mortality and complication rates are higher for low-volume surgeons and centers; and 4) surgery appears cost-effective (compared with commonly cited cost per QALY thresholds) and possibly dominant in patients with type 2 diabetes⁵³⁻⁵⁵.

RCT data comparing surgery to non-surgical treatment and examining mortality or obesity-related comorbidity are lacking. In addition, there is a paucity of long-term (≥ 5 year) RCT data – including both comparisons between different surgical options and between surgical and non-surgical treatments. Notably, a small 2-year RCT comparing AGB to lifestyle modification in 60 patients with early type 2 diabetes just failed to meet criteria for inclusion in our review because it enrolled some patients with mild obesity (i.e., those with BMI levels lower than currently recommended thresholds for surgery). Remission of type 2 diabetes was much higher in the group receiving gastric banding (73% vs. 13%; RR 5.5, 95% CI, 2.2–14.0)⁵⁶.

In contrast to the lack of available RCT data, abundant observational data comparing surgery to non-surgical care have been reported. A previous systematic review of observational data⁹ (136 studies; 22094 patients) reported that surgery resulted in the improvement/resolution of major obesity related comorbidities (hypertension, sleep apnea, diabetes and dyslipidemia) in 78–86% of subjects. The Swedish

Table 3. Description and Outcomes of Hospital and Surgeon Volume-Outcome Studies

Author, Year	Dataset, Time period	Surgery, Sample size	Exposure	Death	Surgical sequelae†
Prospective cohort Smith ³⁹ 2010	Multiple Hospitals 2005–2007	RYGB 3,409	Surgeon	2.0% 0–24 cases/year 0.7% 25–49 cases/year 0.3% 50–99 cases/year 0.1% ≥100 cases/y [ref]	Adj RR: 1.0 [ref] 0–24 cases/year 0.61 (0.30,1.25) 25–49 cases/year 0.41 (0.22,0.79) 50–99 cases/year 0.35 (0.16,0.76) ≥100 cases/year
Chevallier ³⁶ 2007	Multiple Hospitals 2002–2003	AGB 1,236	Surgeon	nr	20.42% 1–2 cases/2 mo 19.61% 3–6 cases/2 mo 18.3% 7–14 cases/2 mo 8.88% ≥15 cases/2 mo [ref]
Registries Kohn ³⁵ 2010	NIS Registry 1998–2006	Any 102,069	Hospital	Adj OR: 0.997 (0.996,0.999) / 1 case	Adj OR: 0.9994 (0.9989,0.9999) / 1 case
Livingston ²⁶ 2007	NIS Registry 2001–2003	GB, JB 51,842	Hospital	Adj OR: 2.22 (1.43,3.45) <125 cases/y vs ≥125 cases/year	nr
Murr ²⁷ 2007	Government Service Registry 1999–2003	Any 19,174	Hospital Surgeon	1.96% 1–9 cases/5y 0.6% 10–99 cases/5y 0.15% 100–199 cases/5y 0.25% 200–499 cases/5y 0.25% ≥500 cases/5y [ref] 1.31% 1–5 cases/5y 0.55% 6–99 cases/5y 0.29% 100–199 cases/5y 0.3% 200–499 cases/5y 0.19% ≥500 cases/5y [ref]	Adj OR: 2.1 (1.2,3.5) 1.3 (1.1,1.5) 0.6 (0.4,0.7) 0.9 (0.8,1.1) 1.0 [ref] 9.55% Adj OR: 2.0 (1.3,3.1) 1.4 (1.1,1.6) 0.9 (0.7,1.1) 1.3 (1.1,1.4) 1.0 [ref] 8.53%
Parker ³¹ 2007	Government Service Registry 2003	GB 24,534	Hospital	1.1% <50 cases/year 0.4% 50–124 cases/year 0.2% ≥125 cases/y [ref]	nr
Weller ²⁸ 2007	Government Service Registry 2003	GB, GP 7,868	Hospital Surgeon	nr	Adj OR: 1.56 (1.01,2.41) ≤100 vs >100 cases/year 1.71 (1.13,2.58) ≤125 vs >125 cases/year 1.75 (1.15,2.65) ≤150 vs >150 cases/year 2.20 (1.46,3.33) ≤200 vs >200 cases/year 4.90% >200 cases/year Adj OR: 1.35 (0.90,2.00) ≤25 vs >25 cases/year 1.15 (0.79,1.66) ≤50 vs >50 cases/year 2.39 (1.59,3.59) ≤100 vs >100 cases/year 2.05 (1.29,3.25) ≤150 vs >150 cases/year 4.61% >150 cases/year
Carbonell ³² 2005	NIS Registry 2000	GB 5,876	Hospital	0.58% <50 cases/year 0.95% 50–99 cases/year 0.87% 100–199 cases/year 0.1% ≥200 cases/y [ref]	14.2% 11.5% 11.6% 7.8% [ref]
Flum ³⁷ 2005	National Insurance Service Registry 1997–2000	Any 16,155	Surgeon	Adj OR: 1.6 (1.3,2.0) Lower half vs Upper half	nr
Nguyen ²⁹ 2004	University Health System Consortium Registry 1999–2002	GB 24,166	Hospital	nr	14.5% <50 cases/year 12.3% 50–100 cases/year 10.2% >100 cases/y [ref]
Courcoulas ³⁰ 2003	Government Service Registry 1999–2001	GB 4,674	Hospital Surgeon	Adj risk 3.52% First tertile (1–4 cases) 6.52% Second tertile (5–32 cases) 0.53% Third tertile (34–887 cases) [ref] Adj risk 4.75% <10 cases/year 0.64% 10–50 cases/year 0.89% 51–100 cases/year 0.33% >100 cases/y [ref]	Adj risk 30.83% 31.75% 16.00% [ref] Adj risk 28.29% 17.92% 15.69% 14.07% [ref]

Table 3. (continued)

Author, Year	Dataset, Time period	Surgery, Sample size	Exposure	Death	Surgical sequelae†
Liu ³³ 2003	Government Service Registry 1996–2000	GB 16,232	Hospital	nr	Adj OR: 2.72 (1.57,4.73) <50 cases/year 2.70 (1.41,5.20) 50–99 cases/year 1.30 (0.74,2.29) 100–199 cases/year 1.00 [ref] 6.60% ≥200 cases/year
Lopez ³⁸ 2002	Government Service Registry 1999	Any 933	Surgeon	0.59% <2 cases/mo 0.52% ≥2 cases/mo [ref]	13.02% 9.03% [ref]
Retrospective cohort Kelles ³⁴ 2009	Single HMO 2004–2007	RYGB 2,167	Hospital	OR: 4.96 (1.73,14.24) <20 vs ≥20 cases/year	nr
			Surgeon	Adj OR: 6.21 (1.90,20.26) <20 vs ≥20 cases/year	

NIS National Inpatient Survey, HMO health maintenance organisation, AGB adjustable gastric banding, GB gastric bypass, JB jejunioleal bypass, GP gastroplasty, NIH National Institutes of Health, Adj adjusted, OR odds ratio, nr not reported

†bolded results are significantly different from the referent category at $P < 0.05$

Obesity Study (SOS)⁵⁷, a multicenter, prospective, matched cohort study of 2010 surgical cases and 2037 medically treated controls (mean BMI 41 kg/m²) was the largest and most methodologically rigorous long-term evaluation of bariatric surgery identified in this review. Surgical cases underwent RYGB (13%), AGB (19%) or vertical-banded gastroplasty (VGB; 68%). Compared to controls, surgery was associated with significantly greater weight reduction of 16.3 kg at 10 years (95% CI, 14.9–17.6);⁵⁸ lower mortality over 15 years (6.3% vs. 5.0%; HR 0.76, 95% CI, 0.59–0.99);⁵⁷ and lower incidence rates of first time cancers over 11 years (primarily in women; HR 0.67; 95% CI 0.53–0.85)⁵⁹. Surgery was also associated with higher rates of remission at 10 years from type 2 diabetes (36% vs. 13%; OR 3.5, 95% CI, 1.6–7.3), hypertension (19% vs. 11%; OR 1.68, 95% CI, 1.1–2.6), hypertriglyceridemia (46% vs. 24%; OR 2.6, 95% CI, 1.9–3.6) and low HDL cholesterol (73% vs. 53%; OR 2.4, 95% CI, 1.4–3.8);⁵⁸ and with statistically and clinically significant improvements in QoL and sleep apnea symptoms^{60,61}. Perioperative mortality in the surgical group was 0.25%; 13% of patients experienced post-operative complications, including bleeding (0.5%), venous thromboembolism (0.8%), wound complications (1.8%), deep infections (2.1%) and pulmonary complications (6.1%)⁵⁸.

Paradoxically, because of the large amount of observational evidence that now exists, long-term RCTs involving non-surgical comparators are now unlikely to be performed because of the perception that surgery is superior⁶². Because of the extended wait lists that exist in many public bariatric programs⁶³, novel study designs such as delayed-start designs could be considered⁶⁴.

The choice between AGB and RYGB (the two most commonly performed procedures), appears to represent a trade-off between weight loss efficacy and risk. AGB is a simpler, shorter procedure that does not carry a long-term risk of malabsorption. It also leads to a lower number of serious complications but consistently produces smaller reductions in weight and a higher requirement for overall reoperations. SG appears similar to RYGB with respect to weight loss efficacy, although further confirmatory data are required. Overall, the choice between these procedures should be made on the basis of patient preference and surgeon experience and training. Further study is specifically needed to fully elucidate the

mechanisms of action of each type of procedure (such as investigating the role of reductions in ghrelin levels post-SG) as this may also clarify the indications for each procedure. For example, emerging data suggest that RYGB may potentially exert weight-independent effects on glycemic control (possibly due to alterations in enteroendocrine signals) and thus this technique may be particularly beneficial in patients with type 2 diabetes⁶⁵.

As most evidence supporting the benefits of surgery comes from observational studies and relatively short-term (<5 years) RCTs performed in experienced, high-volume centers, the reported results may overestimate the benefits of surgery and underestimate the risks. Metabolic bone disease and associated fractures (particularly following diversionary procedures) are examples of potential risks that remain understudied⁶⁶. Conversely, ongoing refinements of bariatric techniques may cause the results of clinical studies to lag behind the benefits of surgery in the 'real world'. For example, the SOS study primarily used VBG—which is now largely obsolete, having been replaced by procedures with superior weight loss efficacy such as RYGB. This underscores the importance of prospective studies aimed at verifying the effectiveness and adverse effects of surgery in contemporary clinical practice. While overall mortality benefit is expected from other types of bariatric surgery, none of the eligible RCTs have demonstrated this. The Longitudinal Assessment of Bariatric Surgery (LABS) is an ongoing, prospective registry in the US that recently reported outcomes in 4,776 patients¹⁰. Thirty-day mortality rates were 0.3% and major complication rates were 4.1%—rates that are very similar to those reported in SOS and also similar to other types of elective, non-bariatric operations⁶⁷.

As severely obese adolescents may experience the same serious obesity-related complications that develop in adults, surgery may be considered after careful multidisciplinary preoperative assessment to assess patient suitability and physical/emotional maturity as well as to confirm a supportive family environment⁶⁸. Proposed indications for surgery in adolescents range from the use of the same criteria as in adults to more stringent BMI cut-offs⁶⁹. Concerns have been raised about whether adolescents truly have the capacity to give informed consent; whether proper adherence to post-operative dietary supplements is feasible;⁷⁰ and whether the possible negative effects of surgery on physical maturation

Table 4. Description and Outcomes of Economic Studies

Author, Year	Efficacy data (study design, sample size, follow-up)	Neumann score (% yes)/ Industry funded	Population (mean BMI, mean age, sex, DM)	Comparators	Base case (Incremental Cost/QALY) (Time horizon)*	Sensitivity analysis
Campbell ⁴⁹ 2010	Cost-utility RCT, n=43, 5 years ¹⁹ Literature review	88 Y (Allergan)	NIH criteria; 40 years; 82% F; 2% DM	LAGB LRYGB No treatment	\$6,033 [lifetime] \$6256 [lifetime]	100% probability that LAGB and LRYGB cost-effective over lifetime at willingness-to-pay of \$50,000
Hoerger ⁵⁰ 2010	Literature review Meta-analysis for remission of DM ⁷⁷	81 N	≥35 kg/m ² ; 35–74 years; 100% DM	GB AGB Standard care	\$8,135 [10 years] incident DM \$13,946 [10 years] prevalent DM \$12,784 [10 years] incident DM \$15,108 [10 years] prevalent DM	95% probability that GB cost-effective for 45–54 years ranged from \$2,300–27,000. 95% probability that AGB cost-effective for 45–54 years ranged from \$0–35,000
McEwen ⁵² 2010	RCT, n=221, 2 years	44 N	52 kg/m ² ; 42 years; 88% F; 36% DM Managed care population	97% RYGB Standard care	\$48,662 [2 years] \$1,425 [lifetime]	\$11,345 [lifetime] in non-DM vs \$8,831 in DM \$1,246 for LRYGB vs \$17,372 for ORYGB
Anselmino ⁴⁸ 2009	Literature review	50 Y (Ethicon)	≥35 kg/m ² ; 100% DM	AGB GB Standard care	-\$4,844 [5 years] Austria -\$5,214 [5 years] Italy \$6,051 [5 years] Spain -\$6,090 [5 years] Austria -\$2,679 [5 years] Italy \$2,107 [5 years] Spain	Results robust when effectiveness for BMI reduction and DM remission with AGB and GB reduced by 20%
Ikramuddin ⁵¹ 2009	PC, n=204, 2 years	75 Y (Covidien)	48 kg/m ² ; 50 years; 78% F; 100% DM	RYGB Standard care	\$23,510 [35 years]	84% probability that RYGB cost-effective over 35 years at a willingness-to-pay of \$50,000
Picot ⁴⁷ 2009	Literature review	100	45 kg/m ² ; 40 years; 90% F; 10% DM	LGB LAGB Standard care	\$11,879 [20 years] \$6,763 [20 years]	Robust to pessimistic estimates of weight loss
	RCT, n=60, 2 years	N	37 kg/m ² ; 49 years; 55% F; 100% DM	LAGB Standard care	\$35,904 [2 years], \$2,953 [20 years]	100% probability that LAGB cost-effective over 20 years
	RCT, n=80, 2 years		34 kg/m ² ; 41 years; 76% F	LAGB Standard care	\$115,230 [2 years], \$24,207 [20 years]	98% probability that LAGB cost-effective over 20 years
Keating ⁴⁶ 2009	RCT, n=60, 2 years	100 Y (Allergan)	37 kg/m ² ; 49; 55% F; 100% DM	LAGB Standard care	-\$1,909 [lifetime]	Mean duration of DM remission must be ≥2y to be cost-effective, ≥10y to be dominant
Salem ⁴⁰ 2008	Literature review	88 Y (Inamed/ Allergan)	40, 50, 60 kg/m ² ; 35, 45, 55 years; M, F; 0% DM	LAGB LRYGB Standard care	\$14,056 at 35 years, 40kg/m ² , M; \$10,754 F [lifetime] \$22,460 at 35y, 40kg/m ² , M; \$17,781 F [lifetime]	ICUR consistently <\$25,000

Table 4. (continued)

Author, Year	Efficacy data (study design, sample size, follow-up)	Neumann score (% yes)/ Industry funded	Population (mean BMI, mean age, sex, DM)	Comparators	Base case (Incremental Cost/QALY) (Time horizon)*	Sensitivity analysis
Ackroyd ⁴¹ 2006	Literature review	69 Y (Ethicon)	≥35 kg/m ² ; 100% DM	LAGB LGB Standard care	Germany -\$5,041 , France -\$6,297 , UK \$4,076 [5 years] Germany -\$5,426 , France -\$6,338 , UK \$3,205 [5 years]	Surgeries consistently cost-saving in Germany and France Surgeries consistently cost-effective in UK
Jensen ⁴² 2005	PC, n=346, 8 years RCT, n=211, 2 years	69 NR	≥40 kg/m ² at 40 years; ≥33 kg/m ² at 18 years 100% F	GB at age 40 years Standard care at age 18 years	\$8,631 [lifetime]	ICUR consistently <\$20,000
Clegg ⁴⁵ 2002	Literature review	81 N	45 kg/m ² ; 40 years; 90% F; 10% DM	LGB LAGB Standard care	\$13,704 [20 years] \$18,581 [20 years]	Consistently cost-effective
Craig ⁴⁴ 2002	Observational study, n=608, 14 years	81 N	40, 50 kg/m ² ; 35–55 years; M, F; 0% DM	GB No treatment	\$39,379 at 35 years, 40kg/m ² , M; \$20,240 F [lifetime] \$14,733 at 35 years, 50kg/m ² , M; \$7,848 F [lifetime]	Cost-effectiveness robust in women Cost-effectiveness sensitive to EWL in men
Cost-minimization						
Paxton ⁴³ 2005	Literature review	31 NR	50 kg/m ² ; 40 years; 85% F	LGB OGB	Cost \$21,391 [lifetime] Cost \$24,762 [lifetime]	None

RCT randomized controlled trial, RC retrospective cohort, PC prospective cohort, NR not reported, NIH National Institutes of Health, BMI body mass index, DM diabetes mellitus, F female, M male, LGB laparoscopic gastric bypass, LAGB laparoscopic adjustable gastric band, LRYGB laparoscopic Roux-en-Y gastric bypass, GB gastric bypass, OGB open gastric bypass, ICUR incremental cost utility ratio, QALY quality-adjusted life-year, AUD Australian dollar, UK United Kingdom, EWL excess weight loss

All prices converted to 2009 \$US (Bureau of Labor Statistics, OECD).

*Results in bold indicate that surgery was the dominant strategy and cost-saving relative to the comparator.

outweigh potential benefits of surgery^{69,71}. Although the benefits and risks of surgery in adolescents appear similar to those in adults, more data are required for this population. Teen-LABS is an ancillary study to LABS that is collecting similar information in the adolescent population and may help to close some of the existing knowledge gaps⁶⁸.

The major limitation of published cost-effectiveness models is that observational data and relatively short-term RCT data were used to model the long-term impact of changes in weight on QoL and health. As such, these models might overestimate the economic attractiveness of surgery, although results were robust over a wide range of sensitivity analyses. In addition, most models assumed that the weight of patients not undergoing surgery would remain stable over the long-term; surgically induced improvements that may occur in common obesity-related comorbidities such as osteoarthritis were usually ignored; and reductions in the indirect costs of obesity were typically not considered. For these reasons, it is also possible that existing models underestimate the true economic attractiveness of surgery. Future studies measuring both direct and indirect costs would help to clarify these issues.

An association between higher volume hospitals/surgeons and lower mortality rates was evident from the studies

reviewed, although the absolute increase in mortality rates are small. Surgeon inexperience is consistently associated with increased morbidity and mortality, although it is difficult to define an exact minimum threshold volume due to differences in this definition across studies. The available evidence does indicate that mortality rates are dramatically higher for surgeons who perform approximately 25 cases or fewer per year. It is therefore recommended that surgeons performing bariatric procedures have not only the prerequisite training and certification but also are consistently and frequently performing such procedures on an ongoing basis. Professional societies have suggested criteria to designate Surgical Centers of Excellence specializing in bariatric surgery⁷². Proposed criteria for such centers include a minimum volume threshold of 125 cases/year (based largely upon the studies we have cited). Public payers such as Medicare and Medicaid currently use these criteria as prerequisites for reimbursement⁷³. Defining absolute procedure volume thresholds and limiting surgeries to designated centers appears to be a practical attempt at quality control across surgical sites but may have the unintended consequence of limiting access to surgery, particularly in patients of lower socioeconomic status served in lower volume centers²⁶. It is notable that an analysis of 253

hospitals in the US reported no difference in in-hospital mortality or short-term complications between designated Centers of Excellence and lower volume centers⁷⁴. Additional studies examining the relation between policies limiting bariatric surgery to higher volume centers and access to such surgery are needed.

Access to bariatric surgery appears to be a particularly severe problem for public payers and health care systems. In Canada, the US and the United Kingdom, far less than 1% of eligible patients currently receive a bariatric procedure and wait lists in Canada average 5 years⁶³. In addition, concerns have been raised regarding potential inequities in access, as men, patients of lower socioeconomic status, ethnic minorities and individuals with more comorbidity appear under-represented amongst surgical recipients⁷⁵. The absence of a widely accepted triage system for selecting surgical candidates is also a major impediment to streamlining wait lists⁷⁶.

Overall, we conclude from the available evidence that bariatric surgery is more efficacious than non-surgical care in reducing weight, with acceptable cost-effectiveness. Procedure-specific differences in efficacy and risks exist and higher surgical volumes are associated with better outcomes. Further study is required to examine long-term benefits, risks and cost-effectiveness and to fully characterize the advantages and disadvantages of different bariatric procedures.

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