Bariatric Surgery for Obesity: A Systematic Review and Meta-Analysis

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Abstract

Obesity is the fifth leading cause of global deaths. The efficacy and safety of obesity treatment is still controversial. The objective of the thesis is to evaluate the efficacy and safety of bariatric surgery, through a systematic review of the current evidence and meta-analysis of important outcomes. Nineteen (19) randomized controlled trials (RCTs) with 1346 participants were included. Bariatric surgery resulted in greater weight loss when compared to non-surgical treatment. Weight loss was also associated with resolution and/or improvement of obesity related comorbidites such as diabetes, hypertension, hyperlipidemia, and sleep apnea. Weight loss and safety varied across the surgical procedures. Biliopancreatic diversion/duodenal switch had the greatest weight loss, followed by sleeve gastrectomy and Roux-en-Y gastric bypass, purely restrictive procedures such as vertical banded gastroplasty and adjustable gastric banding resulted in the least weight loss. Long term, high quality, and adequately powered trials are still needed to support the available evidence.

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ABBREVIATIONS

AGB	adjustable gastric banding
BMI	body mass index
BPD	biliopancreatic diversion
BPD/DS	biliopancreatic diversion with duodenal switch
CDC	Centers for Disease Control and Prevention
CI	confidence interval
GBP	gastric bypass
GERD	gastroesophageal reflux disease
HBG	horizontal banded gastroplasty
HG	horizontal gastroplasty
JB	jejunoileal bypass
LAGB	laparoscopic adjustable gastric banding
LBPD/DS	laparoscopic biliopancreatic diversion with duodenal switch
L RYGB	laparoscopic Roux-en-Y gastric bypass
LSG	laparoscopic sleeve gastrectomy
LVBG	laparoscopic vertical banded gastroplasty
MD	mean difference
NIH	National Institutes of Health
RCT	randomized controlled trial
RYGB	Roux-en-Y gastric bypass
SD	standard deviation
SF-36	Medical Outcomes Study 36-item short-form health survey
SG	sleeve gastrectomy
UK	United Kingdom
US	United States of America
VBG	vertical banded gastroplasty
WHO	World Health Organization

1.0 Background

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health[1]. The main cause of obesity and overweight is an energy imbalance between calories consumed and calories expended. However, multiple factors have been linked to obesity including, genetic[2], biochemical[3], and behavioral[4] as well as environmental, social and economic factors[5]. The link to obesity is through interaction of these factors rather than the influence of any single factor.

Obesity is a worldwide epidemic, with more than 1.5 billion overweight adults[6]. Overweight and obesity remains a major health challenge, and are considered to be the fifth leading risk for global death and a major burden on health care systems[6].

Diet therapy with exercise supplemented with pharmacotherapy, with or without organization supervision, generally achieved only minimal and often transient effects with poor long term results[7, 8]. The raise in the prevalence of obesity led to increase interest in the surgical approach to treat obesity, and in 1991, the National Institutes of Health established guidelines for surgical therapy of morbid obesity now known as bariatric surgery[9].

The objective of this thesis is to evaluate the effectiveness and safety of surgical and non-surgical treatments for obesity and whether they modify clinically important outcomes, including weight loss, comorbidity modifications to diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea in adolescents and the adult obese population.

1.1 Classification

Body Mass Index (BMI) is a simple index of weight for height. It is the most commonly used measure for classifying overweight and obesity in adults, both at the population as well as the individual level. It is calculated as weight in kilograms divided by the square of the height in meters (kg/m^2). The World Health Organization (WHO) defines overweight

as a BMI of 25 or more, obesity as a BMI of 30 or more, and morbid obesity as a BMI of 40 or more (Table 1) [10, 11].

Table 1: International BMI Classification of Adult Overweight and Obesity [10, 11]

Classification	BMI	Risk of Comorbidities
Normal range	18.5 – 24.99	Average
Overweight	≥ 25.0	
Pre-obese	25.0 – 29.99	Increased
Obese	≥ 30.0	
Obese class 1	30.0 – 34.99	Moderate
Obese class 2	35.0 – 39.99	Severe
Obese class 3	≥ 40.0	Very Severe

For children and teens, BMI is age and sex specific and is referred to as BMI for age. After BMI is calculated for children, the BMI number is plotted on the CDC growth charts to obtain a percentile ranking. Percentiles which are age and sex specific are used to assess the size and growth patterns of children. The growth charts classify the weight status categories into underweight, healthy weight, overweight, and obese[12] (Table 2).

Table 2: BMI Age-Related Weight Status Categories and Percentiles[12]

Weight Status Category	Percentile Range
Underweight	Less than the 5th percentile
Healthy weight	5th percentile to less than the 85th percentile
Overweight	85th to less than the 95th percentile
Obese	Equal to or greater than the 95th percentile

1.2 Epidemiology

WHO estimated that as of 2008, there were 1.5 billion overweight adults, and more than 200 million obese men and 300 million obese women in the world. overall it was estimated that more than one in ten of the world's adult population was obese[6]. Another study estimated the world epidemic of overweight to involve close to 1.7 billion individuals[13]. Canada, USA, UK, and Australia have more than doubled their rate of obesity in the last two decades [14, 15]. In the US, the prevalence of overweight and obesity in adults is estimated at 66.3% and 32.2% respectively [16] and the prevalence of morbid obesity (BMI ≥40) is approximately 5.1%[17]. In Canada morbid obesity affects 3% of Canadians[18].

According to the WHO in 2010, close to 43 million children under five were overweight. Approximately 35 million overweight children were living in developing countries and 8 million in developed countries.[6]. In the US, according to the National Health and Nutrition 2003-2004 Examination Survey (NHANES) close to 17.1% of children and adolescents aged 2 to 19 were overweight[16]. In Canada in 2005, the measured rate of obesity for youth 12 to 17 was 9.4%, which almost doubled the self-reported rate of 4.9%.[19].

1.3 Health consequences of obesity

WHO reported that overweight and obesity were the fifth leading risk for global deaths[6]. Obesity is associated with increases in the prevalence of obesity comorbidities (e.g. type 2 diabetes, hyperlipidemia, hypertension, obstructive sleep apnea, heart disease, stroke, asthma, back and lower extremity weight-bearing degenerative problems, several forms of cancer, depression)[20] (Table 3).

WHO estimated that, 44% of the diabetes cases worldwide, 23% of the heart disease and up to 41% of certain cancer are attributed to overweight and obesity, and as a result of overweight or obesity, more than 2.8 million adults die each year worldwide [6, 21]

There is a linear relationship between BMI and mortality; the longer the duration of obesity the greater the risk[11]. Obesity is associated with substantial loss of life expectancy; it is estimated that a 25-year-old morbidly obese man will lose 12 years of life which represents a loss of 22% in the expected remaining lifespan when compared to a normal weight individual, which translates into 12-fold increased risk of mortality [11, 22]

Table 3: WHO Estimated Risk for the Obese Developing Obesity-Related Diseases[10]

Greatly increased (RR > 3)	**Moderately increased (RR = 2-3)**	**Slightly increased (RR = 1-2)**
Type 2 diabetes	Coronary heart disease	Cancer (breast cancer in postmenopausal women, endometrial cancer, colon cancer)
Dyslipidaemia	Hypertension	Reproductive hormones abnormality
Insulin resistance	Osteoarthritis	Polycystic ovary syndrome
Sleep apnea	Hyperurcemia and gout	Impaired fertility
Breathlessness		Low back pain
Gall bladder disease		Increased risk for anesthesia complications
		Fetal defect associated with maternal obesity

In children and adolescents, obesity is associated with increased risk for cardiovascular diseases including hypertension and dyslipedaemia, abnormal glucose metabolism, hepatic steatosis, sleep apnea, and most importantly persistence of obesity with all the associated risk to adulthood[10](Table 4)

Table 4: WHO Estimated Risk for the Obese Child Developing Obesity-Related Diseases[10]

High Risk	Intermediate risk	Low risk
Faster growth	Hepatic steatosi	Orthopedic complications
Psychosocial problems	Abnormal glucose metabolism	Sleep apnea
persistence into adulthood		Polycystic ovary syndrome
Dyslipidemia		Psudotumor cerebri
		Cholelithasis
		Hypertension

1.4 Interventions

1.4.1 Medical therapy

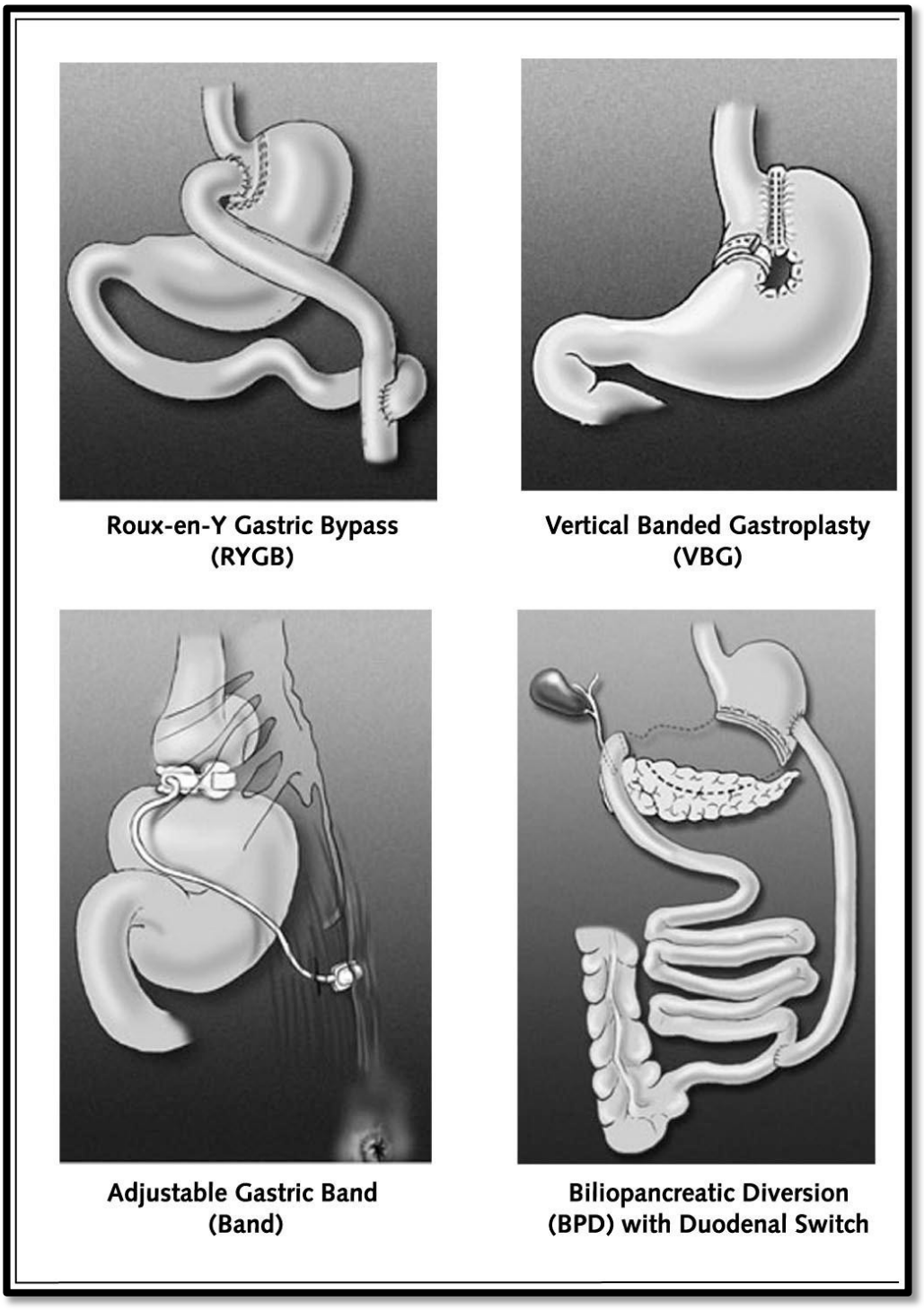
Medical therapy options are limited. Behavioral therapy consisting of reducing energy intake, improving eating behaviors, and increasing exercise and activity, supplemented with pharmacotherapy, generally achieved only minimal and often transient effects[7, 8]
The National Institutes of Health (NIH) Consensus Conference (1991) recognized that medical therapy for severe obesity had been uniformly unsuccessful in treating the problem.[23]

1.4.2 Surgical therapy

In 1991, the National Institutes of Health established guidelines for surgical therapy of morbid obesity (BMI≥40 or BMI≥35 in the presence of significant comorbidities), now referred to as bariatric surgery[9](Figure 1).

The rise in the prevalence of obesity led to increase interest in surgical treatments to achieve weight loss and in 2008, approximately 350,000 operations were performed worldwide -- 220,000 of these in the US and Canada. The most commonly performed procedures were laparoscopic adjustable gastric banding (AGB; 42.3%), laparoscopic standard Roux-Y gastric bypass (RYGB; 39.7%), and total sleeve gastrectomies 4.5%.[24]

Figure 1: Various Surgical Procedures for Obesity



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1.4.2 a) Gastric bypass

The first gastric bypass was reported in 1967 by Mason and Ito[25]. In the Roux en-Y gastric bypass (RYGB), the upper stomach is divided using surgical staples to create a gastric pouch about 20-30 ml in capacity. The gastric pouch is connected to the alimentary or the roux limb that is about 100 cm long, joining the 30 to 45cm long biliary limb, which forms the common limb. Adjustments of the procedure have been used to increase malabsorption and increase weight loss by lengthening the Roux-en-Y limb to 100–150 cm. This procedure can be performed laparoscopically or using open techniques. Weight loss is achieved by limiting gastric capacity as well as causing malabsorption and inducing hormonal changes.

1.4.2 b) Adjustable gastric banding

Non-adjustable gastric banding was first reported in 1978 by Wilkinson and Peloso[26], but the first report on the clinical use of adjustable gastric band was in 1986 by Lubomyr Kuzmak[27]. Adjustable gastric banding is considered one of the least invasive bariatric surgery procedures. An inflatable gastric band is placed horizontally around the proximal part of the stomach which is connected to a subcutaneous port. The subcutaneous port creates a pouch by inflating the band which controls the rate of emptying of the pouch and meal capacity. Moreover, the diameter of the band can be adjusted to the individual needs of the patient. This procedure can be done laparoscopically or using open techniques.

1.4.2 c) Biliopancreatic diversion with duodenal switch

Biliopancreatic diversion was first reported in 1978 by Scopinaro[28], and is now commonly performed by adding the duodenal switch component. It is primarily a malabsorptive procedure involving resection of the stomach along the greater curvature. As in sleeve gastrectomy, the pylorus is preserved with an aggressive intestinal bypass; the alimentary and biliary limbs join to form the common channel which is less than 100 cm in length. This procedure can be done laparoscopically or using open techniques.

1.4.2 d) Sleeve gastrectomy

Sleeve gastrectomy was first reported by Doug Hess in 1988 as part of what is now known as the duodenal switch procedure[29]. For some patients at high risk from bariatric surgery, particularly those with a BMI of more than 60, a sleeve gastrectomy is considered to be a bridging procedure. In a sleeve gastrectomy procedure about 80% of the stomach along the greater curvature is divided and removed to form a sleeve or a tube-shaped stomach followed in 6-12 months by a conversion to either a gastric bypass or a duodenal switch. However, for some, enough weight loss is achieved with the sleeve gastrectomy alone and it can be considered the sole treatment for obesity in selective patients. This procedure can be done laparoscopically or using open techniques.

1.4.2 e) Vertical banded gastroplasty

Gastroplasty procedures were introduced by Gomez in 1981[30] and Mason in 1982[31]. In these procedures, the fundus of the stomach is stapled, creating a small gastric pouch about 50 ml in size. With the band surrounding the outlet to the remaining distal stomach, a 10-13mm channel is created which limit the size of the meal and induce early satiety and decrease caloric intake. Vertical banded gastroplasty (VBG) can be done laparoscopically or using open techniques. Currently, VBG is not frequently done and it has been largely replaced by other procedures. However, it has been often used as a comparator intervention frequently, for this reason it is included in this review.

2.0 Methods – Systematic Review

A systematic review of the medical literature was carried out in an attempt to answer the research question: What is the relative effectiveness and safety of surgical treatments for obesity and do they modify clinically important outcomes, including weight loss, comorbidity modifications to diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea in adolescents and the adult obese population?

2.1 Literature Search Strategy

The search strategies were developed with input from an information specialist. The following bibliographic databases were searched on the Ovid interface: MEDLINE Daily Update, MEDLINE In-Process & Other Non-Indexed Citations (1950 to December 8 2010), EMBASE (1947 to December 8 2010) and the Cochrane Library (until the fourth quarter 2010).

The search strategy used both controlled vocabulary -- the National Library of Medicine's MeSH (Medical Subject Headings) -- and keywords, such as: *obesity/ surgery, gastric bypass, sleeve gastrectomy, bariatric, gastric banding, anastomosis, Roux-en-Y* and *biliopancreatic diversion* (including duodenal switch). See Appendix A for the search strategy. Methodological filters were applied to limit the retrieval to randomized controlled trials. The search was not restricted to language.

Grey literature (literature that is not commercially published) was identified by searching health technology assessment websites and related agencies. These electronic searches were supplemented by hand searching the bibliographies of key papers, and contacting appropriate experts in the field.

2. 2 Study Selection Method

A study was eligible for inclusion if it satisfied each of the criteria listed below:

• **Study design**: Randomized controlled trial (RCT).

• **Population**: Adults who fulfill the definition of obesity i.e BMI more than 30, and adolescents who fulfill the definition of obesity for age, sex, and height.

• **Interventions**: Five types of bariatric surgery procedures -- Roux-en-Y gastric bypass, vertical banded gastroplasty, adjustable gastric banding, biliopancreatic diversion (BPD) and sleeve gastrectomy.

• **Comparators**

- Surgical procedure versus usual care (no treatment or medical management e.g. very low calorie diet.
- Head-to-head comparisons to a surgical procedure.

• **Outcomes**: Percent of excess weight loss (EWL), BMI loss, weight changes (Kg), safety, and resolution of obesity related comorbidities (diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea).

Once citations from the literature search were obtained, two independent reviewers (H.A., J.P.) performed an initial screening of articles by examining titles, abstracts and keywords for relevance to the research question. A screening log was used to track this process. Differences between reviewers were discussed and resolved by consensus.

Articles were then retrieved and reviewed by the same two independent reviewers and selected for final inclusion in the review if they satisfied the inclusion criteria described in Section 3.2. Caution was exercised to ensure that duplicate publications of the same study or published articles of a single center study, which were part of a larger multi-center study, were not included in the analysis. In the case of studies published several times, only those providing relevant and updated data were selected. Differences between reviewers were discussed and resolved by consensus. In cases where consensus was not achieved, a third reviewer (G.W.) was added to the selection process. Studies for which only abstracts were available were not considered.

2.3 Data Extraction Strategy

A draft data extraction form (Appendix B1) was designed to document all relevant information available in the selected studies. One reviewer (H.A.) extracted data from the selected studies, and a second reviewer (J.P.) checked the extracted data for accuracy. Any differences were resolved by consensus.

2.4 Study Quality Assessment

Methodological quality of the studies was assessed using the SIGN50 (Appendix B2). A Guideline Developer's Handbook published by the Scottish Intercollegiate Guidelines Network [32] which considered the appropriateness and clarity of the question, randomization, concealment, blinding, baseline comparability, group difference, outcome measurement, drop out, intention-to-treat analysis, site result, overall bias, and funding.

The risk of bias in the included studies was assessed using *The Cochrane Handbook for Systematic Reviews of Interventions* [33] (Appendix B3) which considered the following factors : sequence generation, concealment, blinding, incomplete data, selective reporting and other bias.

The same two reviewers independently assessed the quality of the included studies. Prior to assessment, a calibration exercise was undertaken to ensure consistency in assessing or scoring between the two reviewers. Differences were discussed and resolved by consensus. In cases where consensus was not achieved, the third reviewer assisted with the study quality assessment process.

2.5 Measures of treatment effect

RevMan 5.1, 2011[34] was used to analyze the result of the studies. Data were summarized in the meta-analysis if they were both clinically and statistically homogeneous. A random effects model was employed. Continuous data was expressed as mean difference (MD). In the few studies where measures of variance were missing from a relevant article, it was imputed from other information provided by the article (e.g. standard error (SE), p-value, 95% confidence interval (CI)).

2.6 Assessment of heterogeneity

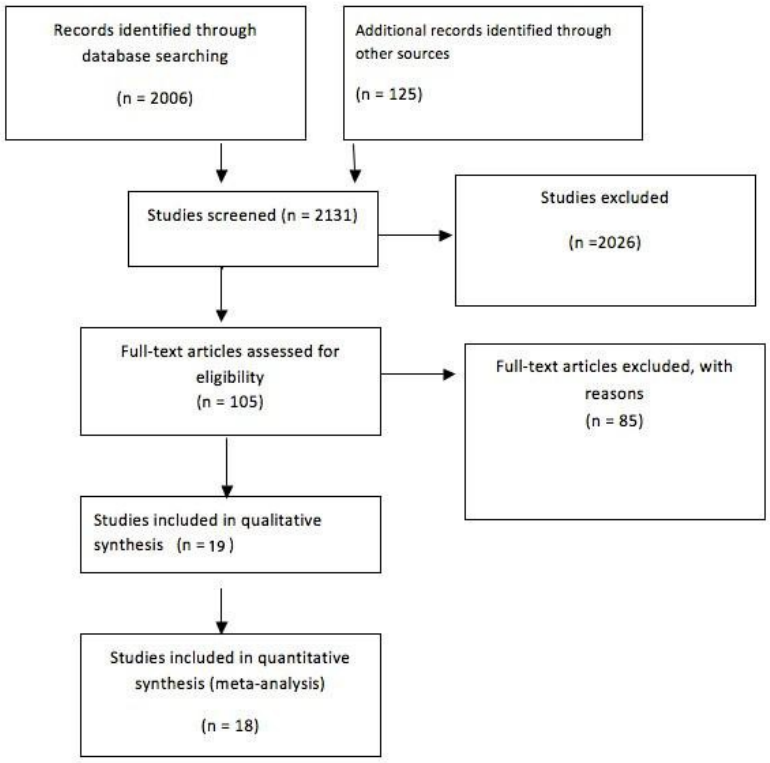
Before the quantitative pooling of the results, the homogeneity of the clinical and methodological characteristics of included studies was evaluated. The characteristics reviewed included study design, inclusion and exclusion criteria, baseline demographics (age, gender), interventions, and clinical outcomes. Heterogeneity was measured with the I^2 statistic, with $I^2 \geq 50\%$ identifying substantial heterogeneity[35].

3.0 Results of the systematic review

3.1 Results of the search

The search of electronic databases resulted in 2006 records. Hand searching of the bibliographies of key papers and contacting appropriate experts resulted in additional 125 records. A total of 2131 records were screened. We excluded 2026 based on title or abstract. We retrieved 105 full text articles. We excluded 85 articles after reviewing the full text (see appendix C 'Characteristics of excluded studies' for further details). A total of 19 articles met the inclusion criteria for the qualitative synthesis and 18 articles met the inclusion criteria for the quantitative synthesis (Figure 2).

Figure 2: Search result flow diagram



3.2 Description of studies

Table 5 provides a summary of the included studies.

Table 5: Summary of Included Studies

Study	Trial Characteristics	Patient Characteristics	Interventions	Outcome	QA
Angrisani 2007	**Design:** RCT, single centre **Sample size:** 51 **Follow-up:** 60 months **Country:** Italy	Age: 34 (9) % Female: 82 BMI: 43.6 (4.1) WT: 117.65 (13)	1- LRYGBP 2- LAGB	BMI, weight, %EWL. Mortality, conversion to an open procedure, postoperative complications leading to reoperation, hospital stay, and improvement in co-morbidities.	–
Dixon 2008	**Design:** RCT, single centre **Sample size:** 60 **Follow-up:** 24 months **Country:** Australia	Age: 46.8 (8) % Female: 53.5 BMI: 37.1 (2.6) WT: 105.7(14)	1- LAGB 2- Conventional treatment	BMI, weight, %EWL. Proportion of participants achieving remission of type 2 diabetes, percentage change in HbA1C levels, blood pressure, waist circumference, and levels of fasting lipids, including total cholesterol, triglycerides, and high-density lipoprotein cholesterol. Changes in medication use, changes in the proportion of participants with the metabolic syndrome, changes in indirect measures of insulin resistance, and adverse events.	+
Himpens 2006	**Design:** RCT, single centre **Sample size:** 80 **Follow-up:** 36 months **Country:** Belgium	Age: 38 (20-65)* % Female: 80 BMI: 38 (30-53)* WT: not reported * median & range.	1-LSG 2-LAGB	BMI, weight, %EWL. Feeling of hunger, craving for eating sweets, GERD, complications and re-operations.	–
Howard 1995	**Design:** RCT, single centre **Sample size:** 42 **Follow-up:** up to 78 months **Country:** USA	Age: 37.3 (2.1)* % Female: 78.5 BMI: not reported WT: max.148(21.5)* * Standard error	1-GBP 2-VBG	%EWL Early postoperative complications such as wound dehiscence, infection and thromboembolism, and late complications including hernia, wound problems, peptic ulcer, gallbladder disease, vitamin deficiency and weight regain.	–

Study	Trial Characteristics	Patient Characteristics	Interventions	Outcome	QA
Karamanakos 2008	**Design:** RCT, single centre **Sample size:** 32 **Follow-up:** 12 months **Country:** Greece	Age: 33.8 (8) % Female: 84.3 BMI: 45.8 (3.6) WT: 123.6(16.4)	1-LRYGB 2-LSG	BMI, %EWL. Blood level of glucose, triglycerides, cholesterol, and high and low density lipoprotein cholesterol, Hb, liver function test as well as fasting ghrelin and fasting PYY, and appetite assessment.	++
Lee 2004	**Design:** RCT, single centre **Sample size:** 80 **Follow-up:** up to 30 months **Country:** Taiwan	Age: 32 (8.2) % Female: 70 BMI: 43.1 6.8) WT: 119.8(23.8)	1.LRYGB 2-LVBG	BMI, %EWL. Operative time, estimated blood loss, dosages required during hospital stay, length to postoperative flatus passage, hospital stay, early, late and major complications. Quality of Life Assessment.	+
MacLean 1995	**Design:** RCT, single centre **Sample size:** 106 **Follow-up:** up to 84 months **Country:** Canada	Age: 39.4 (8.6) % Female: not reported BMI: 49(6.9) WT: not reported	1-RYGB 2-VBG	BMI, % EWL, Reinhold classification Reoperation rate.	–
Mingrone 2003	**Design:** RCT, single centre **Sample size:** 79 **Follow-up:** 12 months **Country:** Italy	Age: 30 - 45 % Female: 65 BMI: 48.1(7.3) WT: 136.4	1- BPD 2- Diet	BMI, weight. Body composition and adipose tissue distribution, hormone measurements, as well as metabolic investigations.	–

Study	Trial Characteristics	Patient Characteristics	Interventions	Outcome	QA
Nguyen 2009	**Design:** RCT, single centre **Sample size:** 197 **Follow-up:** 48 months **Country:** USA	Age: 43.6 (10.4) % Female: 76.5 BMI: 46.5 (5.4) WT: 131.1 (21.1)	1-LRYGB 2-LAGB	BMI, % EWL. Perioperative and late outcomes, weight loss, quality of life, and costs. operative time, estimated blood loss, length of hospital stay, number of patients requiring intensive care unit (ICU) stay, time to return to normal activities and work, morbidity, and mortality.	++
Nilsell 2001	**Design:** RCT, single centre **Sample size:** 59 **Follow-up:** up to 60 months **Country:** Sweden	Age: 38.5 (19-59) % Female: 76.0 BMI: 43.3 (4.6) WT: 123.5 (17.7)	1-AGB 2-VBG	BMI, weight. Complications, need for revisional surgery, reflux symptoms and the patient's own evaluation.	+
O'Brien 2006	**Design:** RCT, single centre **Sample size:** 80 **Follow-up:** 24 months **Country:** Ausralia	Age: 41.2 (6.7) % Female: 76.2 BMI: 33.6 (1.6) WT: 94.8 (11.5)	1-LAGB 2- Intensive Medical Program	BMI, weight, % EWL, % of patients who lost more than 50% of excess weight at 2 years. Health, quality of life, and side effects of treatment.	++
O'Brien 2010	**Design:** RCT, single centre **Sample size:** 50 **Follow-up:** 24 months **Country:** Australia	Age: 16.5 (1.3) % Female: 68 BMI: 41.3 (4.6) WT: 118 (19.6)	1-LAGB 2-Supervised lifestyle intervention	BMI, weight, % EWL. Health, quality of life, and adverse events resulting from treatment or from failure of compliance with the protocol.	++
Olbers 2005	**Design:** RCT, single centre **Sample size:** 83 **Follow-up:** 24 months **Country:** Sweden	Age: 35.5 (26-61) % Female: 73.4 BMI: 42.4 (4.1) WT: 123.6 (15.7)	1-LRYGB 2-LVBG	BMI, % EWL, and the need for remedial surgical intervention. Complication rates, postoperative lung function and time to mobilization.	+
Peterli 2009	**Design:** RCT, single centre **Sample size:** 27 **Follow-up:** 3 months **Country:** Switzerland	Age: 39.8 (10.4) % Female: not reported BMI: 46.3 (6.5) WT: 128.3 (25.6)	1-LRYGB 2-LSG	BMI, weight, % EWL. GLP-1, insulin, PYY, and ghrelin, glucose, triglycerides, and cholesterol.	++

Study	Trial Characteristics	Patient Characteristics	Interventions	Outcome	QA
Reis 2010	**Design:** RCT, single centre **Sample size:** 20 **Follow-up:** 24 months **Country:** Brazil	Age: 39.4 (11.2) % Female: 0 BMI: 54.8 (6.9) WT: 164.3 (24.1)	1-LRYGB 2- Conventional Rx.	BMI, weight. International Index of Erectile Function (IIEF-5) questionnaire. Serum total (TT) and free testosterone (FT), oestradiol, prolactin (PRL), luteinizing (LH) and follicle-stimulating (FSH) hormones.	++
Scozzari 2009	**Design:** RCT, single centre **Sample size:** 100 **Follow-up:** 84 months **Country:** Italy	Age: 37.7 (20-58) % Female: 81 BMI: 44.4 (40-50) WT: 120.1 (90-175)	1-LAGB 2-LVBG	BMI, % EWL, Reinhold classification. Surgical time, anesthesiology time, conversion rate, intraoperative and postoperative morbidity, 60-day mortality, and length of hospital stay. Long-term complications, additional procedures, readmissions, and hospital stay. Reoperation rate	+
Sovik 2010	**Design:** RCT, 2 centres **Sample size:** 60 **Follow-up:** 12 months **Country:** Norway & Sweden	Age: 35.5 (6) % Female: 70 BMI: 55 (3.3) WT: 162 (22)	1-LRYGB 2-LBPD/DS	BMI, weight, % EWL. Complications and readmission rate.	+
Sugerman 1987	**Design:** RCT, single centre **Sample size:** 40 **Follow-up:** 36 months **Country:** USA	Age: 38(10) % Female: 90 % ideal WT: 219 (45)	1-RYGB 2-VBG	Weight, % EWL, percentage decreases in weight, percentage of ideal weight achieved. Complications and mortality. Laboratory result.	-
Van Dielen 2005	**Design:** RCT, single centre **Sample size:** 100 **Follow-up:** 24 months **Country:** Netherland	Age: 38.1 (9.1) % Female: 80 BMI: 46.6 (6.2) WT: not reported	1-LAGB 2- VBG	BMI, % EWL. Hospital length of stay, early and late Postoperative complications and mortality. Reoperation rate.	+

QA= Qualitative Assessment

3.2.1 Design

All included studies were randomized control trials.

3.2.2 Sample sizes

Sample size ranged from 20 in Reis 2010[36] to 197 in Nguyen 2009[37]

3.2.3 Setting

All the studies were single centre randomized control trials except for one trial[38] which was conducted in two centres, Norway and Sweden**.** Three trials were done in each of the following countries: Australia, Italy, and USA; two trials in Sweden; one trial in: Belgium, Brazil, Canada, Greece, Netherlands, Switzerland and Taiwan.

3.2.4 Participants

All trial participants were adults except for one trial[39] where the trial participants were adolescents who were eligible to be included in the trial if they were between 14 to 18 years old. The average age of adults was 36.1 years of age. Most trial participants were female except in the one trial[40] where all participants were male.

Most studies included participants with a BMI of 40 or higher or a BMI of 35 with an obesity-related comorbidity. Dixon 2008[41] included participants with a BMI of 30 to 40 and Type 2 diabetes. O'Brien 2006[42] participant's BMI were less than 35, Søvik 2010[38] included participants with a BMI between 50 and 60, and Reis 2010[40] excluded participants with comorbidities requiring treatment. Other studies had an upper limit of a BMI of 50[43-45], or 60 as in Nguyen 2009[37].

3.2.5 Interventions

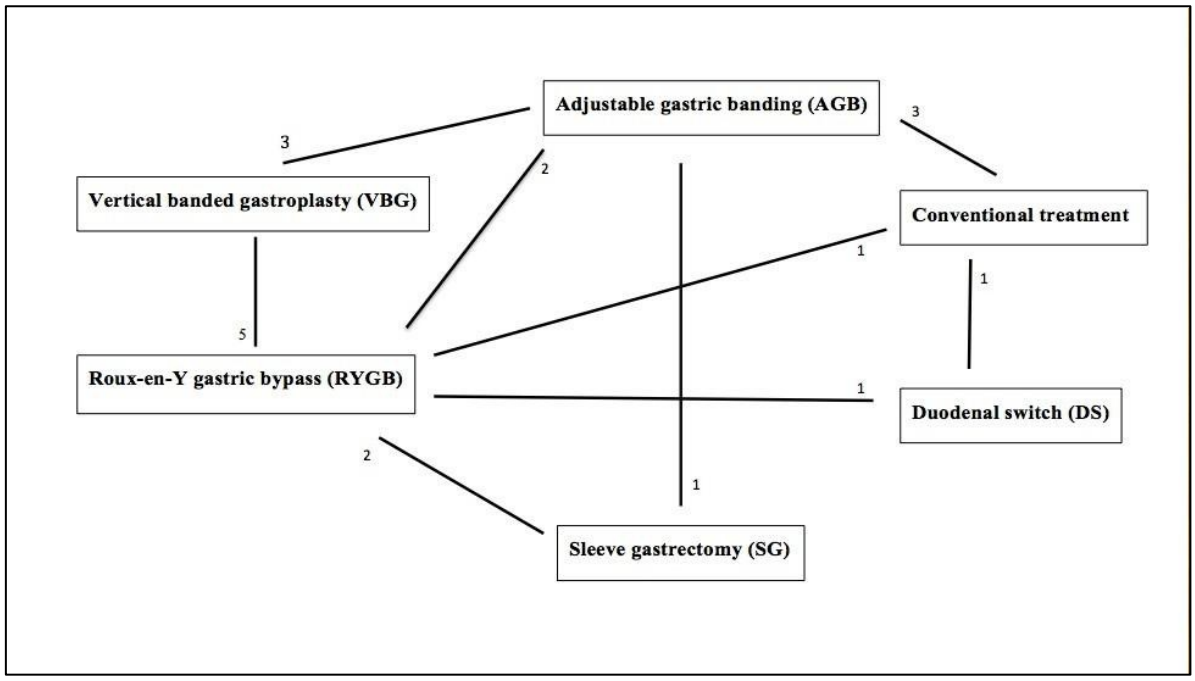
The included studies compared variety of interventions, see Figure 3 for the visual display of the comparisons. Five RCTs[39-42, 46] compared surgical interventions to non-surgical interventions. Four of the five were done in an adult population[40-42, 46] and one RCT was done in an adolescent population[39]. Of the five RCTS, three compared adjustable gastric banding to conventional therapy[39, 41, 42], one compared laparoscopic Roux-en-Y gastric

bypass (LRYGB) with conventional therapy[40], and the fifth RCT compared biliopancreatic diversion to diet[46].

There were 14 RCTs comparing different surgical procedures:

- Five RCTs compared Roux-en-Y gastric bypass (RYGB) with vertical banded gastroplasty (VBG)[44, 47-50]
- Three RCTs compared vertical banded gastroplasty (VBG) with adjustable gastric banding (AGB)[45, 51, 52]
- Two RCTs compared laparoscopic Roux-en-Y gastric bypass (LRYGB) with laparoscopic adjustable gastric banding (LAGB)[37, 43]
- Two RCTs compared laparoscopic Roux-en-Y gastric bypass (LRYGB) with laparoscopic sleeve gastrectomy (LSG)[**53, 54**]
- One RCT compared laparoscopic Roux-en-Y gastric bypass (LRYGB) with laparoscopic biliopancreatic diversion with duodenal switch (LDS)[38]
- One RCT compared laparoscopic adjustable gastric banding (LAGB) with laparoscopic sleeve gastrectomy (LSG)[55]

Figure 3: Network of Comparisons: of Surgical and Non-Surgical Interventions



3.2.6 Outcomes

All the studies reported on weight changes but used different measures, mostly BMI, weight and percentage of excess weight loss. For the studies that did not report measure of variance, (i.e. standard deviation and confidence intervals), these were imputed to be included in the meta-analysis. Resolutions of comorbidities were reported in eight trials[39, 41-43, 52-55]. All trials reported on safety and adverse events except four trials[40, 46, 53, 54].

3.3 Excluded studies

Eighty-five articles were excluded after retrieving the publications. Forty articles were excluded because the comparison was between two techniques of the same procedure. Sixteen articles were excluded because of study design; 15 studies were excluded because the comparison arm was horizontal gastroplasty; 6 studies because one of the comparison arms was jejunoileal bypass both of which are no longer performed. Four studies had no relevant control, three articles were multiple publications, and one was an abstract. (Appendix C)

3.4 Quality of the included studies

3.4.1 Sign 50

Table 6 provide summary of the quality assessment using Sign 50.

Two reviewers independently assessed the included studies using the SIGN 50 quality assessment tool addressing the following criteria:
a) Study question
Three[47, 49, 52] trials poorly addressed the study question, all other trials were either "well covered" or "adequately addressed".

b) Randomization
Three trials[46, 47, 55] poorly addressed randomization; all other trials were either "well covered" or "adequately addressed".

c) Allocation concealment
Seven trials[41, 46, 47, 49, 52, 55, 56] did not address concealment methods, all other trials were either "well covered" or "adequately addressed".

d) Blinding
One trial[53] reported blinding as to the type of the procedure involved the patient and the medical staff, and the independent data collector, all other trials did not address blinding adequately.

e) Baseline group comparability
All trial's treatment and the control groups were similar at the start of the trial.

f) Group treatment comparability
In all the trials the only difference between the groups was the treatment under investigation.

g) Outcome measurement
Three trials[47, 49, 51] poorly addressed measurement of all relevant outcomes in a standard, valid and reliable way, all other trials were either "well covered" or "adequately addressed".

With respect to other SIGN 50 criteria 4 trials[39, 47, 50, 56] reported ≥ 20% withdrawal rate in either study group and one study[38] was multicentre but did not report the results separately by site. Funding was reported in only 7 trials. Two were funded by industry[41, 42], two by government agencies[52, 56] and three by a combination of industry and government [38, 39, 54]. For the overall assessment score we awarded six studies a minus, eight studies a plus and five studies a double plus.

Table 6: Sign 50 Quality assessment of the included studies.

Sign 50	*Angrisani 2007*	*Dixon 2008*	*Himpens 2006*	*Howard 1995*	*Karamanakos 2008*	*Lee 2004*	*Maclean 1995*	*Mingrone 2002*	*Morino2003*	*Nguyen 2009*
1.1 Question	B	A	A	C	A	B	C	A	B	A
1.2 Randomized	B	A	C	C	A	B	B	C	B	A
1.3 Concealed	B	D	D	D	A	B	D	D	A	B
1.4 Blinding	D	D	D	D	B	D	D	D	D	D
1.5 Baseline Comparability	B	A	B	A	B	A	B	C	A	B
1.6 Group Differences	B	A	B	B	A	A	B	B	B	B
1.7 Outcome Measurement	B	A	B	C	A	A	C	A	A	A
1.8 Dropouts: Treatment % Control %	LRYGB 0% LAGB 3%	LAGB 3.3% Medical 13.3%	D	GBP 70% VBG 73%	0%	D	D	0%	D	LRYGB 16.9% LAGB 6.7%
1.9 TT	D	B	D	D	A	B	C	A	D	B
1.10 Site Results	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
2.1 Bias (++, + , -)	_	+	_	_	++	+	_	_	+	++
3.8 Funding	D	IND	D	D	D	D	D	D	D	D

A = Well Covered, B = Adequately Addressed, C = Poorly Addressed, D = Not Addressed, NR = Not Reported.

Sign 50	*O'Brien 2006*	*O'Brien 2010*	*Olbers 2005*	*Peterli 2009*	*Reis 2010*	*Scozzari 2009*	*Sovik 2010*	*Sugerman 1987*	*Van Dielen 2005*	*Nilsell 2001*
1.1 Question	A	B	A	A	A	B	A	B	C	A
1.2 Randomized	A	A	A	A	A	B	A	A	B	B
1.3 Concealed	A	A	D	A	B	A	B	B	D	B
1.4 Blinding	D	D	D	D	B	D	D	D	D	D
1.5 Baseline Comparability	A	A	A	A	A	A	A	B	B	A
1.6 Group Differences	A	A	A	A	A	B	A	B	B	A
1.7 Outcome Measurement	A	A	B	A	A	A	A	B	A	C
1.8 Dropouts:	LAGB 7.0%	LAGB 4.0%	LAGB 4.0%			LAGB 18.4%	LRYGB 0%	GBP 10.0%		AGB 16.9%
Treatment %				0%	0%				0%	
Control %	Medical 17.0%	Medical 28.0%	Medical 28%			LVBG 19.6%	DS 3.5%	VBG 20.0%		VBG 12.5%
1.9 ITT	B	A	D	A	A	B	D	D	B	D
1.10 Site Results	NA	NA	NA	NA	NA	NA	D	NA	NA	NA
2.1 Bias (++, + , -)	++	++	+	++	++	+	+	_	+	+
3.8 Funding	IND	IND + GOV	GOV	IND + GOV	D	D	IND + GOV	D	GOV	D

A = Well Covered, B = Adequately Addressed, C = Poorly Addressed, D = Not Addressed, NR = Not Reported.

3.4.2 Risk of bias in included studies

Figure 4 and Figure 5 provide a graphical summary of the results of risk of bias for the included studies. For more detailed assessment of the risk of bias of included trials see (Appendix D).

Figure 4: Risk of bias summary: review authors' judgements about each risk of bias item for each included study

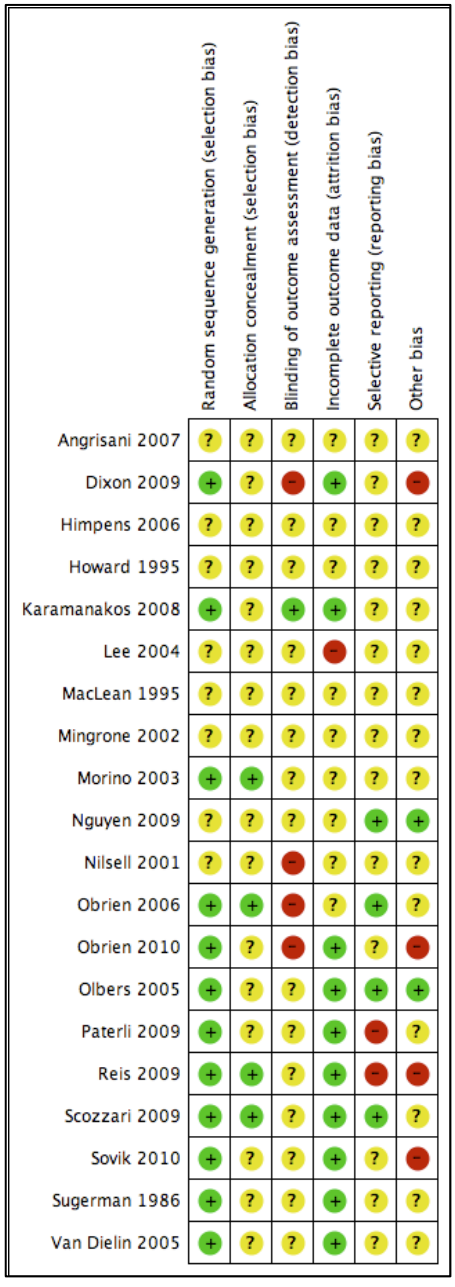
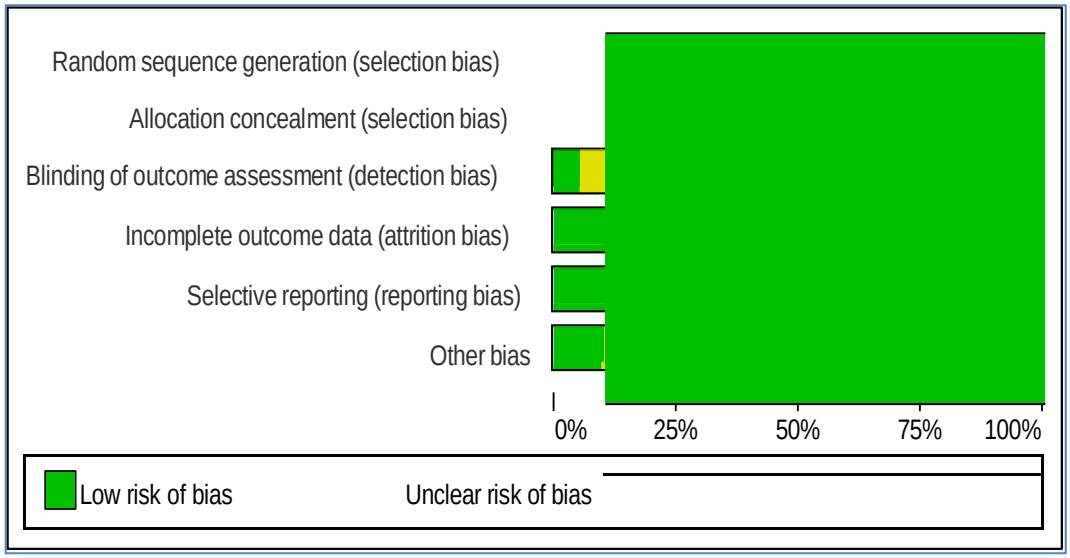


Figure 5: Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.



3.4.2.1 Sequence generation

Adequate sequence generation was described in 11 trials[38-42, 44, 45, 50, 52-54] All were computer driven except for one trial used shuffling cards[50].

3.4.2.2 Allocation

Adequate concealment methods were described in three studies [40, 42, 45]. Most other trials did not report the allocation process in sufficient details to determine concealment.

3.4.2.3 Blinding

Four trials reported that outcome assessors were not blinded[39, 41, 42, 51]; one trial was blinded[53] and the remaining trials did not report blinding.

3.4.2.4 Incomplete outcome data

Five trials had a complete follow up in both groups[40, 46, 52-54], one trial[49] reported complete follow up in an earlier report but this information was not provided in the latest report. Three trials provided the number of dropouts along with the reasons for the dropout[39, 44, 50] Six trials did not report the reasons for the dropout[37, 41, 42, 45, 47, 51]. Two trails did not report on missing data[48, 55].

3.4.2.5 Selective reporting

Adverse events were either not reported or not reported adequately in five trials[40, 46, 51, 53, 54]. All outcomes were pre-specified in the methods section and reported as results in four trials[37, 42, 44, 45]. No measures of variance were reported in one trial [55]. one trial[49] used the Reinhold classification to describe postoperative weight changes[57]

3.4.2.6 Other potential bias

Three trials were sponsored by a government body together with private industry[38, 39, 54]**;** two trials were sponsored by private industry[41, 42] and two trials were sponsored by a government institute[44, 52]

One trial[43] stated that surgeons were in the early phase of the learning curve for laparoscopic Roux-en-Y gastric bypass (LRYGB) compared with laparoscopic adjustable gastric banding (LAGB). In another trial[38] not all participating surgeons performed all types of procedures, and in one trial[49] the results were not reported by the original treatment assignment. Two trials[39, 41] had their participants involved in a program for two to three months prior to surgery fulfilling the best practice recommendations for diet and physical activity. One trial[40] was conducted on males only and one trial[54] reported only a three month follow up. One trial[50] was terminated nine months after randomization because a statistically significant difference of $p < 0.05$ was noted in favor of one of the treatments which was agreed upon prior to conducting the study.

3.5 Publication bias and other sensitivity analyses

There were too few studies in any particular comparison to assess publication bias or sensitivity analysis.

4.0 Results: Effect of Interventions

4.1 Weight changes

There were three primary end points in the meta-analysis: percent of excess weight loss (%EWL), body mass index (BMI), and weight (WT), measured at one, two and three years. Figures for the one year result were included in the main text, two and three years results were presented in appendix E.

4.1.1 Percent of excess weight loss (% EWL)

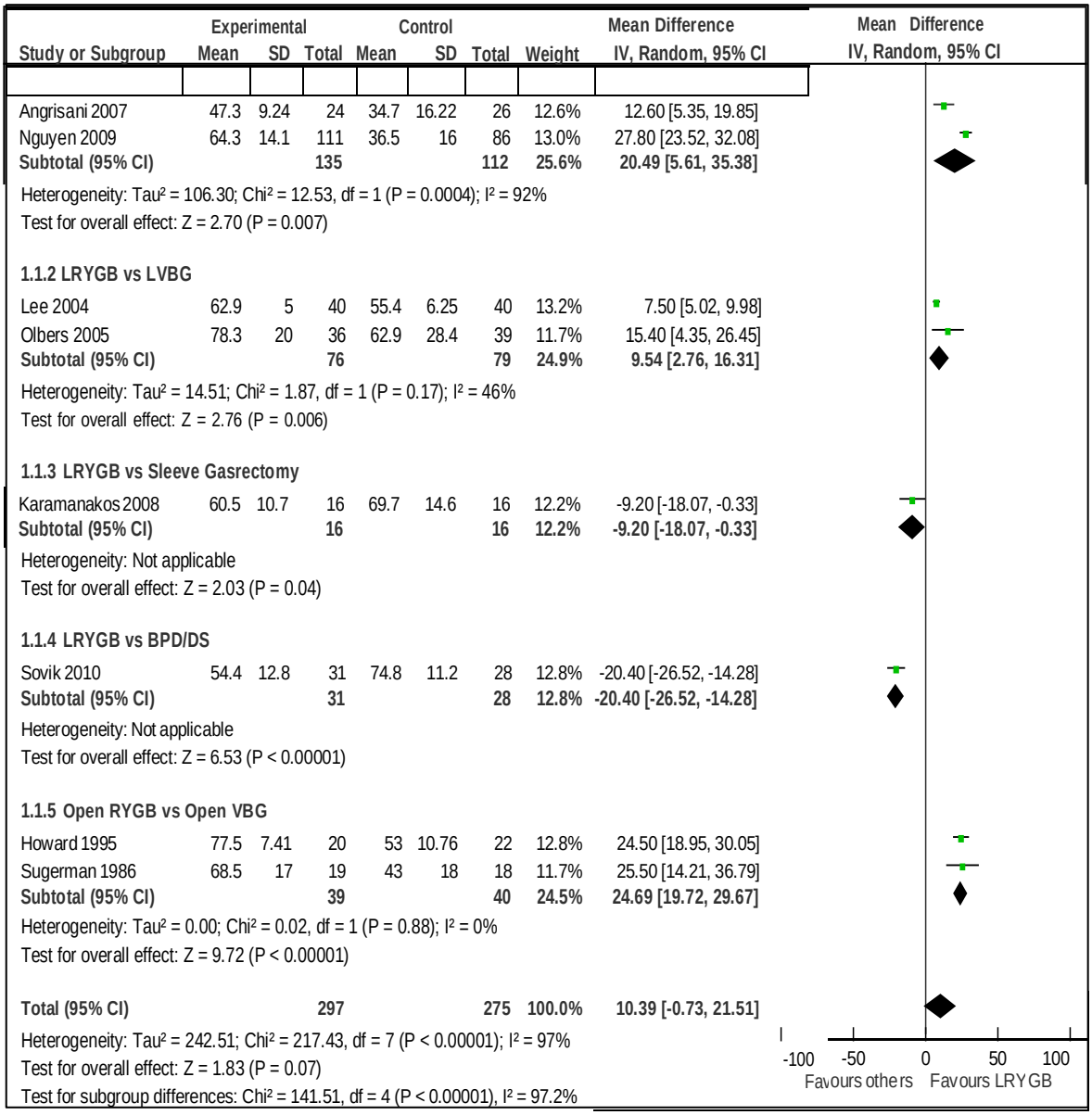
4.1.1 a) Gastric bypass

For % EWL there were studies available for the following comparison: two trials[37, 43] compared LRYGB to LAGB (247 participants)**;** two trials[44, 48] compared LRYGB to LVBG**;** one trial[53] compared LRYGB to LSG; one trial[38] compared LRYGB to LDS; two trials[47, 50] compared open RYGB to open VBG; and one trial[40] compared LRYGB to conventional therapy.

Based on the evidence, LRYGB produced a significantly greater percent of excess weight loss when compared to LAGB at 1 year [MD 20.5% (95% CI: 5.6 to 35.4)] (Figure 6) with the percent of excess weight loss maintained at 3 year follow up (MD 22.2% [95% CI: 12.7 to 31.7]) (Appendix E, Figure E2). A substantial heterogeneity was noted is this comparison ($I^2 = 92\%$) with a stronger treatment effect noted in Nguyen 2009 study, where patients with higher BMI were included in the study compared Angrisani 2007 who excluded patients with BMI higher than 50. Variations in the surgical technique were also noted between the two studies specifically the length of the Roux limb where it has been shown to have a linear relationship with weight loss[58].

LRYGB also resulted in a significant weight loss when compared to LVBG at 1 year [MD 9.5% (95% CI: 2.8 to 16.3)] (Figure 6), and at 2 years [MD 18.5% (95% CI: 16.3 to 20.7)] with I^2 statistics less than 50% (Appendix E, Figure E1). Open RYGB had significant weight loss when compared to open VBG at 1 year [MD 24.7% (95% CI: 19.7 to 29.8)], in this comparison our meta-analysis indicated no heterogeneity (I^2= 0%) (Figure 6). At 2 years when compared to conventional therapy, LRYGB produced a significantly greater percent excess weight loss [MD 74.6% (95% CI: 61.7 to 87.5)] (Appendix E, Figure E1), but produced less percent excess weight loss when compared to sleeve gastrectomy at 1 year (MD -9.2% [95% CI: -18.3 to -0.3]), and duodenal switch at 1 year (MD -20.4% [95% CI: -26.5 to -14.3]) (Figure 6).

Figure 6: Percent of excess weight loss at 1 year: Gastric Bypass

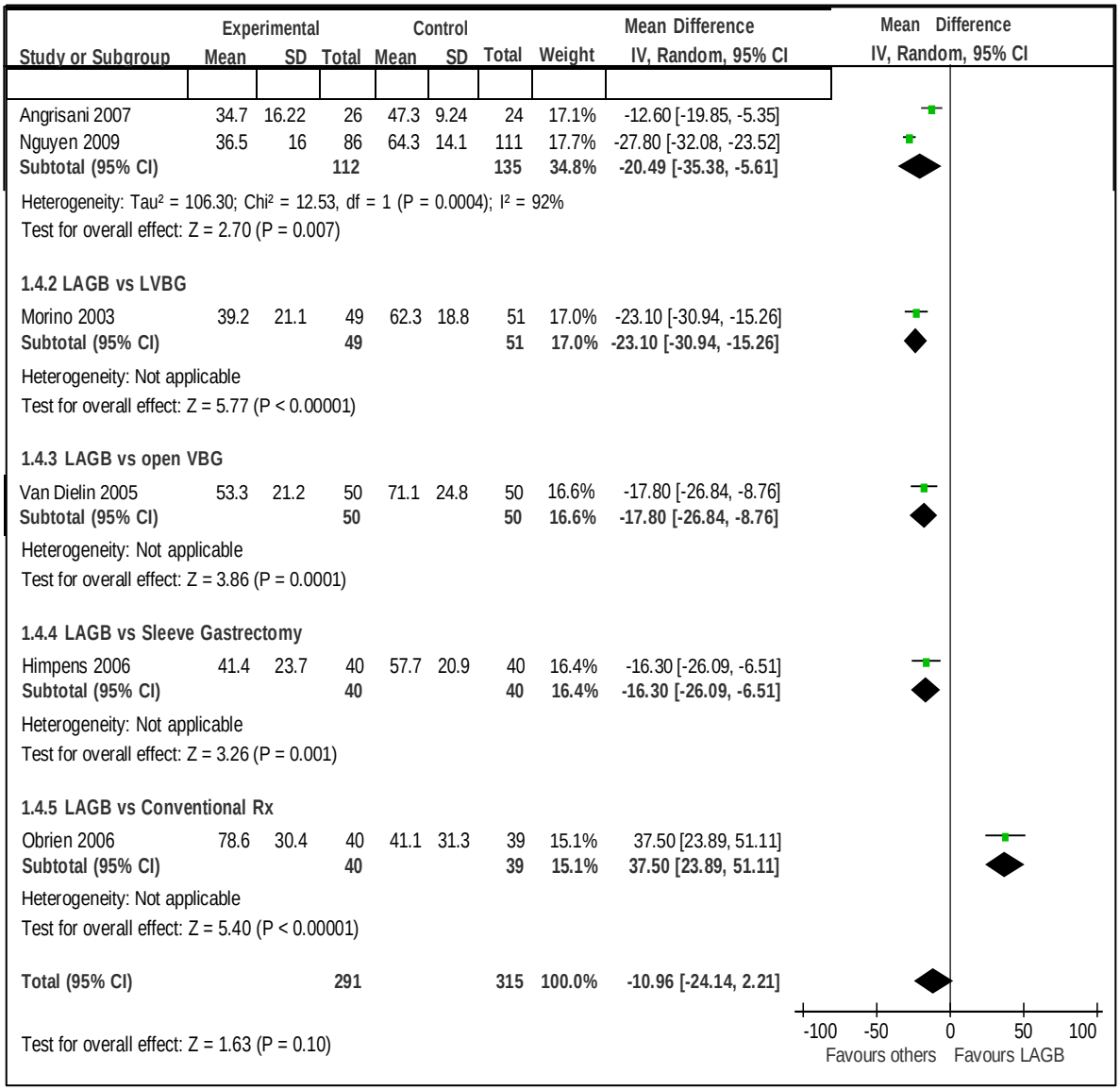


4.1.1 b) Adjustable gastric banding (AGB)

For the % EWL for LAGB there were studies available for the following comparisons: two trials compared LAGB to LRYGB (247 participants)[37, 43]; one trial[59] compared LAGB to LVBG (100 participants) and the longer follow up of the same trial[45], one trial[52] compared LAGB to open VBG (100 participants); one trial[55] of 80 participants compared LAGB to sleeve gastrectomy; and three trials with a total of 189 participants compared LAGB to conventional treatment[39, 41, 42] .

Based on the evidence, LAGB appeared to be inferior to all other surgical procedures in terms of weight loss, and only superior to conventional treatment at 1 year [MD 37.5% (95% CI: 23.9 to 51.1)] (Figure 7), which was maintained and increased at the 2- year follow up [MD 61.7 % (95% CI: 54.6 to 68.8)] (Appendix E, Figure E7) . LAGB produced significantly less %EWL compared to LRYGB (as discussed previously); LVBG at 1 year [MD -23.1 % (95% CI: -30.94 to -15.3)] (Figure 7), and at 3 years [MD -19.1 % (95% CI: -26.7 to -11.6)] (Appendix E, Figure E8), as well as sleeve gastrectomy at 1 year [MD -16.3 % (95% CI: -26.1 to -6.5)] (Figure 7), and at 3 years [MD -18.0 % (95% CI: -28.3 to -7.7)] (Appendix E, Figure E8). LAGB also produced less %EWL compared to open VBG [MD -17.8% (95% CI: -26.8 to -8.8)] at 1 year (Figure 7) and at 2 years [MD -15.2 % (95% CI: -24.8 to -5.6)] (Appendix E, Figure E7).

Figure 7: Percent of excess weight loss at 1 year: Adjustable Gastric Banding



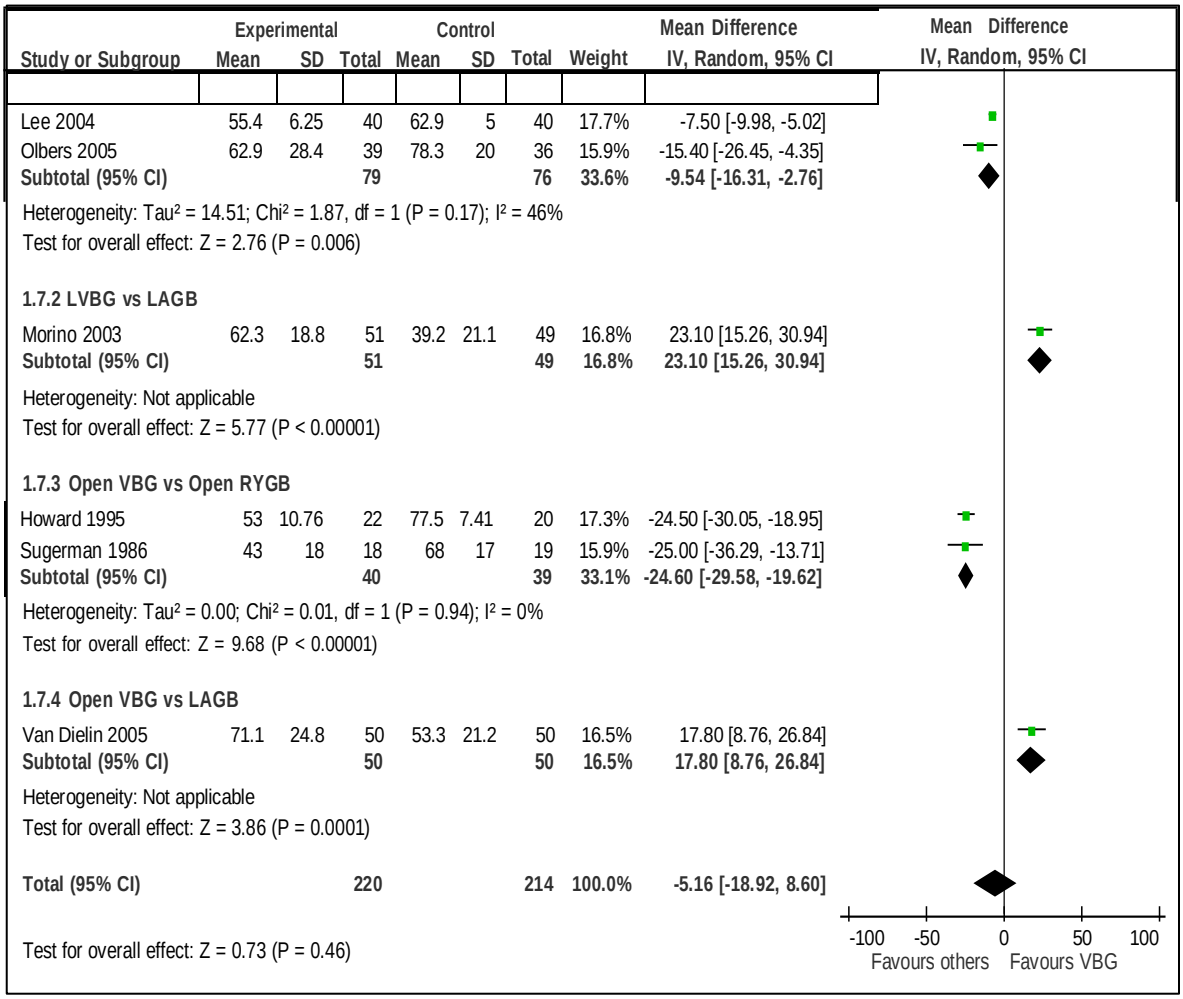
4.1.1 c) Vertical banded gastroplasty (VGB)

Studies comparing % EWL for VGB included: two trials[44, 48] that compared LRYGB to LVBG; one trial[59] with 100 participants comparing LAGB to LVBG, and the more extensive follow up of the same trial[45]**;** two trials[47, 50] compared open VBG to open RYGB (82 participants) ; one trial[52] with 100 participants compared open VBG to LAGB.

Based on the evidence, both LVBG and open VBG were inferior in terms of weight loss when compared to LRYGB and open RYGB at 1 year, [MD -9.5% (95% CI: -16.3 to -

2.8)], and [MD -24.6% (95% CI: -29.6 to -19.6)] respectively (Figure 8), which was maintained at 2 and 3 years(Appendix E, Figure E13 and E14). LVBG and open VBG were superior in terms of weight loss when compared to LAGB at 1 year [MD 23.1% (95% CI: 15.3 to 30.9)], and [MD 17.8% (95% CI: 8.8 to 26.8)] respectively (Figure 8), and the weight loss was maintained at 2 and 3 years follow-up (Appendix E, Figure E13 and E14).

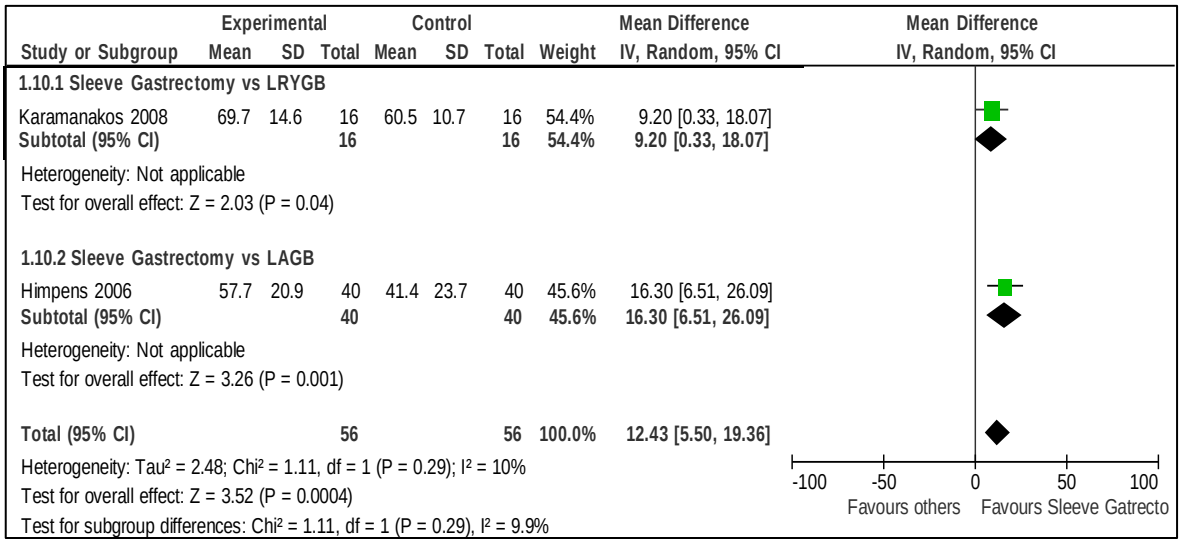
Figure 8: Percent of excess weight loss at 1 year: Vertical banded gastroplasty



4.1.1 d) Sleeve gastrectomy

One trial[53] with 32 participants, compared sleeve gastrectomy to LRYGB for %EWL and one trial[55] with 80 participants compared sleeve gastrectomy to LAGB. Based on the evidence from these studies, sleeve gastrectomy was shown to produce superior weight loss at 1 year when compared to LRYGB [MD 9.2 % (95% CI: 0.33 to 18.1)] and LAGB [MD 16.3% (95% CI: 6.5 to 26.1)] (Figure 9), and the weight loss was maintained at 3 year follow-up (Appendix E, Figure E19).

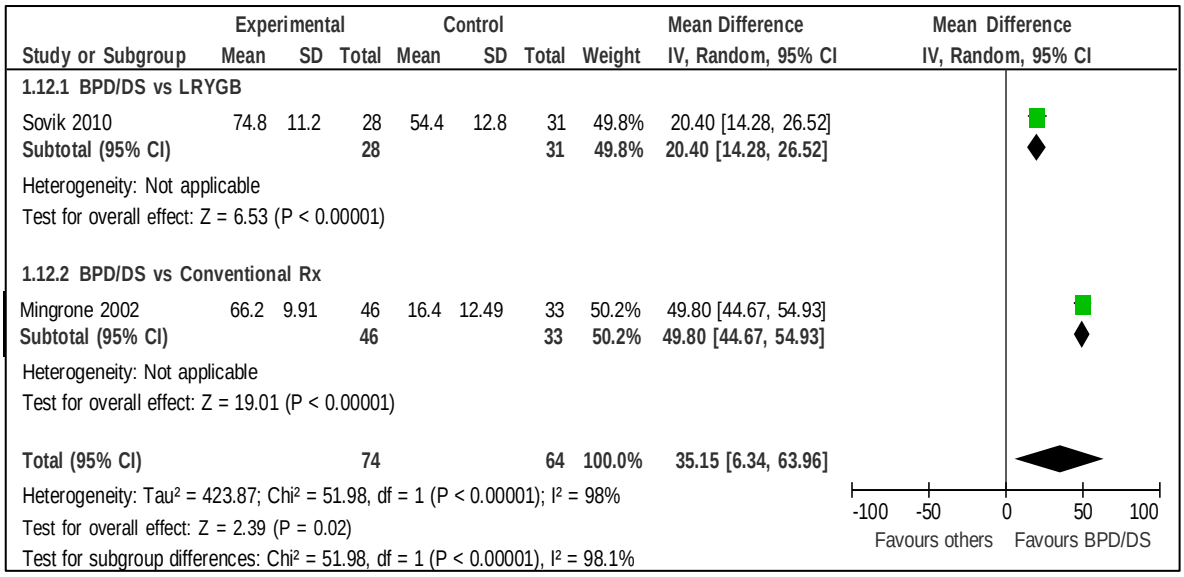
Figure 9: Percent of excess weight loss at 1 year: Sleeve gastrectomy



4.1.1 e) Biliopancreatic diversion with duodenal switch BPD/DS

For % EWL using the BPD/DS procedure, one trial[38] compared BPD/DS to LRYGB and one trial[46] compared BPD/DS to conventional therapy. Based on the evidence at 1 year, BPD/DS produced a significantly superior % EWL compared to LRYGB [MD 20.4% (95% CI: 14.3 to 26.5)] and conventional therapy [MD 49.8% (95% CI: 44.7 to 54.9)] (Figure 10).

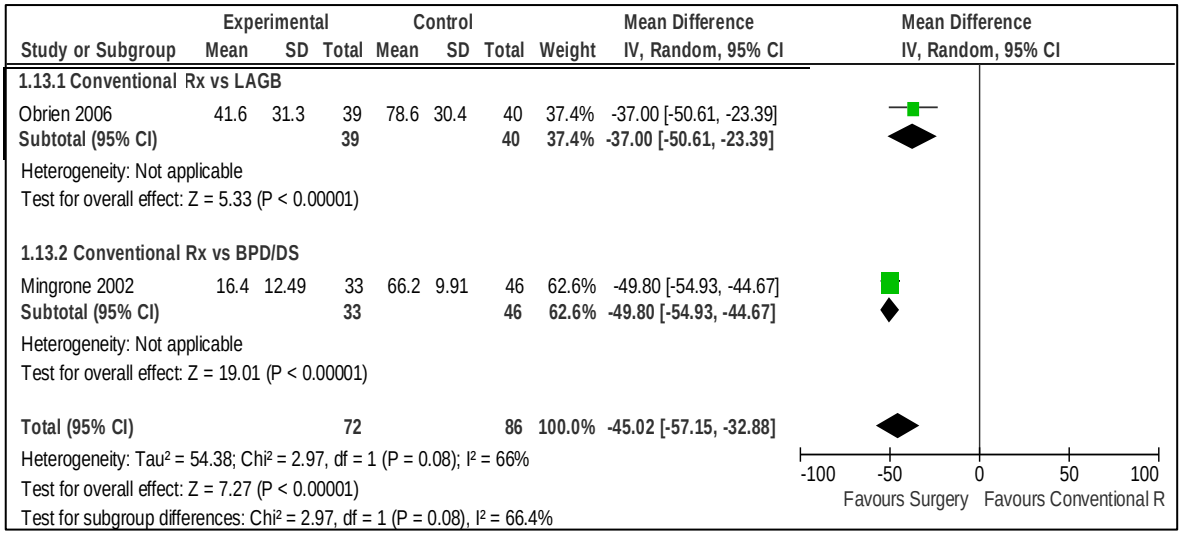
Figure 10: Percent of excess weight loss at 1 year: Biliopancreatic diversion with duodenal switch



4.1.1 f) Conventional therapy

Three trials compared conventional therapy to LAGB based on %EWL[39, 41, 42]. One trial[40] compared conventional therapy to LRYGB and one trial[46] compared conventional therapy to BPD/DS. Based on the evidence in all the comparisons, surgical interventions produced a significantly superior percent excess weight loss compared to conventional therapy (Figure 11) and the result was maintained at 2 year follow-up (Appendix E, Figure E21).

Figure 11: Percent of excess weight loss at 1 Year: Conventional therapy

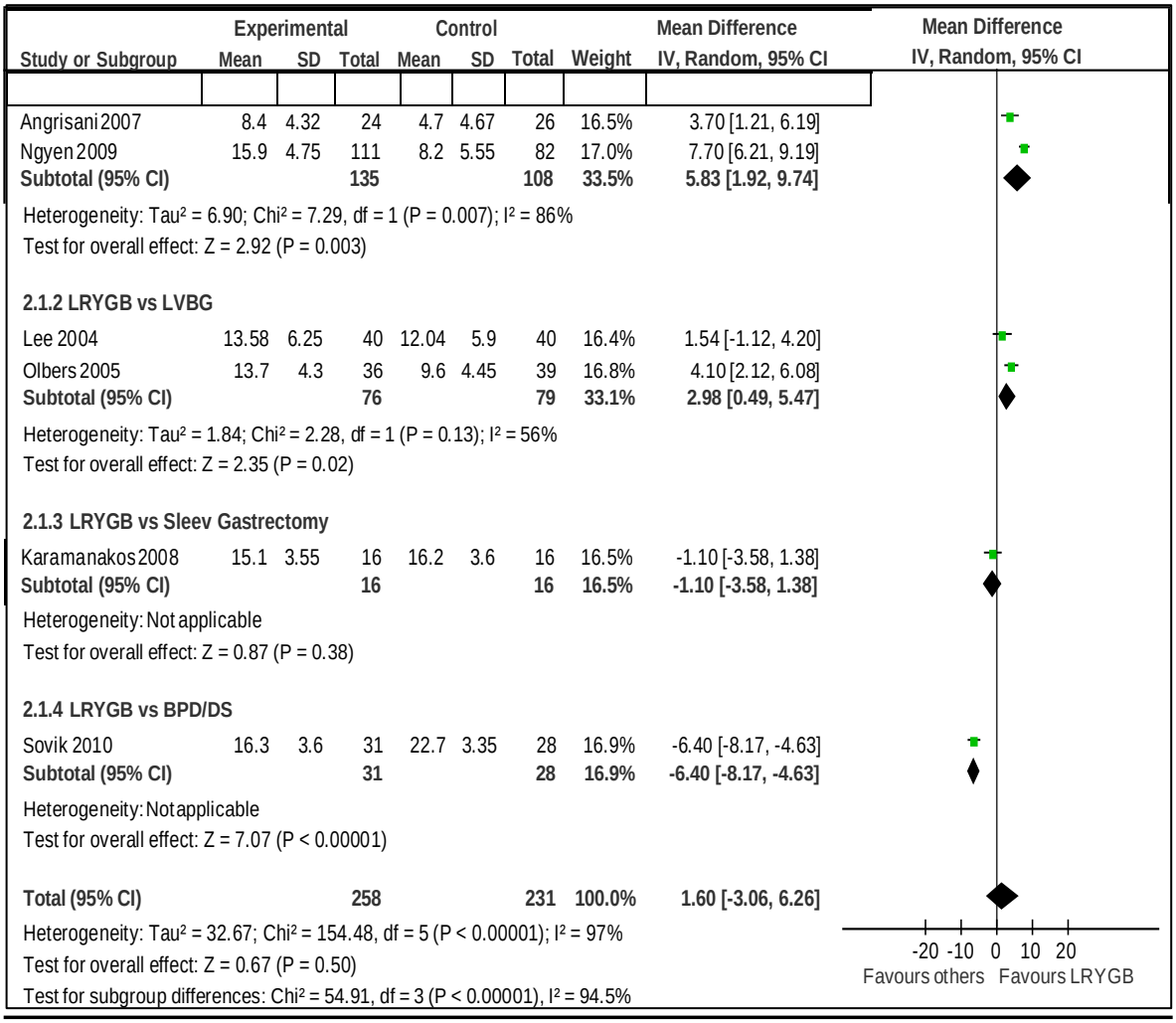


4.1.2 Body mass index (BMI)

4.1.2 a) Gastric bypass (GBP)

LRYGB produced a significantly greater body mass index unit loss compared to LAGB at 1 year [MD 3.7 kg/m² (95% CI: 1.2 to 6.2)] (Figure 12), with the BMI unit losses increased and maintained at the 3-year follow up [MD 7.0 kg/m² (95% CI: 5.6 to 8.3)] (Appendix E, Figure E4). LRYGB compared to conventional therapy produced a significantly greater BMI loss at 2 years [MD 23.0 kg/m² (95% CI: 17.5 to 28.5)] (Appendix E, Figure E3), and also when compared to LVBG at 1 year [MD 3.0 kg/m² (95% CI: 0.5 to 5.5)] (Figure 12) and 2 years [MD 4.7 kg/m² (95% CI: 3.0 to 6.4)] with I^2 statistics of 56% indicating heterogeneity which could be explained by the variation in the surgical technique. (Appendix E, Figure E3). LRYGB produced less BMI unit loss compared to sleeve gastrectomy at 1 year [MD -1.1 kg/m² (95% CI: -3.58 to 1.38)] and when compared to biliopancreatic diversion with duodenal switch at 1 year, the difference was substantial and significant (MD -6.4 kg/m² [95% CI: -8.7 to -4.6]) (Figure 12).

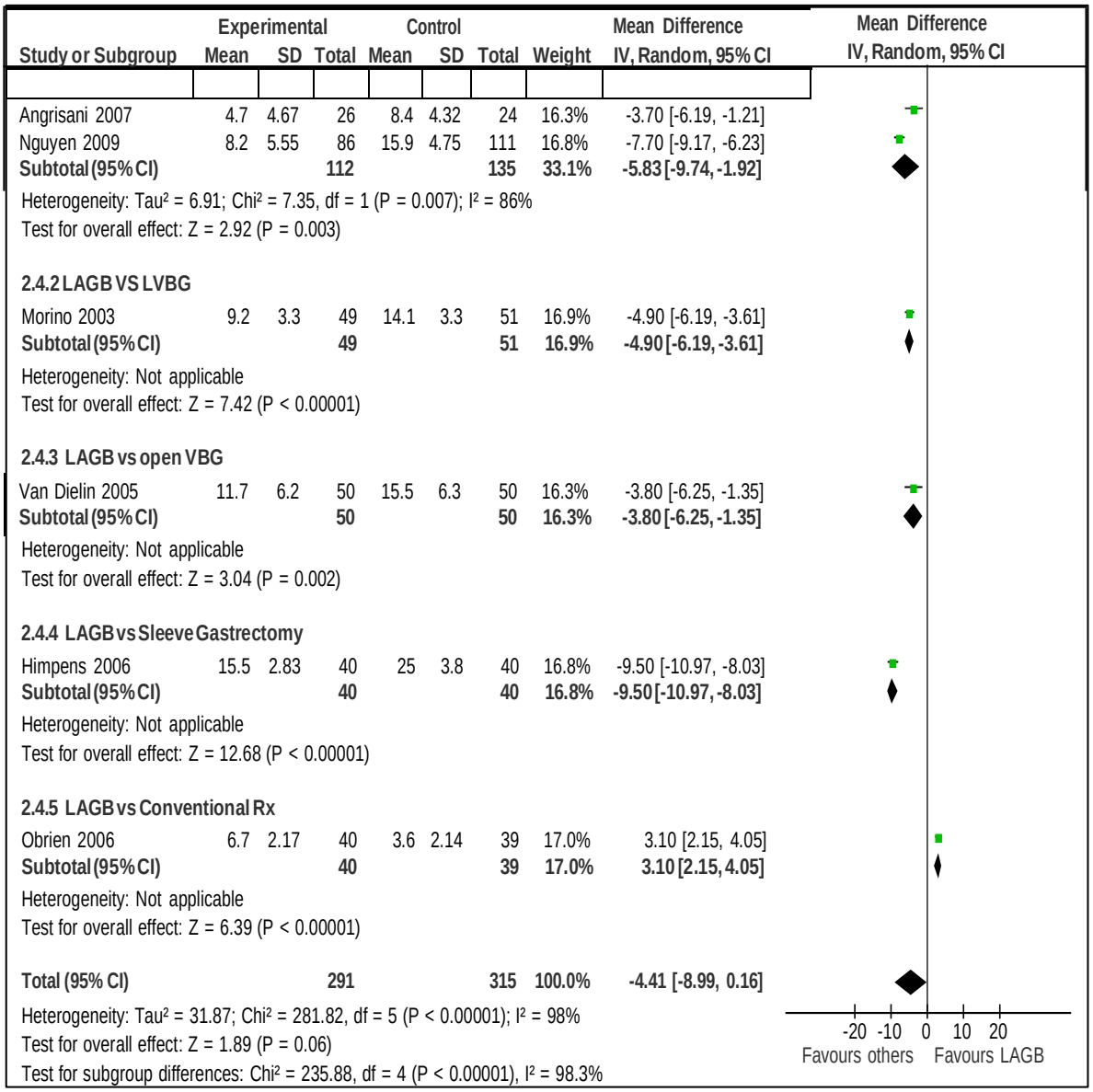
Figure 12: BMI loss at 1 Year: Gastric Bypass



4.1.2 b) Adjustable gastric banding (AGB)

LAGB was only superior in terms of BMI unit loss when compared to conventional treatment at 1 year [MD 3.1 kg/m² (95% CI: 2.2 to 4.1)] (Figure 13). This loss was maintained and the BMI unit loss was increased at the 2-year follow up [MD 7.6 kg/m² (95% CI: 4.9 to 10.2)] (Appendix E, Figure E9). However, LAGB produced significantly less BMI unit loss compared to LVBG at 1 year (MD -4.9 kg/m² [95% CI: -6.2 to -3.6]) (Figure 13) and at 3 years (MD -4.5 kg/m² [95% CI: -5.9 to -3.1]) (Appendix E, Figure E10), as well as compared to open VBG at 1 year [MD -3.8 kg/m² (95% CI: -6.25 to -1.35)] and 2 years [MD -3.5 kg/m² (95% CI: -5.6 to -1.1)] (Appendix E, Figure E9). LAGB produced less BMI unit loss compared to sleeve gastrectomy at 1 year [MD -9.5 kg/m² (95% CI: -11.0 to -8.0)] (Figure 13), which was maintained at the 3 year follow up (Appendix E, Figure E10)

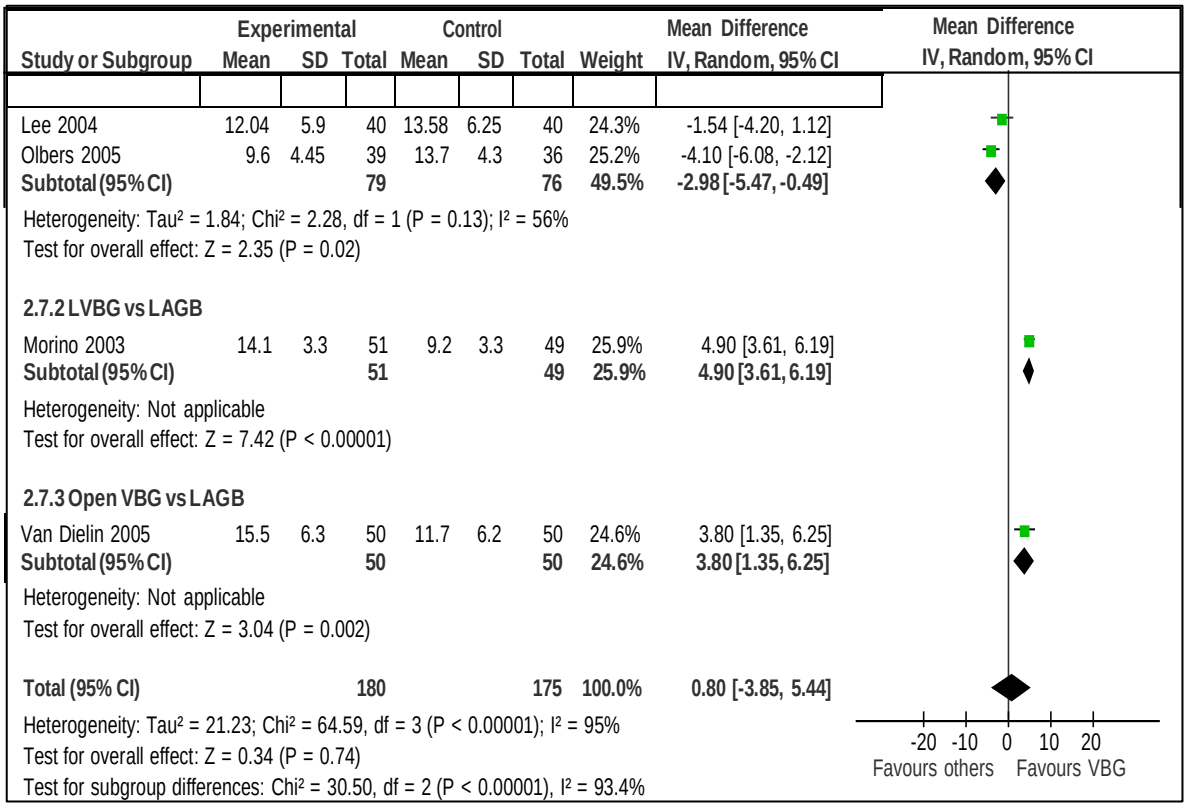
Figure 13: Body mass index loss at 1 year: Adjustable gastric banding



4.1.2 c) Vertical banded gastroplasty (VGB)

Based on the evidence, LVBG produced significantly more BMI unit loss compared to LAGB at 1 year [MD 4.9 kg/m² (95% CI: 3.6 to 6.2)] (Figure 14), as well as open VBG compared to LAGB at 1 year [MD 3.8 kg/m² (95% CI: 1.4 to 6.3)] (Figure 14), with the result maintained at the 2- and 3-year follow up (Appendix E, Figure E15 and E16). LVBG produced significantly less BMI unit loss compared to LRYGB at 1 year [MD -3.0 kg/m² (95% CI: -5.5to -0.5)] (Figure 14), as well as the 2-year follow up (Appendix E, Figure E15).

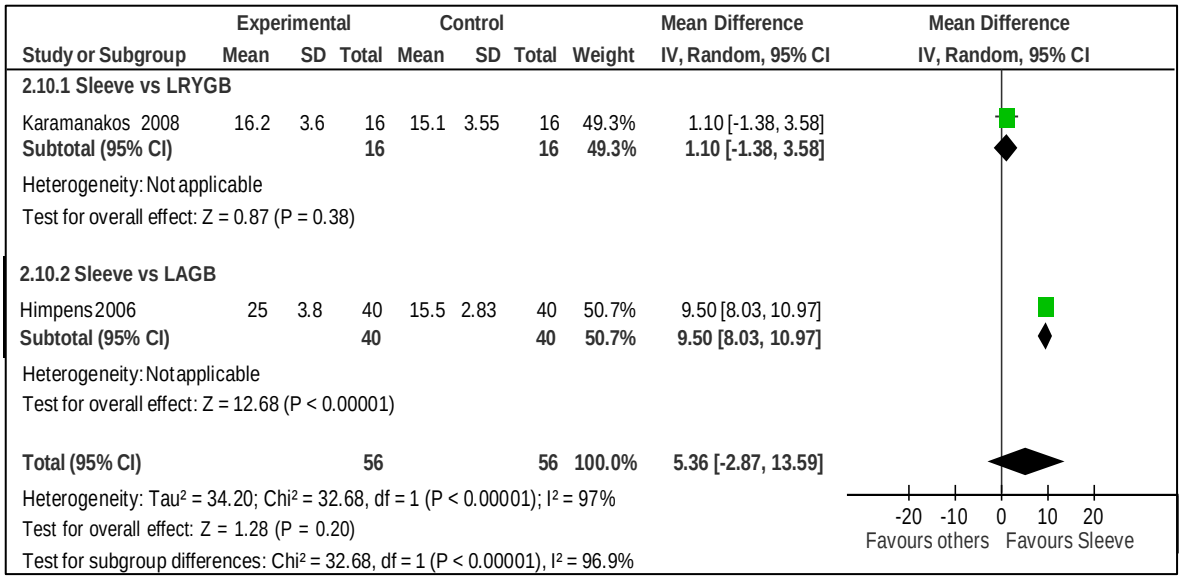
Figure 14: Body mass index loss at 1 year: Vertical banded gastroplasty



4.1. 2 d) Sleeve gastrectomy

Sleeve gastrectomy produced significantly more BMI unit loss compared to LAGB at 1 year [MD 9.5 kg/m² (95% CI: 8.0 to 11.0)] (Figure 15) with the results maintained at the 3-year follow up (Appendix E, Figure E20). When sleeve gastrectomy compared to LRYGB, sleeve gastrectomy produced more but not significantly more BMI unit loss at 1 year [MD 1.1 kg/m² (95% CI: -1.4 to 3.58)] (Figure 15).

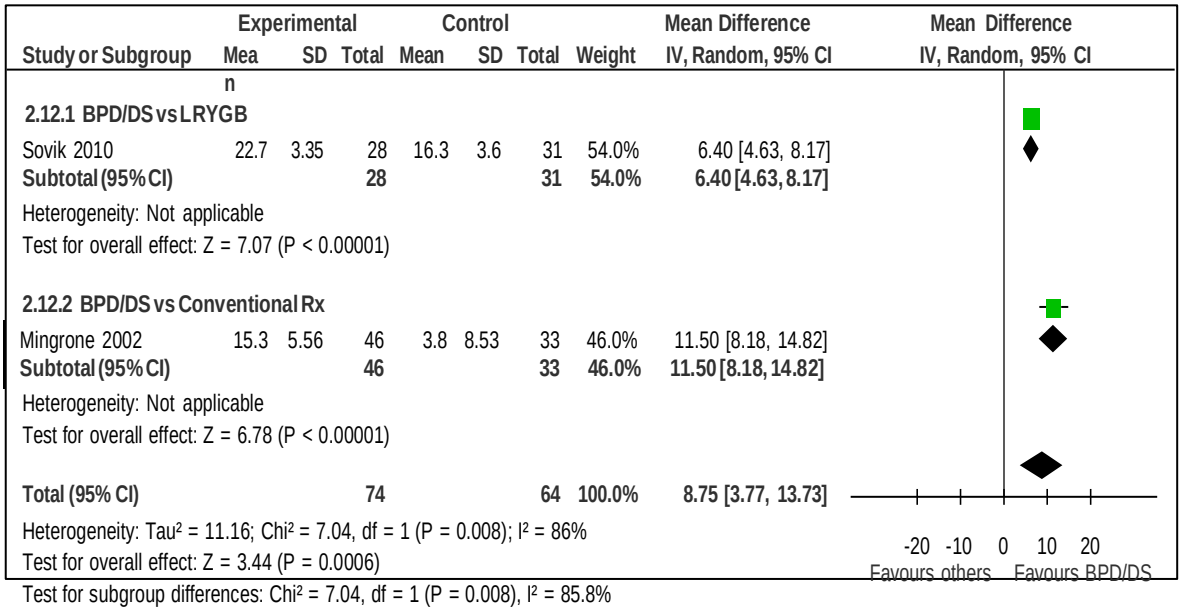
Figure 15: Body mass index loss at 1 year: Sleeve gastrectomy



4.1.2 e) Biliopancreatic diversion with duodenal switch BPD/DS

BPD/DS produced significantly more BMI unit loss compared to LRYGB at 1 year [MD 6.4 kg/m² (95% CI: 4.6 to 8.2)] as well as when compared to conventional therapy at 1 year [MD 11.5 kg/m² (95% CI: 8.2 to 14.8)] (Figure 16).

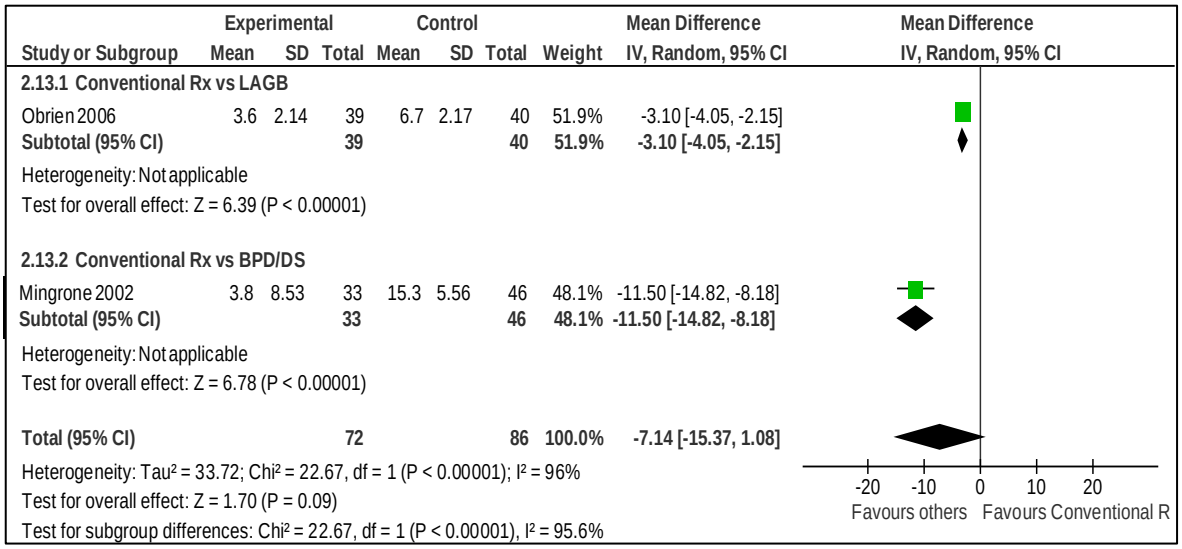
Figure 16: Body mass index loss at 1 year: Biliopancreatic diversion with duodenal switch



4.1.2 f) Conventional therapy

Conventional therapy produced significantly less BMI unit loss compared to surgical interventions. At 3 years, there were significantly less BMI units lost when conventional therapy compared to LAGB [MD -7.5 kg/m² (95% CI: -10.2 to -4.9)], as well as when conventional therapy compared to open RYGB [MD -23.0 kg/m² (95% CI: -28.5 to -17.5)] (Appendix E, Figure E22). Conventional therapy also produced significantly less BMI unit loss when compared to BPD/DS at 1 year (MD -11.5 kg/m² [95% CI: -14.8 to -8.2]) (Figure 17).

Figure 17: Body mass index loss at 1 year: Conventional therapy

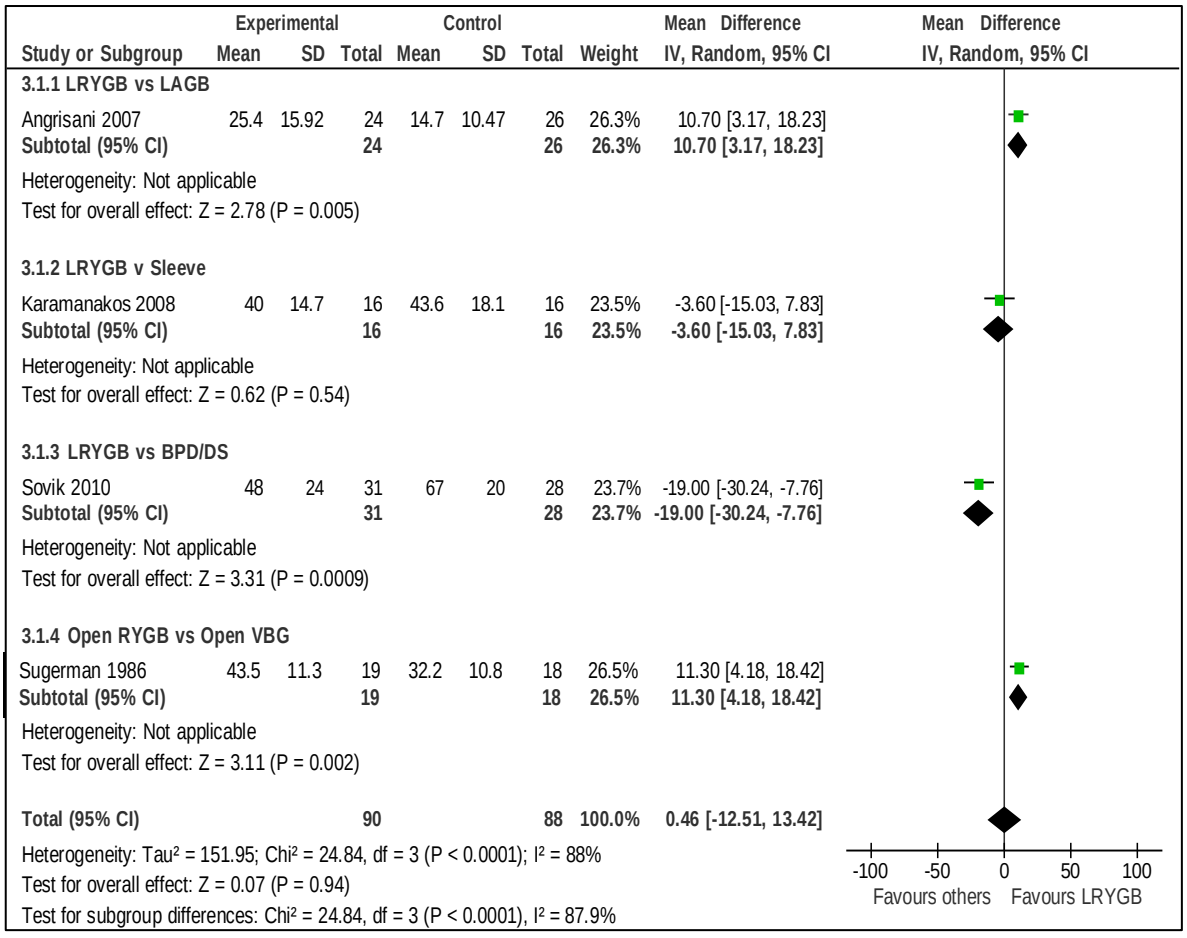


4.1.3 Weight (Kg)

4.1.3 a) Gastric bypass (GBP)

LRYGB produced a significantly greater weight loss when compared to LAGB at 1 year [MD 10.7 Kg (95% CI: 3.17 to 18.2)] (Figure 18), with the weight loss increased and maintained at the 3-year follow up [MD 16.3 Kg (95% CI: 7.8 to 24.8)] (Appendix E, Figure E5). LRYGB compared to conventional therapy produced a significantly greater weight loss at 2 years (MD 69.1 Kg [95% CI: 49.5 to 88.8]) (Appendix E, Figure E5). When open RYGB was compared to open VBG at 1 year a significantly greater weight loss was achieved [MD 11.3 Kg (95% CI: 4.2 to 18.4)](Figure 18). LRYGB produced less weight loss when compared to sleeve gastrectomy at 1 year [MD -3.6 Kg (95% CI: -15.0 to 7.8)] and BPD/DS at 1 year [MD -19.0 Kg (95% CI: -30.2 to -7.8)] (Figure 18).

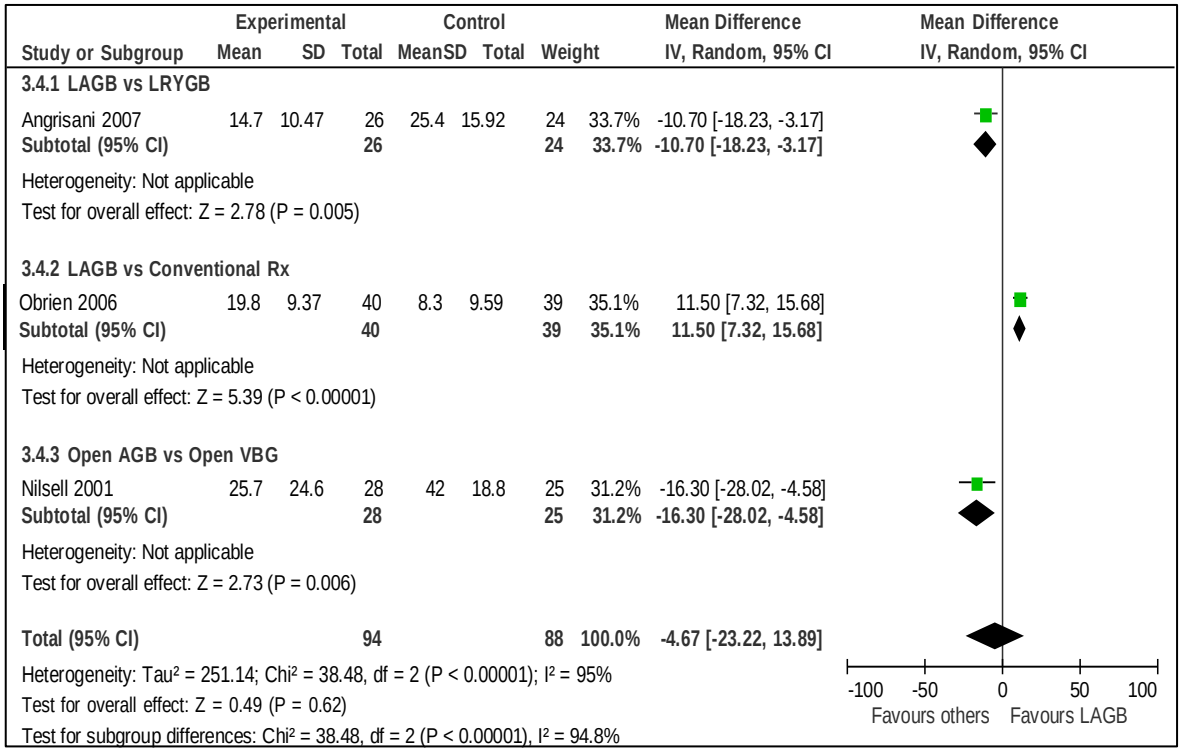
Figure 18: Weight loss (Kg) at 1 year: Gastric bypass



4.1.3 b) Adjustable gastric banding (AGB)

LAGB is only superior in terms of weight loss when compared to conventional treatment at 1 year [MD 11.5 Kg (95% CI: 7.32 to 15.68)] (Figure 19), which was maintained and increased the weight loss at 2 years follow up [MD 22.7 Kg (95% CI: 14.9 to 30.6)] (Appendix E, Figure E11). LAGB produced significantly less weight loss when compared to LRYGB at 1 year [MD -10.7 Kg (95% CI: -18.2 to -3.2)] (Figure 19), with more profound difference at 3 years [MD -16.3 Kg (95% CI: -24.8 to -7.8)] (Appendix E, Figure E12) . Open AGB produced significant less weight loss when compared to open VBG at 1 year [MD -16.3 Kg (95% CI: -28.0 to -4.6)] (Figure 19) and to an even lesser degree at 2 years (MD -2.0 Kg [95% CI: -13.7 to -9.7]) (Appendix E, Figure E11) , but at 3 years open AGB produced greater weight loss than open VBG (MD 8.0 Kg [95% CI: -4.3 to 20.3]) (Appendix E, Figure E12).

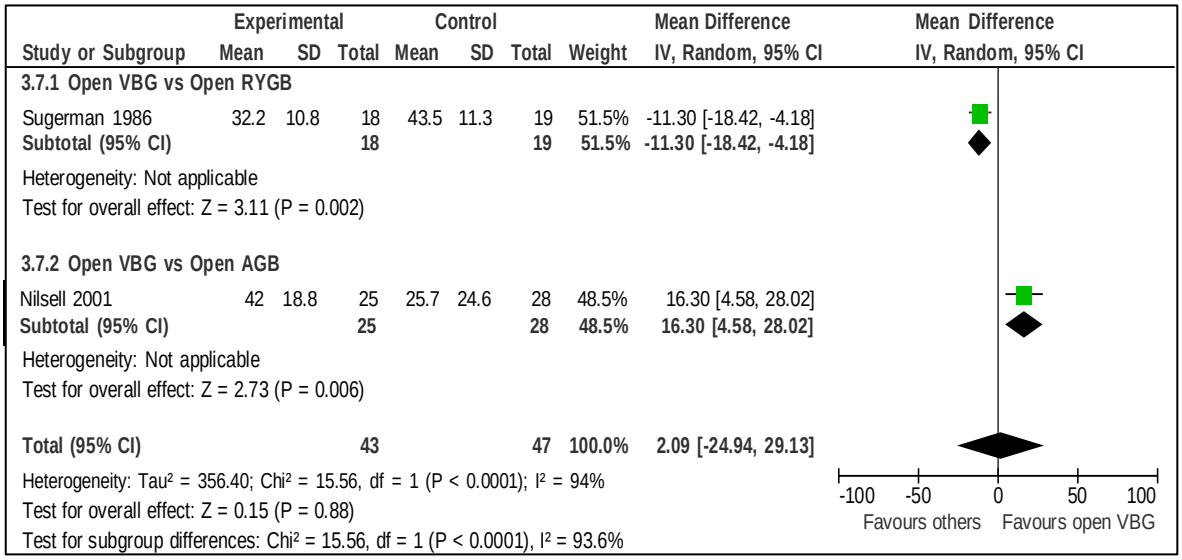
Figure 19: Weight loss (Kg) at 1 year: Adjustable gastric banding



4.1.3 c) Vertical banded gastroplasty (VGB)

When open VBG was compared to open RYGB, less weight loss was achieved in the VBG group at 1 year [MD -11.3 Kg (95% CI: -18.4 to -4.2)] (Figure 20) which was maintained at the 2- and 3-year follow up (Appendix E, Figure E 17 and E18). As previously discussed, open VBG produced more weight loss at 1 and 2 years compared to open AGB (Figure 20 and Appendix E, Figure E17), however, open AGB produced more weight loss at 3 years (Appendix E, Figure E18).

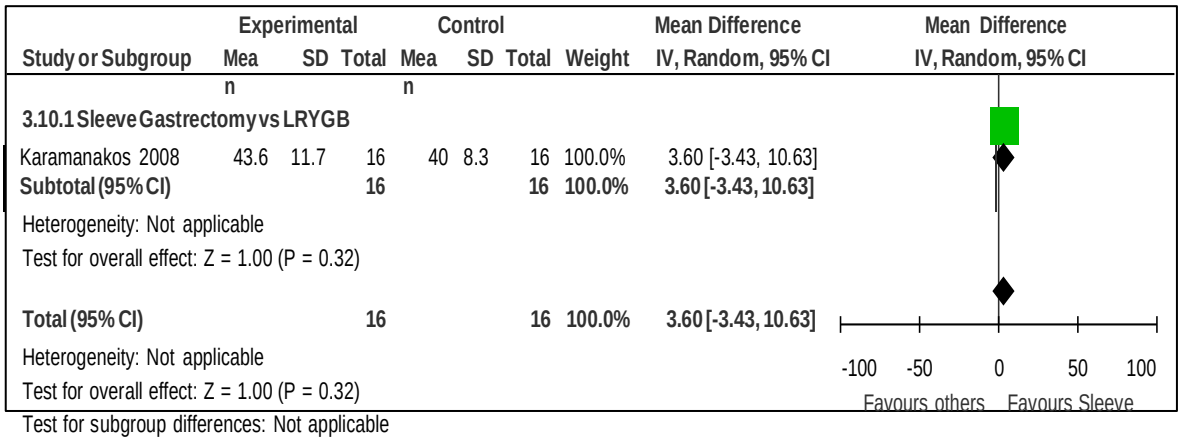
Figure 20: Weight loss (Kg) at 1 year: Vertical banded gastroplasty



4.1.3 d) Sleeve Gastrectomy

Only one trial reported changes in weight (Kg), comparing sleeve gastrectomy to LRYGB, which showed more but not significant weight loss in the sleeve gastrectomy group at 1 year [MD 3.6 Kg (95% CI: -3.4 to 10.6)] (Figure 21).

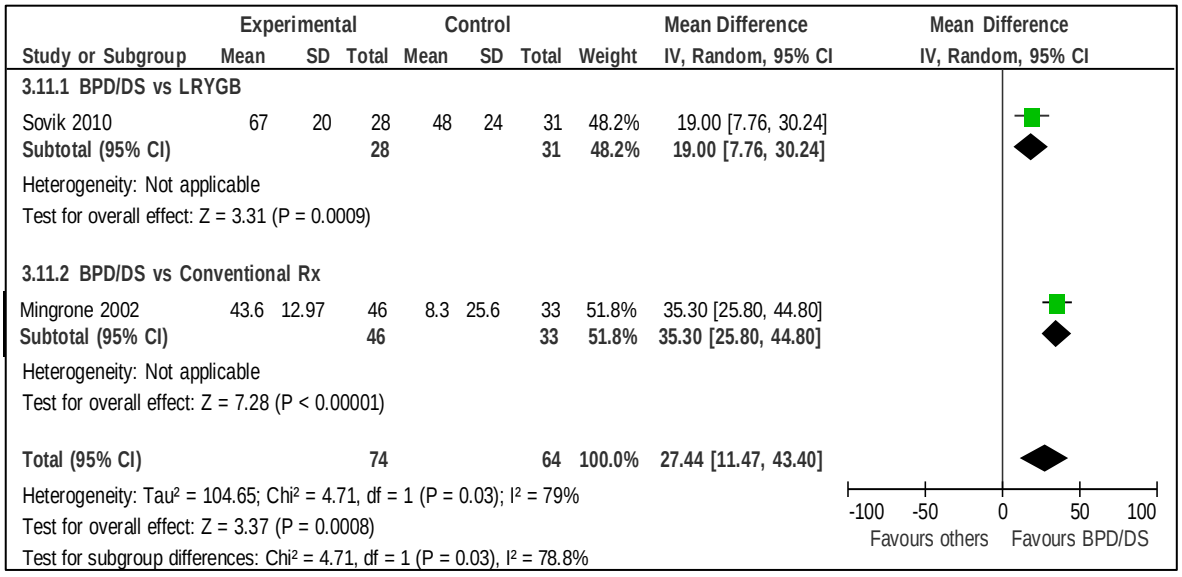
Figure 21: Weight loss (Kg) at 1 year: Sleeve gastrectomy



4.1.3 e) Biliopancreatic diversion with duodenal switch (BPD/DS)

BPD/DS produced significantly more weight loss compared to LRYGB at 1 year [MD 19 Kg (95% CI: 7.8 to 30.2)] and more profound results compared to conventional therapy at 1 year [MD 35 Kg (95% CI: 25.8 to 44.8)] (Figure 22).

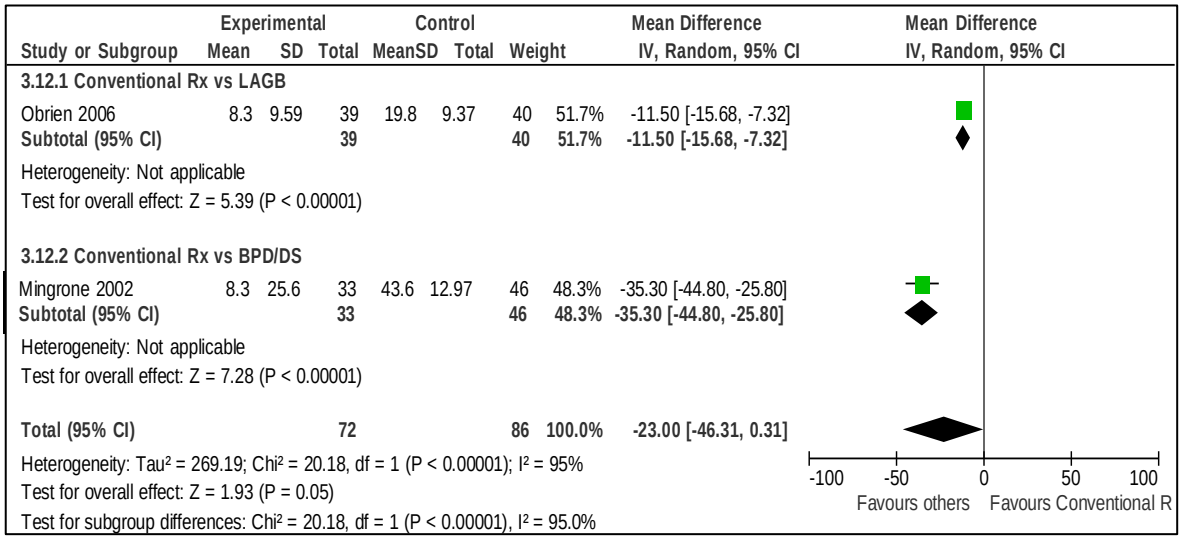
Figure 22: Weight changes (Kg) at 1 year: Biliopancreatic diversion with duodenal switch



4.1.3 f) Conventional Therapy

Conventional therapy produced significantly less weight loss compared to surgical interventions. At 2 years, significantly less weight was lost with conventional therapy compared to LAGB [MD -22.7 Kg [95% CI: -30.6 to -14.9)], as well as when compared to open RYGB [MD -69.1 Kg (95% CI: -88.7 to -49.5)] (Appendix E, Figure E23). Conventional therapy also produced significantly less weight loss compared to BPD/DS at 1 year [MD -35.3 Kg (95% CI: -44.8 to -25.8)] (Figure 23).

Figure 23: Weight loss (Kg) at 1 year: Conventional therapy



4.2 Resolution of comorbidities

4.2.1 Surgical interventions vs non-surgical interventions

Five RCTS[36, 39, 41, 42, 46] (Dixon 2008, O'Brien 2006, O'Brien 2010, Mingrone 2003, Reis 2010) compared surgical to nonsurgical interventions. Four of the five were conducted in adult[36, 41, 42, 46] populations (Dixon 2008, O'Brien 2006, Mingrone 2003, Reis 2010) and one in adolescents[39] (O'Brien 2010). Of the five RCTS: three compared adjustable gastric banding to conventional[39, 41, 42] (Dixon 2008, O'Brien 2006, O'Brien 2010). One trial[36] compared laparoscopic Roux-en-Y gastric bypass (LRYGB) to conventional therapy (Reis 2010) and one RCT[46]compared biliopancreatic diversion and duodenal switch to diet (Mingrone 2003).

Dixon 2008[41] conventional therapy program focused on weight loss by lifestyle modification which was individually structured to reduce energy intake and intake of fat, to encourage intake of high-fiber foods and physical activity to 10,000 steps per day and 200 minutes per week of structured activity.

O'Brien 2006[42] conventional therapy program centred on the use of behavioural modification, very low-calorie diet, and pharmacotherapy as well as education and professional support on appropriate eating and exercise behaviour.

O'Brien 2010[39] conventional therapy program, which was applied to adolescents between 14 and 18 years, focused on reduced energy intake (depending on age and weight status), increased activity (target of 10,000 steps per day on pedometer) with a structured exercise schedule of at least 30 minutes a day and behavioural modification.

Mingrone 2003[46] conventional therapy program was only focused on diet, and patients were assigned to a diet protocol (20 kcal/kg FFM, 55% carbohydrates, 30% fat, and 15% proteins).

Reis 2010[36] conventional program consisted of general multidisciplinary team direction without intensive structured program.

Dixon 2008[41]**,** at 2 years 22/30 (73%) randomized to the surgical program and 4/30 (13%) to the conventional therapy program ($P < 001$) achieved remission of type 2 diabetes. Dixon 2008[41], also reported that greater percentage of weight loss was independently associated with remission of type 2 diabetes (Cox-Snell $R2=0.46$, $P < 001$) (Table 7).

Table 7: Resolution of comorbidites by Dixon 2008[41] at 2 years: LAGB vs conventional therapy

Comorbidities	**Surgical Group**	**Conventional Group**	
Achieved remission of type 2 diabetes	22/30 (73%)	4/30 (13%)	P < 0.001
Not using pharmacotherapy for glycemic control	24/28 (86%)	4/26 (15%)	
Not using Metformin	25/28 (89%)	8/26 (30%) NS	P < 0.001
Not using other oral hypoglycemic agents	8/9 (89%)	1/8 (13%) NS	P = 0.006
Not using insulin	1/1 (100%)	0/3 (0%) NS	P < 0.001
Not using antihypertensive agents	14/20 (70%)	0/15 (0%) NS	P < 0.001
Not using lipid lowering agents	8/12 (67%)	1/8(13%) NS	P = 0.02
HbA1c > 6.2%	4/28 (14%)	20/26 (77%)	

Dixon 2008[41] found that participants in the surgical group had significantly lower mean levels of HbA1c and fasting plasma glucose at 2 years ($P < 001$ for both). At baseline, 93% of the surgical patients and 86% of the conventional group were using pharmacotherapy for glycemic control. At 2 years, the numbers were 13% and 73%, respectively. In the surgical group at 2 years, there were fewer using metformin (10% vs 93%, $P < 001$) , and other hypoglycemic therapy (3% vs 30%, P=.006). There were no significant changes in the use of therapy for diabetes in the conventional group.

The use of antihypertensive agents and lipid lowering agents in the surgical group was significantly reduced throughout the follow up (69% at baseline and 20% at 2 years, $P <$ 001) (41% at baseline and 13% at 2 years, P=.02) respectively. There were no significant changes in the use of antihypertensive agents and lipid lowering agents in the conventional group (Table 7).

O'Brien 2006[42] reported statistically significant differences between the surgical and the medical group in the resolution of metabolic syndrome (93% vs 46%, P= 0.006) respectively at 2 years, compared to 37.5% of patients in each group before treatment. This signified a significant reduction in the proportion of patients with metabolic syndrome during the study period in the surgical group (P < 0.001) but not in the medical group (P = 0.22) (table 8).

Table 8: Resolution of metabolic syndrome at 2 year: LAGB vs conventional therapy

Resolution of metabolic syndrome	Surgical group	Conventional group	Between group difference
O'Brien 2006[42]	14/15 (93%) P < 0.001	7/15 (46%) P = 0.22	P = 0.006
O'Brien 2010[39]	9/9 (100%) P < 0.008	6/10 (60%) P =.12	P = 0.025

O'Brien 2010[39] surgical group had no metabolic syndrome at 2 years compared to 36% at the beginning of the study (P < 0.008), whereas more than 22% of the adolescents who completed the study in nonsurgical still have metabolic syndrome compared to 40% at the start (P = 0.12). The proportion of patients with metabolic syndrome was significantly different between the two groups at 2 years (P = 0.025) (Table 8).

O'Brien 2010[39] surgical group had significant reduction in systolic and diastolic blood pressure P< 0.002 and P < 0.01 respectively, as well as significant reduction in triglycerides level P< 0.001 vs P = 0.12 in the lifestyle group, and improvement in HDL cholesterol levels P< 0.005 vs P = 0.18 in the lifestyle group**.** The improvement of insulin sensitivity in the surgical group was greater than in the lifestyle group (*P*<.001) as well as improvement in the ß cell function

Mingrone 2003[46] and **Reis 2010**[36] did not report on any co-morbidities resolution.

4.2.2 Resolution of comorbidities among different surgical procedures

4.2.2 a) Gastric bypass (GBP) vs adjustable gastric banding (AGB)

There were two RCTs[37, 43] comparing laparoscopic Roux-en-Y gastric bypass (LRYGB) with laparoscopic adjustable gastric banding (LAGB). The overall quality assessment for **Angrisani 2007**[43] is (+), and **Nguyen 2009**[37] is (++), for more details about the quality of the study see appendix D.

Angrisani 2007[43] reported resolution of diabetes, sleep apnea, and hyperlipdemia in all patients who suffered from these co-morbidities prior to entrance into the study. In the LRYGB group, 2 patients had hyperlipidemia, 1 had hypertension, and 1 had type 2 diabetes. In the LAGB group, 3 patients had hypertension and 1 had sleep apnea.

Nguyen 2009[37], did not report on resolution of co-morbidities.

4.2.2 b) Gastric bypass (GBP) vs sleeve gastrectomy (SG)

There were two RCTs[53, 54] comparing laparoscopic Roux-en-Y gastric bypass (LRYGB) with laparoscopic Sleeve gastrectomy (LSG). The overall quality assessment for **Karamanakos 2008**[53] is (++), and **Peterli 2009**[54] is (++),or more details about the quality of the study see appendix D.

Karamanakos 2008[53] reported significant reduction in glucose and triglyceride levels in both groups (LRYGBP, P = 0.03, LSG, P = 0.001) and (LRYGBP, P = 0.04; LSG, P = 0.01) respectively. There were two diabetic patients in the LRYGBP group. By the end of the study, diabetes was resolved completely. No significant reduction in levels of total and LDL cholesterol were found in either group.

Peterli 2009[54] demonstrated a dramatic improvement in glycemic control despite the short term follow up (3 months) in both groups.

4.2.2 c) Adjustable gastric banding (AGB) vs sleeve gstrectomy (SG)

There was one RCT[55] comparing laparoscopic adjustable gastric banding (LAGB) with laparoscopic sleeve gastrectomy (LSG). The overall quality assessment for **Himpens** 2006[55] is (-), For more details about the quality of the study see appendix D.

Himpens 2006[55] reported only on the resolution of gastroesophageal reflux disease (GERD) in 5 out of 6 (83%) patients in the adjustable gastric banding group and in 6 out of 8 (75%) patients in the sleeve gastrectomy group.

4.2.2 d) Gastric bypass (GBP) vs biliopancreatic diversion with duodenal switch (BPD/DS)

There was one RCT[38] comparing laparoscopic Roux-en-Y gastric bypass (LRYGB) with laparoscopic biliopancreatic diversion with duodenal switch (LBPD/DS). The overall quality assessment for **Søvik 2010**[38] was (+), for more details about the quality of the study see appendix D.

Søvik 2010*[38]*, reported comorbidities on patient's baseline characteristics, but did not report on the resolution of comorbidities.

4.2.2 e) Adjustable gastric banding (AGB) vs vertical banded gastroplasty (VBG)

There were 4 RCTs[45, 51, 52, 59] comparing adjustable gastric banding (AGB) with vertical banded gastroplasty (VBG); one RCT[45] is longer follow up of another study[59]. One RCT[59] compared laparoscopic adjustable gastric banding (LAGB) with laparoscopic vertical banded gastroplasty (LVBG); the second RCT[52] compared laparoscopic adjustable gastric banding (LAGB) with open vertical banded gastroplasty (VBG); the third[51] compared open adjustable gastric banding (AGB) with open vertical banded gastroplasty (VBG). The overall quality assessment for **Morino 2003[59]** is (+), **Scozzari** 2009[45] is (+), **Nilsell** 2001[51] is (+), **Van Dielen** 2005[52] is (+). For more details about the quality of the study see appendix D.

Van Dielen 2005[52] reported that all co-morbidities have a tendency to decrease over time in both groups, and that joint problems, pulmonary problems and diabetes showed the greatest improvemen after surgery. 83% of the patients with diabetes were no longer requiring treatment after 1 year. Joint problems had resolved in 68% of patients with these problems and pulmonary problems had resolved in 65% of patients with these co-morbidities preoperatively (Table 9).

Table 9: Resolution of comorbidites by Van Dielen 2005[52]: VBG vs LAGB

Resolved Co-morbidity	VBG	LAGB
No. of patients with co-morbidity	27/42 (65%)	21/39 (53%)
Joint problems	22/29 (75%)	18/28 (64%)
Pulmonary problems	5/8 (63%)	6/9 (67%)
Diabetes mellitus	6/7 (86%)	4/5 (80%)
Hypertension	2/10 (20%)	2/7 (29%)
Cardiovascular problems	1/3 (33%)	0/2 (0%)
Hypercholesterolemia	1/2 (50%)	0/2 (0%)
Reflux disease	2/2 (100%)	3/3 (100%)
Sleep apnea	1/1 (100%)	1/1 (100%)

Morino 2003[59], Scozzari 2009[45], and Nilsell 2001[51] did not report on resolution of co-morbidities.

4.2.2 f) Gastric bypass (GBP) vs vertical banded gastroplasty (VBG)

Five RCTs[44, 47-50] compared Roux-en-Y gastric bypass (RYGB) with vertical banded gastroplasty (VBG) and one RCT was no longer a follow-up of a previous study. Two RCTs compared laparoscopic Roux-en-Y gastric bypass (LRYGB) with laparoscopic vertical banded gastroplasty (LVBG); four RCTs compared open Roux-en-Y gastric bypass (RYGB) with open vertical banded gastroplasty (VBG).The overall quality assessment for **Howard 1995[47]** is (-), **Lee 2004[48]** is (+), **MacLean 1995[49]** is (-), **Olbers 2005[44]** is (+), **Sugerman 1985[50]** is (-). For more details about the quality of the study see appendix D.

Lee 2004[48] reported significant reduction in obesity-related clinical and laboratory abnormalities including blood pressure, blood glucose level, cholesterol level, triglyceride levels, uric acid levels, and liver function test. **Howard 1995**[47]**, MacLean 1995**[49]**, Olbers 2005**[44] **and Sugerman 1985**[50] did not report the resolution of co-morbidities.

4.3 Adverse events (Morbidity and Mortality)

4.3.1 Surgical interventions vs non-surgical interventions

Dixon 2008[41] reported, that of the thirty patients in the LAGB group, one developed superficial wound infection; two patients had gastric pouch enlargement that was treated by laparoscopic revision and replacement of the band; one had eating difficulty and persistent regurgitation despite normal investigation and workup. The band was removed; one patient had postoperative fever which resolved spontaneously; one patient had an episode of minor hypoglycemia; and one patient had intolerance to metformin (Table 10).

Table 10: Adverse events by Dixon 2008: LAGB vs conventional therapy

Adverse Event	Number of Patients (%)
Surgical Group N = 30	
Access port site infection	1 (3%)
Gastric pouch enlargement	2 (6%)
Eating difficulty and persistent regurgitation	1 (3%)
Postoperative fever	1 (3%)
Hypoglycemic episode	1 (3%)
Gastrointestinal intolerance to metformin	1 (3%)
Operative interventions	3 (10%)
Conventional therapy group N = 30	
Gastrointestinal problems	2 (6%)
Persistent diarrhea with metformin	1 (3%)
Vasculitic rash	1 (3%)
Multiple hypoglycemic episodes	1 (3%)
Angina and transient cerebral ischemic episode	1 (3%)
Intolerance to meal replacement	2 (6%)

Of the 30 patients in the conventional group, two had gastrointestinal adverse effects from the medications, one developed diarrhea with metformin, one developed rash with rosiglitzone, both resolved after discontinuing the medication. Other adverse events included multiple hypoglycemic episodes in one patient, one patient developed angina and transient cerebral ischemic episodes, and two patients were intolerant of the meal replacement (Table 10).

O'Brien 2006[42] reported more adverse events in the non-surgical group (58%) than the LAGB group (18%). Of the 39 patients in LAGB group, one developed infection at the 5 mm port site, , four developed prolapse of the posterior gastric wall through the band treated by revision, one patient developed acute cholecystitis treated by elective uncomplicated laparoscopic cholecystectomy . Of the 31 patients in the nonsurgical group, one patient could not tolerate the very low calorie diet, eight patients could not tolerate the oral drug, orlistat, three chose not to use this drug and four patients developed acute cholecystitis which was treated by an elective uncomplicated laparoscopic cholecystectomy (Table 11).

Table 11: Adverse events by O'Brien 2006: LAGB vs conventional therapy

Adverse Events	Number of Patients
Conventional therapy group (n = 25)	
Total events	18 (58%)
Intolerance to very low-calorie diet	1 (3%)
Intolerance to orlistat	8 (26%)
Acute cholecystitis	4 (13%)
(cholecystectomy)	5 (16%)
Loss to follow-up	4 (13%)
Surgical group (n = 25)	
Total events	7 (18%)
5 mm port site infection	1 (2.6%)
Acute cholecystitis	1(2.6%)
Cholecystectomy	4 (10%)
Prolapse, posterior (laparoscopic revision)	1 (4%)
Loss to follow-up	5 (13%)

In O'Brien 2010[39], 12 of the 25 (48%) patients in the surgical group developed complications; all of them occurred more than 30 days after the procedure. Six patients developed proximal pouch dilation, two had needle stick injury to the tubing, all required revisional surgery with either replacement of the band or the access port. One patient developed acute cholecystitis treated by cholecystectomy; one patient required admission for depression that was diagnosed prior to entry into the study and found to be secondary to parental divorce. In the lifestyle group**,** 11 of the 25 (44%) patients developed adverse events. Seven patients withdraw from the study; six of them had gained weight at the time of withdrawal. One patient required multiple hospital admissions and was diagnosed with bipolar disorder and benign intracranial hypertension, and one patient developed acute cholecystitis treated by cholecystectomy (Table 12).

Table 12: Adverse events by O'Brien 2010: LAGB vs conventional therapy

Adverse Events	Number of Patients
Conventional therapy group (n = 25)	
Depression	1 (4%)
Benign intracranial hypertension	1 (4%)
Acute cholecystitis (cholecystectomy)	1 (4%)
Loss to follow-up	7 (28%)
Surgical group (n = 25)	
Proximal gastric enlargement	6 (24%)
Needle stick injury to the tubing	2(8%)
Acute cholecystitis (cholecystectomy)	1 (4%)
Depression	1 (4%)

Mingrone 2003[46] did not report adverse events.

4.3.2 Adverse events of different surgical procedures

4.3.2 a) Gastric bypass (GBP) vs adjustable gastric banding (AGB)

Angrisani 2007[43] classified complications into those occurring early < 30 days, and those occurring late > 30 days. There were no early complications necessitating reoperation in the LAGB group.However, in the LRYGB group, one patient presented with acute abdominal discomfort three days after surgery and required reoperation for jejunal perforation. The patient had a long postoperative stay. One patient had a posterior leak at the gastrojejunal anastomosis discovered intraoperatively and the leak was repaired by interrupted sutures after conversion of the procedure to an open procedure. Late complications in the form of gastric pouch dilation occurred in two patients from the LAGB group which was treated by band removal. One patent in the LRYGB group presented with small bowel obstruction 15 months after the surgery and was diagnosed with an internal hernia requiring small bowel resection**.**

A more extensive report on complications was provided by **Nguyen 2009**[37]. In the gastric bypass group, early complications were as follows: two patients developed postoperative gastrointestinal hemorrhage, one required reoperation by laparoscopy and oversewing of the stable line and the other patient was treated with endoscopy and epinephrine injection. Five patients developed small bowel obstruction. Obstruction was caused by scar at the transverse colon obstructing the Roux limb, obstruction at the jejunojejunostomy, Richter hernia at the port site, obstruction at the gastrojejunostomy, and internal herniation. In the gastric band group, two major early complications developed. One patient developed obstruction requiring replacement of the band and a patient developed renal insufficiency which was managed conservatively.

Nguyen 2009[37], found that late major complications were significantly higher in the gastric bypass group than the band group (26.1% vs. 11.6%, respectively, *P*<0.01). Of the 118 patients in the gastric bypass group, 17 developed anastomotic stricture requiring endoscopic dilation, 2 had internal hernias, 3 had ventral hernias, 2 developed marginal ulcers requiring revision of the anastomosis, 2 had abdominal pain requiring laparoscopy, one had bowel obstruction, one developed peripheral neuropathy, one died due to alcohol/drug abuse. In the gastric banding group, 3 required port revision, 2 patients developed band obstruction requiring removal, 2 had slippage requiring slippage reduction. Two patients had poor weight loss requiring revisional surgery and conversion to a sleeve gastrectomy. One patient developed erosion of the band requiring its removal (Table 13).

Table 13: Adverse events by Nguyen 2009: Gatric bypass vs gastric banding

Complications	**Gastric bypass N = 111**	**Gastric Banding N = 86**	**P value**
Number of patients with complications	50 (45.0%)	15 (17.4%)	P < 0.001
Early complications	24 (21.6%)	6 (7.0%)	P < 0.001
Late complications	43 (38.7%)	10 (11.6%)	P < 0.001
30-day re-admission	6 (5.4%)	0 (0%)	P = 0.04
30-day reoperation	6 (5.4%)	1 (1.2%)	NS
Late reoperation	8 (7.2%)	10 (11.6%)	NS
90 day- mortality	0 (0%)	0 (0%)	NS
1 Year- mortality	1 (0.9%)	0 (0%)	NS

4.3.2 b) Gastric bypass (GBP) vs sleeve gastrectomy (SG)

Karamanakos 2008[53] and Peterli 2009[54] did not report on complications.

4.3.2 c) Adjustable gastric banding (AGB) vs sleeve gastrectomy (SG)

Himpens 2006[55] classified complications into those requiring reoperation and those not requiring reoperation. Out of the 40 patients in the gastric banding group, complications not requiring reoperation at 3 years were shoulder pain in 3 patients (8.5%), frequent vomiting in 10 patients (28.5%), poor choice of alimentation in 17 patients (48.5%) and gastric ulcer in 1 patient. After 3 years, complications following sleeve gastrectomy which did not require reoperations were as follows: frequent vomiting in 5 patients (16.6%), poor choice of alimentation in 8 patients (26.6%), mineral defiance in 3 patients.

Complications requiring reoperation occurred in 9 patients; 3 had gastric pouch dilation treated by band removal in 2 patients and laparoscopic conversion to Roux-en-Y gastric bypass (LRYGBP) in the third patient; 2 patients had insufficient weight loss; one patient had gastric erosion and all three were treated with conversion to Roux-en-Y gastric bypass (RYGBP); 3 patients presented with disconnection of the port and had it reconnected. In the sleeve gastrectomy group, 2 patients had complications requiring reoperation; one patient had intraperitoneal bleeding and was treated with laparoscopy; one patient had ischemia of the sleeve and was treated with laparoscopic total gastrectomy, and 2 patients presented with insufficient weight loss treated with conversion to laparoscopic duodenal switch (DS).

4.3.2 d) Gastric bypass (GBP) VS biliopancreatic diversion with Duodenal switch (BPD/DS)

In the laparoscopic Roux-en-Y gastric bypass (LRYGB), two patients developed leaks from gastrojejunostomy; both required reoperation. In laparoscopic biliopancreatic diversion with duodenal switch (LDS), two patients developed leaks from the duodenal stump; one required reoperation and one was treated conservatively with percutaneous drainage; three patients required late reoperation, one had omental resection secondary to an inflammatory reaction in transverse mesocolon of unknown origin; one patient had laparotomy for

peritonitis ten months after the laparoscopic duodenal switch (LDS) and ascites was the only finding; one patient had laparoscopic bile duct exploration and cholecystectomy for gall stones developed 11 months after the original operation; and two patients developed severe metabolic disturbances (hypoalbuminemia and iron deficiency). There were no statistically significant differences in rate of complications and the rate of reoperation between the two groups.

4.3.2 e) Adjustable gastric banding (AGB) vs vertical banded gastroplasty (VBG)

In the earlier report, **Morino 2003[59],** found no significant statistical difference ($P = 0.754$) in the early postoperative morbidity between the LAGB group (6.1%) and the LVBG group (9.8%). One patient in the LAGB group had band slippage on the seventh postoperative day and was treated with laparoscopic repositioning; one patient had port infection and one had a hematoma at the port site.

In the LVBG group, one patient developed a staple line fistula on the second postoperative day and was treated with conversion to an open gastric bypass: two patients developed prolonged postoperative fever, resolved with non-operative treatment; two patients developed respiratory failure which was resolved with conservative treatment.

Scozzari 2009[45] provided a long term follow-up of the same group up to 7 years and found that the rate of complications at 3 years was 36.7% (18/49) in LAGB vs 15.7% (8/51) in LVBG ($P < 0.05$), and a non-statistically significant difference at 7 years of 55.1% (27/49) vs 47.1% (24/51) respectively. At 7 years in the LAGB group, 22.4% (11/49) developed pouch dilation. One patient had the band replaced, six patients had the band removed, two patients had a conversion to LVBG after the band removal, and two patients achieved a clinical improvement by a complete band desufflation; 12.2% (6/49) developed GERD; three patients improved with medical therapy and band desufflation; two patients had the band removed, and one patient had a conversion to Roux-en-Y gastric bypass (RYGB); 6.1% (3/49) had complete food intolerance(treated with either conversion to vertical banded gastroplasty or gastric bypass); 6.1% (3/49) had poor weight loss or weight increase (treated with either conversion to vertical banded gastroplasty or gastric bypass); 2.0%

(1/49) had band erosion (treated with removal of the band); 2% (1/49) had no compliance (treated with conversion to gastric bypass); and 4.1% (2/49) developed complications of the port.

In the LVBG at seven years, 21.6% (11/51) developed GERD (8 patients were treated with medical therapy and 3 required conversion to Roux-en-Y gastric bypass due to persistent symptoms despite medical therapy); 7.8% (4/51) had a bolus obstruction (all treated with endoscopic removal of the bolus); 5.9% (3/51) developed pouch dilation; 3.9% (2/51) had stenosis at the gastric pouch outlet (treated with endoscopic dilation); 3.9% (2/51) had complete food intolerance; 2.0% (1/51) developed a pouch-to-fundus fistula; and 2.0% (1/51) had a leak. The rate of reoperation at 7 years was 46.9% (23/49) in the LASGB group and 7.8% (4/51) in the LVBG group ($P < 0.001$).

Nilsell 2001[51] reported that 1/30 in LVBG developed anastomotic leak requiring surgery. There were no postoperative deaths or early reoperations in either group. In LAGB, 3/29 (10.3%) had late reoperations; 2/29 (6.8%) had pouch dilation (treated with replacement of the band); 1/29 (3.4%) had the band removed on request; 1/29 (3.4%) had band erosion that had not been operated on prior to publication. In the LVBG group, 10/30 (33.3%) had late reoperations, mainly for stricture of the stoma, intolerance of solid food, and stable line disruption; 4/30 (13.3%) had the band removed; 3/30 (10%) had a gastrogastrostomy done; 1/30 (3.3%) replaced the band with a longer one; and 2/30 (6.6%) had converted to gastric banding.

Van Dielen 2005[52] reported that in the VBG group, 9/50 (18%) patients developed early postoperative complications; two patients had splenectomy secondary to iatrogenic injury; three patients had a leak and sepsis requiring reoperation; two patients developed temporary outlet obstruction treated with endoscopic dilation; three patients developed pneumonia; one patient had urinary tract infection; two patients died, one from sepsis after a leak and one from pneumonia**.**

In the LAGB group, 2/50 (4%), were converted to open procedure due to technical difficulties, 1/50 (2%) had a conversion to gastric bypass due to gastric perforation during retrogastric tunneling. Concerning long term complications, in the VBG group, 18/50 (38%) needed revisional surgery, 15 due to stable line disruption, two patients due to food intolerance, and one patient due to insufficient weight loss. In addition to the 18 patients, eight developed an incisional hernia, six patients had endoscopy for outlet stenosis, and two patients developed peroneal nerve paralysis secondary to rapid weight loss. In the LAGB group, 20/50 (40%) needed revisional surgery, 12 for pouch dilation which was treated with band repositioning in 8 patients, reduction and refixation of the pouch in 3, and 1 patient was treated with replacement of the band; 2 patients for band leakage, 2 for band erosion, and 4 for access port problems.

4.3.2 f) Gastric bypass (GBP) vs vertical banded gastroplasty (VBG)

Howard 1995[47] reported that, as an early complication, only one patient developed wound infection (no report was given to which group this patient belonged). There were no deaths, leaks, pulmonary embolism, or wound dehiscence in either group. For late complications, 25% of patients in the GBP group developed symptomatic ulcer disease, half of these patients required surgical interventions and one of these patients had mesh erosion in addition to symptomatic ulcer disease. Four and five patients in the GBP and the VBG group respectively developed gall stone disease.

Lee 2004[48] found the rate of early postoperative complications to be higher in the GBP group compared to the VBG group (17.8% vs 2.5%, $P<0.05$). One patient in the GBP group had a conversion to open procedure due to retrogastric adhesion; two patients developed anastomotic leak requiring reoperation; one developed intra-abdominal abscess requiring percutaneous drainage and total parenteral nutrition. Four patients developed minor upper gastrointestinal bleeding, sutured nasogastric tube, and minor leaks. All of these patients recovered with conservative management. In the VBG group, one patient developed minor stable line leak as well as wound infection and recovered with conservative management.

The rate of late postoperative complication was higher in the GBP (4/40) group than the VBG (2/40) group (10% vs 5%). Two patients (5%) in the VBG group developed reflux esophagitis and one required revisional surgery. In the GBP group, one patient developed anastomotic stricture requiring endoscopic dilatation, two developed marginal ulcers requiring blood transfusion and one patient developed pyothorax requiring percutaneous drainage.

MacLean 1995[49] found in their early results that the rate of reoperations in the VBG was higher than the GBP group (23/54, 43% vs 12/52, 23%). Reoperation in the VBG group was mainly for stenosis in 11 patients, enlarged orifice in 7 patients, stable line disruption in 2 patients, clinical failure in 2 patients, and abscess in 1 patient. In the GBP group, reoperations occurred for stable line fistula between the gastric pouch and the fundus of the stomach in 12 patients and 7 patients had stomach ulcers.

There were no deaths in either group. At the 6.5 year follow-up, 20 of the 52 patients in the GBP group, and 29 of the 54 in the VBG group had conversions, mostly to isolated gastric bypass.

Olbers 2005[44] reported no conversions to open procedure, and no thrombotic complications in either group. The rate of reoperations did not differ statistically between the two groups (5/37 LRYGB group vs 1/46 in LVBG group)(P = 0.080). The rationale for reoperation and the procedure performed was not provided.

In the LRYGB, three patients had bleeding requiring reoperation; one had a suspected leak (tachycardia, pain and fever and/or requiring exploratory surgery); one patient had stenosis; two patients had minor bleeding (need for postoperative blood transfusion or a fall in hemoglobin more than 3·0 g/dl); one developed intra-abdominal abscess and was treated with antibiotics as an outpatient. In the LVBG group, one patient had a leak, four had minor bleeding, and one patient had a deep infection.

Sugerman 1985[50] reported that out of 20 patients in the VBG group, four patients failed to lose weight; one patient was found to have stable line disruption and the others had intact stable lines. All subsequently converted to RYGBP. One patient was killed by her husband, she had only lost 8% of her excess weight in 2 years. In the RYGBP group, two patients died, one on the fourth postoperative day presumed secondary to arrhythmia, and the second patient died after 13 months. He had had a history of complete heart block with a permanent pacemaker.

At 2 years, the RYGB group had a significantly ($P < 0.05$) lower level of vitamin B12 (286 +/- 149 ng/ml) compared to (461+/- 226 ng/ml) in the VBG group. This improved with patient education to a non-significant difference at 3 years (411 +/- 149 ng/ml) in the VBG and (410 +/-310 ng/ml) in the RYGB group. Three patients in the RYGB group continued to receive B12 injections because of low levels.

Five patients in RYGB group had intractable vomiting and were found to have stomal stenosis. They were treated with endoscopic dilation. One patient was diagnosed with marginal ulcer and responded well to medical therapy. In the VBG group one patient developed stomal erosions which responded well to medical therapy.

5.0 Discussion

5.1 Summary of main results

5.1.1 Weight loss

Bariatric surgery was more effective than conventional therapy for weight loss. The effectiveness of bariatric procedures varied across the procedures, where malabsorptive procedures such as biliopancreatic diversion had the greatest weight loss results. Second to BPD was sleeve gastrectomy. Malabsorptive and restrictive procedures such as Roux-en-Y gastric bypass resulted in intermediate weight loss and restrictive procedures such as AGB and VBG caused the least amount of weight loss.

5.1.2 Resolution of co-morbidities

Bariatric surgery participants had greater improvement in obesity-related comorbidities compared to participants in the conventional therapy program. One trial[41], compared LAGB to conventional therapy in type 2 diabetic patients and found a higher remission rate in the surgical group (73% vs 13% $P < 0.001$). In addition, patients in this study discontinued antihypertensive medications (70% vs 0% $P < 0.001$) and lipid lowering agents (67% vs 13% $P = 0.02$). Similar findings were reported by two other trials[39, 42] compared LAGB to conventional therapy and found more patients with resolution of metabolic syndrome following bariatric surgery (93% vs 46% $P = 0.006$) and (100% vs 60% $P < 0.025$) respectively. One trial[43] compared LRYGB to LAGB and reported resolution of diabetes, sleep apnea, and hyperlipidemia in all patients who suffered from these co-morbidities prior to entrance into the study. **Himpens 2006[55]** compared sleeve gastrectomy to LAGB and found resolution of gastroesophageal reflux disease (GERD) in more than 75% of participants following surgery. **Karamanakos 2008[53]** compared LSG to LRYGB and found significant reduction in glucose and triglyceride levels in both groups following surgery, as well as resolution of diabetes in all participants in the LRYGB group. **Van Dielen 2005[52]** compared LAGB to open VBG and found that all co-morbidities had a tendency to decrease over time in both groups. Joint and pulmonary problems as well as diabetes showed the greatest improvement in co-morbidities after surgery. **Lee 2004[48]**

compared LRYGB to LVBG and found significant reduction in obesity-related clinical and laboratory abnormalities including blood pressure, blood glucose level, cholesterol level, triglyceride levels, uric acid levels, and liver function test.

5.1.3 Adverse events

5.1.3 a) Gastric bypass

GBP was associated with more early complications when compared to AGB and to a lesser degree when compared to VBG. However, GBP has led to fewer reoperations and late complications when compared to AGB or VBG.

5.1.3 b) Adjustable gastric banding

AGB was associated with increased risk of procedure-specific complications, which included band slippage and pouch dilation. This subsequently led to more reoperations such as conversion to other types of bariatric surgery procedures or procedure reversal.

5.1.3 c) Sleeve gastrectomy

Laparoscopic sleeve gastrectomy had generally fewer complications not requiring reoperation as well as complications that required reoperation compared to laparoscopic adjustable gastric banding.

5.1.3 d) Biliopancreatic diversion with duodenal switch (BPD/DS)

Biliopancreatic diversion with duodenal switch (BPD/DS) led to more but not significantly more numbers of perioperative complications as well as late complications and readmission compared to RYGB.

5.1.3 e) Vertical banded gastroplasty

VBG with longer follow-up was associated with increased risk of reoperations because of clinical failure or complications such as stable line disruption, GERD, stricture of the stoma, and intolerance to solid food.

5.1.3 f) Conventional therapy

More participants in the conventional group withdrew from the study and most of them had gained weight prior to withdrawal. The adverse events of conventional therapy were mainly intolerance to diet program to side effects to the prescribed medications such as rash, diarrhea, or hypoglycemic episodes secondary to metformin. More participants in the conventional group developed acute cholecystitis and required cholecystectomy. Two participants developed rare but serious side effects, angina and transient cerebral ischemic episode in one, and bipolar disorder and benign intracranial hypertension in the second.

5.2 Concordance with the current evidence

This review is in an agreement with other reports from observational studies as well as systematic reviews and meta-analysis.

In 2004, Sjo̊ stro̊ m et. al.[60] published a land mark cohort study in the New England Journal of Medicine with a total of 4047 participants, of these 2010 underwent bariatric surgery (gastric banding, vertical banded gastroplasty, or gastric bypass) and contemporaneously matched obese participants treated conventionally and all followed for 10 years, found that weight has increased in the conventional treated group by 1.6 %, where weight has decrease in the surgical group by 16.1%. Recovery from obesity related comorbidites such as hypertension, diabetes, hypertriglyceridemia, and hyperuricemia was more frequent in the surgical group than in the conventional group, both at 2 and 10 years.

Foley et. al[61] reported resolution of preoperative hypertension in 66% of patients following gastric restrictive procedures, and the amount of weight loss significantly predicted the reduction of hypertension.

A systematic review and meta-analysis that included observational studies to evaluate the impact of bariatric surgery on type 2 diabetes and found to have dramatic impact where 78.1% of the participants in the surgical group had complete resolution of type 2 diabetes and 86.6% had their diabetes improved or resolved, as well as similar result in term of

weight loss, where biliopancreatic diversion/duodenal switch had the greatest weight loss followed by gastric bypass, and least for banding procedures[62].

Greenburg et al[63] published a systematic review and meta-analysis on 342 patients who underwent various bariatric surgery procedures, and concluded that bariatric surgery significantly reduces the apnea hypopnea index. However, the patients will likely need continued treatment for OSA, as the mean apnea hypopnea index after surgical weight loss was consistent with moderately severe OSA. To our knowledge this is the only report in disagreement with our review.

Christou et al demonstrated that bariatric surgery resulted in significant risk reductions for developing cardiovascular, cancer, endocrine, infectious, psychiatric, and mental disorders in 1035 patients compared with 5746 controls with a 5-year follow-up, as well as reduction of the relative risk of death by 89% (95% CI, 73%-96%)[64].

In terms of safety, Morino et al[65] retrospectively analyzed 13,871 patients submitted to bariatric surgery (adjustable gastric banding, vertical banded gastroplasty, gastric bypass, and biliopancreatic diversion) and concluded that Mortality after bariatric surgery is a rare event, with overall 60 days mortality risk of 0.25%, and that mortality after bariatric surgery is influenced by different risk factors including type of surgery, prolonged operative time, comorbidities, and volume of cases performed in each center.

Trends in mortality up to 2 years after bariatric surgery was investigated by Buchwald et al[66] through a systematic review and meta-analysis of 85,048 patients and found that, the early and late mortality rates after bariatric surgery are low and can be subjected to risk stratification. The overall ≤30-day mortality for bariatric surgery was 0.28%, and the ≥30 day to 2-year mortality for the bariatric surgery was 0.35%. Mortality varied across the surgical procedures, where adjustable gastric band had the lowest mortality and biliopancreatic diversion with duodenal switch had the highest mortality rates. Subgroup analysis showed that super obese (BMI≥50), males, presence of comorbidities, and elderly have higher mortality risk after bariatric surgery.

5.3 Limitations

Although the nature of obesity required a long term follow-up to evaluate efficacy and safety, most trials only provided short term follow-up (median follow-up was 2 years) and trials which provided a longer follow-up had high dropout rates.

Published trials did not provide enough detail to adequately assess the risk of bias, which consequently remains uncertain. Inadequate allocation concealment can lead to an overestimation of the treatment effect[67], and adequate allocation concealment is crucial to avoid selection bias in controlled trials. Only 3 trials reported adequate concealment, which is considered a low risk of selection bias.

Some variance measures necessary for meta-analysis were missing from a few trials, and this is considered a limitation to this review, as not all the data were available.
Some procedures were assessed in only two trials such as sleeve gastrectomy and biliopancreatic diversion, and some trials did not report on safety at all.

Although most trials reported weight changes in a standardized way i.e. %EWL, changes in BMI, changes in weight, different definitions were used for other outcomes such as complications.

The data in general was statically homogenous, we encountered heterogeneity in two occasions where Roux-en-Y gastric bypass was part of the comparison. The difference in the effect estimate could be explained by the variation in the length of the Roux limb which is known to affect the degree of weight loss.

The surgical techniques in bariatric surgery have evolved, although most bariatric surgery done today uses laparoscopic techniques. Some of the trials included in this review used the open approach. Similarly, VBG is almost never done now, but was included in this review as it forms one arm in some comparisons.

5.4 Conclusion

Bariatric surgery was more effective than conventional therapy i.e. diet, exercise, and life style modifications for the treatment of obesity. Weight loss associated with bariatric surgery led to improvement and remission of co-morbidities such as type 2 diabetes, hypertension, hypercholesterolemia, as well as significant reduction in the use of hypoglycemic agents, antihypertensive agents, and lipid lowering agents.

Weight loss varied across the procedures, where biliopancreatic diversion with duodenal switch achieved the greatest weight loss, followed by sleeve gastrectomy, gastric bypass, followed by vertical banded gastroplasty, and finally adjustable gastric band achieved the least weight loss.

Bariatric surgery was associated with possible adverse events, which varied across the spectrum of procedures. However, the trials were not adequately powered to address the adverse events. Procedures such adjustable gastric banding and vertical banded gastroplasty were associated with higher risk of reoperations and/or conversion to other bariatric procedures. Gastric bypass and biliopancreatic diversion has led to more early complications when compared to other procedures.

There was not enough evidence to evaluate the efficacy and safety of bariatric surgery in adolescents as there was only one randomized control trial done in this age group.

Reference List

1. World Health Organization World health statistics annual 1995. *World Health Orgnization*(1996).

2. Hofbauer K G. Molecular pathways to obesity. *International Journal of Obesity* **26**, S18-S27 (2002).

3. Ravussin,E. & Gautier,J.F. Metabolic predictors of weight gain. *Int. J Obes Relat Metab Disord.* **23 Suppl 1**, 37-41 (1999).

4. Stice,E., Presnell,K., Shaw,H., & Rohde,P. Psychological and behavioral risk factors for obesity onset in adolescent girls: a prospective study. *J Consult Clin Psychol.* **73**, 195-202 (2005).

5. Hazuda,H.P., Haffner,S.M., Stern,M.P., & Eifler,C.W. Effects of acculturation and socioeconomic status on obesity and diabetes in Mexican Americans. The San Antonio Heart Study. *Am. J Epidemiol.* **128**, 1289-1301 (1988).

6. World Health Organization. *Overweight and obesity*. Factsheet no.311. *World HealthOrganization*(2011).

7. Avenell,A. *et al.* What are the long-term benefits of weight reducing diets in adults? A systematic review of randomized controlled trials. *J Hum. Nutr. Diet.* **17**, 317-335 (2004).

8. Avenell,A. *et al.* What interventions should we add to weight reducing diets in adults with obesity? A systematic review of randomized controlled trials of adding drug therapy, exercise, behaviour therapy or combinations of these interventions. *J Hum. Nutr. Diet.* **17**, 293-316 (2004).

9. National Institutes of Health Consensus Development Panel. Gastrointestinal surgery for severe obesity. *Ann Intern Med* **115**, 961 (1991).

10. World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser.* **854**, 1-452 (1995).

11. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* **894**, 1-253 (2000).

12. National Center for Chronic Disease Prevention and Health Promotion **Healthy weight - it**'s **not a diet it**'s **a lifestyle**. *Division of Nutrition,Physical Activity,and Obesity*,(2011).

13. Deitel,M. Overweight and obesity worldwide now estimated to involve 1.7 billion people. *Obes Surg* **13**, 329-330 (2003).

14. Lobstein T International Comparisons of Obesity Trends, Determinants and Responses. Evidence Review. *Foresight Tackling Obesities:* **Future Choices Vol. 2007, issue http://www.foresight.gov.uk.**, (2007).

15. Katzmarzyk,P.T. & Mason,C. Prevalence of class I, II and III obesity in Canada. *CMAJ.* **174**, 156-157 (2006).

16. Ogden,C.L. *et al.* Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* **295**, 1549-1555 (2006).

17. Hedley,A.A. *et al.* Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. *JAMA* **291**, 2847-2850 (2004).

18. Tjepkema M *Measured Obesity. Adult obesity in Canada: Measured height and weight. Statistics Canada* **Cat. No. 82-620-MWE2005001**, (2012).

19. Shields,M. *Measured Obesity. Overweight Canadian children and adolescents. Statistics Canada* **Cat. No. 82-620-MWE2005001**, (2012).

20. Must,A. *et al.* The disease burden associated with overweight and obesity. *JAMA* **282**, 1523-1529 (1999).

21. World Health Organization . *World Health Report 2002.* **Available at: http://www.iotf.org. Accessed January 13, 2004.**, (2004).

22. Fontaine,K.R., Redden,D.T., Wang,C., Westfall,A.O., & Allison,D.B. Years of life lost due to obesity. *JAMA* **289**, 187-193 (2003).

23. National institutes for health consensus Gastrointestinal surgery for severe obesity. *American Journal of Clinical Nutrition.* **55(supplement 5)**, S615-S619 (1992).

24. Buchwald,H. & Oien,D.M. Metabolic/bariatric surgery Worldwide 2008. *Obes Surg* **19**, 1605-1611 (2009).

25. Mason,E.E. & Ito,C. Gastric bypass in obesity. *Surg Clin North Am.* **47**, 1345-1351 (1967).

26. Wilkinson,L.H. & Peloso,O.A. Gastric (reservoir) reduction for morbid obesity. *Arch. Surg* **116**, 602-605 (1981).

27. Kuzmak,L.I. A simple technique to reverse stapling gastric restriction operations. *Curr. Surg* **44**, 462-466 (1987).

28. Scopinaro,N., Gianetta,E., Civalleri,D., Bonalumi,U., & Bachi,V. Bilio-pancreatic bypass for obesity: II. Initial experience in man. *Br. J Surg* **66**, 618-620 (1979).

29. Hess,D.S. & Hess,D.W. Biliopancreatic diversion with a duodenal switch. *Obes Surg* **8**, 267-282 (1998).

30. Gomez,C.A. Gastroplasty in morbid obesity: a progress report. *World J Surg* **5**, 823-828 (1981).

31. Mason,E.E. Vertical banded gastroplasty for obesity. *Arch. Surg* **117**, 701-706 (1982).

32. Sign 50. A guideline developer's handbook. *Scottish Intercollegiate Guidelines Network*(2011).

33. Higgins JPT,A.D. Chapter 8 : Assessing risk of bias in included studies . *Cochrane Handbook for Systematic Reviews of Interventions*(2012).

34. The Nordic Cochrane Centre **RevMan 2011** Review Manager (RevMan). 5.1. *The Cochrane Collaboration*(2011).

35. Higgins,J.P., Thompson,S.G., Deeks,J.J., & Altman,D.G. Measuring inconsistency in meta-analyses. *BMJ* **327**, 557-560 (2003).

36. Reis,L.O. *et al.* Erectile dysfunction and hormonal imbalance in morbidly obese male is reversed after gastric bypass surgery: a prospective randomized controlled trial. *International Journal of Andrology.* **33**, 736-744 (2001).

37. Nguyen,N.T., Slone,J.A., Nguyen,X.M.T., Hartman,J.S., & Hoyt,D.B. A prospective randomized trial of laparoscopic gastric bypass versus laparoscopic adjustable gastric banding for the treatment of morbid obesity: Outcomes, quality of life, and costs. *Annals of Surgery.* **250**, 631-639 (2009).

38. Sovik,T.T. *et al.* Randomized clinical trial of laparoscopic gastric bypass versus laparoscopic duodenal switch for superobesity. *British Journal of Surgery.* **97**, 160-166 (2010).

39. O'Brien,P.E. *et al.* Laparoscopic adjustable gastric banding in severely obese adolescents: a randomized trial. *JAMA.* **303**, 519-526 (2010).

40. Reis,L.O. *et al.* Erectile dysfunction and hormonal imbalance in morbidly obese male is reversed after gastric bypass surgery: a prospective randomized controlled trial. *International Journal of Andrology.* **33**, 736-744 (2001).

41. Dixon,J.B. *et al.* Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *JAMA.* **299**, 316-323 (2008).

42. O'Brien,P.E. *et al.* Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program: A randomized trial. *Annals of Internal Medicine.* **144**, 625-633 (2006).

43. Angrisani,L., Lorenzo,M., & Borrelli,V. Laparoscopic adjustable gastric banding versus Roux-en-Y gastric bypass: 5-year results of a prospective randomized trial. *Surgery for Obesity & Related Diseases.* **3**, 127-132 (2007).

44. Olbers,T., Fagevik,O., Maleckas,A., & nroth,H. Randomized clinical trial of laparoscopic Roux-en-Y gastric bypass versus laparoscopic vertical banded gastroplasty for obesity. *British Journal of Surgery.* **92**, 557-562 (2005).

45. Scozzari,G., Farinella,E., Bonnet,G., Toppino,M., & Morino,M. Laparoscopic adjustable silicone gastric banding vs laparoscopic vertical banded gastroplasty in morbidly obese patients: long-term results of a prospective randomized controlled clinical trial. *Obesity Surgery.*(2008).

46. Mingrone,G. *et al.* Sex hormone-binding globulin levels and cardiovascular risk factors in morbidly obese subjects before and after weight reduction induced by diet or malabsorptive surgery. *Atherosclerosis.* **161**, 455-462 (2002).

47. Howard,L. *et al.* Gastric bypass and vertical banded gastroplasty - A prospective randomized comparison and 5-year follow-up. *Obesity Surgery.* **5**, 55-60 (1995).

48. Lee,W.J., Huang,M.T., Yu,P.J., Wang,W., & Chen,T.C. Laparoscopic vertical banded gastroplasty and laparoscopic gastric bypass: a comparison. *Obesity Surgery.* **14**, 626-634 (2004).

49. MacLean,L.D., Rhode,B.M., Forse,R.A., & Nohr,C. Surgery for obesity - An update of a randomized trial. *Obesity Surgery.* **5**, 145-153 (1995).

50. Sugerman,H.J., Starkey,J.V., & Birkenhauer,R. A randomized prospective trial of gastric bypass versus vertical banded gastroplasty for morbid obesity and their effects on sweets versus non-sweets eaters. *Annals of Surgery.*(1987).

51. Nilsell,K., rne,A., stedt,S., Apelman,J., & Pettersson,N. Prospective randomised comparison of adjustable gastric banding and vertical banded

gastroplasty for morbid obesity. *European Journal of Surgery.* **167**, 504-509 (2001).

52. van,D., Soeters,P.B., de,B., & Greve,J.W. Laparoscopic adjustable gastric banding versus open vertical banded gastroplasty: a prospective randomized trial. *Obesity Surgery.* **15**, 1292-1298 (2005).

53. Karamanakos,S.N., Vagenas,K., Kalfarentzos,F., & Alexandrides,T.K. Weight loss, appetite suppression, and changes in fasting and postprandial ghrelin and peptide-YY levels after Roux-en-Y gastric bypass and sleeve gastrectomy: a prospective, double blind study. *Annals of Surgery.* **247**, 401-407 (2008).

54. Peterli,R. *et al.* Improvement in glucose metabolism after bariatric surgery: comparison of laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy: a prospective randomized trial. *Annals of Surgery.* **250**, 234-241 (2009).

55. Himpens,J., Dapri,G., & re,G.B. A prospective randomized study between laparoscopic gastric banding and laparoscopic isolated sleeve gastrectomy: results after 1 and 3 years. *Obesity Surgery.* **16**, 1450-1456 (2006).

56. Olbers,T., Fagevik,O., Maleckas,A., & nroth,H. Randomized clinical trial of laparoscopic Roux-en-Y gastric bypass versus laparoscopic vertical banded gastroplasty for obesity. *British Journal of Surgery.* **92**, 557-562 (2005).

57. Reinhold,R.B. Critical analysis of long term weight loss following gastric bypass. *Surg Gynecol. Obstet.* **155**, 385-394 (1982).

58. Lee,S., Sahagian,K.G., & Schriver,J.P. Relationship between varying Roux limb lengths and weight loss in gastric bypass. *Curr. Surg* **63**, 259-263 (2006).

59. Morino,M., Toppino,M., Bonnet,G., & del,G. Laparoscopic adjustable silicone gastric banding versus vertical banded gastroplasty in morbidly obese patients: a prospective randomized controlled clinical trial. *Annals of Surgery.* **238**, 835-841 (2003).

60. Sjostrom,L. *et al.* Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N. Engl. J Med* **351**, 2683-2693 (2004).

61. Foley,E.F., Benotti,P.N., Borlase,B.C., Hollingshead,J., & Blackburn,G.L. Impact of gastric restrictive surgery on hypertension in the morbidly obese. *Am. J Surg* **163**, 294-297 (1992).

62. Buchwald,H. *et al.* Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. *Am. J Med* **122**, 248-256 (2009).

63. Greenburg,D.L., Lettieri,C.J., & Eliasson,A.H. Effects of surgical weight loss on measures of obstructive sleep apnea: a meta-analysis. *Am. J Med* **122**, 535-542 (2009).

64. Christou,N.V. *et al.* Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients. *Ann Surg* **240**, 416-423 (2004).

65. Morino,M. *et al.* Mortality after bariatric surgery: analysis of 13,871 morbidly obese patients from a national registry. *Ann Surg* **246**, 1002-1007 (2007).

66. Buchwald,H., Estok,R., Fahrbach,K., Banel,D., & Sledge,I. Trends in mortality in bariatric surgery: a systematic review and meta-analysis. *Surgery* **142**, 621-632 (2007).

67. Schulz,K.F., Chalmers,I., Hayes,R.J., & Altman,D.G. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* **273**, 408-412 (1995).

68. Bhandari,M. *et al.* Association between industry funding and statistically significant pro-industry findings in medical and surgical randomized trials. *CMAJ.* **170**, 477-480 (2004).

Appendix A

Search strategy

Database: EMBASE Classic+EMBASE <1947 to 2010 December 08>

Search Strategy:

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1 exp obesity/ (190374)

2 (obese or obesity).tw. (152446)

3 (overweight or over weight).tw. (30802)

4 weight reduction/ (61831)

5 (weight loss or weight reduc$).tw. (57607)

6 or/1-5 (285628)

7 *bariatric surgery/ (2756)

8 (bariatric adj5 (surg$ or procedure$)).tw. (5150)

9 ((anti?obesity or antiobesity) adj2 (surg$ or operat$)).tw. (25)

10 (obesity adj5 (surg$ or operat$)).tw. (4173)

11 gastroenterostomy/ (3686)

12 Roux Y anastomosis/ (4329)

13 exp gastrectomy/ (38408)

14 biliopancreatic bypass/ or gastric banding/ (3191)

15 ("gastric bypass" or "gastric surgery" or "restrictive surgery" or "restrictive procedure").tw. (6750)

16 ((jejuno?ileal or jejunoileal) adj bypass).tw. (892)

17 (gastrointestinal adj (surg$ or diversion$)).tw. (1625)

18 ((biliopancreatic or bilio?pancreatic) adj (diversion or bypass)).tw. (644)

19 ((gastric or silicon) adj band$).tw. (2195)

20 gastrectom$.tw. (22496)

21 gastroplast$.tw. (1801)

22 surgical stapling/ and stomach/ (29)

23 stomach stapl$.tw. (11)

24 lap band$.tw. (248)

25 "Roux-en-Y".tw. (4881)

26 (malabsorptive adj (surg$ or procedure$)).tw. (122)

27 mason$ procedure.tw. (17)

28 duodenal switch$.tw. (371)

29 (lagb or rygb or lrygb).tw. (1059)

30 or/7-29 (63157)

31 random$.tw. (637061)

32 placebo$.tw. (162964)

33 double-blind$.mp. (157496)

34 clinical trial$.tw. (195686)

35 Randomized controlled trial/ (288550)

36 Randomization/ (53339)

37 or/31-36 (942937)

38 6 and 30 and 37 (814)

39 (animal$ not human$).sh,hw. (3503311)

40 38 not 39 (793)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1950 to Present>

Search Strategy:

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1 exp obesity/ (106278)

2 (obese or obesity).af. (157899)

3 Overweight/ (5806)

4 (overweight or over weight).tw. (24669)

5 Weight Loss/ (17972)

6 (weight loss or weight reduc$).tw. (45703)

7 or/1-6 (198196)

8 exp Bariatric Surgery/ (9957)

9 (bariatric adj5 (surg$ or procedure$)).tw. (4040)

10 exp Obesity/su [Surgery] (7162)

11 ((anti?obesity or antiobesity) adj2 (surg$ or operat$)).tw. (19)

12 (obesity adj5 (surg$ or operat$)).tw. (3407)

13 exp Gastroenterostomy/ or Anastomosis, Roux-en-Y/ or Gastrectomy/ or Biliopancreatic Diversion/ (29163)

14 ("gastric bypass" or "gastric surgery" or "restrictive surgery" or "restrictive procedure").tw. (5384)

15 ((jejuno?ileal or jejunoileal) adj bypass).tw. (763)
16 (gastrointestinal adj (surg$ or diversion$)).tw. (1306)
17 ((biliopancreatic or bilio?pancreatic) adj (diversion or bypass)).tw. (551)
18 ((gastric or silicon) adj band$).tw. (1779)
19 gastrectom$.tw. (14419)
20 gastroplast$.tw. (1434)
21 stomach stapl$.tw. (9)
22 lap band$.tw. (206)
23 "Roux-en-Y".tw. (4174)
24 (malabsorptive adj (surg$ or procedure$)).tw. (87)
25 mason$ procedure.tw. (15)
26 duodenal switch$.tw. (305)
27 (lagb or rygb or lrygb).tw. (865)
28 or/8-27 (48005)
29 7 and 28 (12295)
30 randomized controlled trial.pt. (307412)
31 controlled clinical trial.pt. (83514)
32 randomi?ed.ab. (264127)
33 placebo.ab. (128653)
34 clinical trials as topic.sh. (153235)
35 randomly.ab. (163273)
36 trial.ti. (95162)
37 or/30-36 (746254)
38 exp animals/ not humans.sh. (3604888)
39 37 not 38 (692168)
40 29 and 39 (732)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <4th Quarter 2010>

Search Strategy:

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1 exp obesity/ (4725)
2 (obese or obesity).af. (7434)
3 Overweight/ (562)
4 (overweight or over weight).tw. (2174)
5 Weight Loss/ (2096)
6 (weight loss or weight reduc$).tw. (4233)
7 or/1-6 (9929)
8 exp Bariatric Surgery/ (321)
9 (bariatric adj5 (surg$ or procedure$)).tw. (111)

10 exp Obesity/su [Surgery] (241)
11 ((anti?obesity or antiobesity) adj2 (surg$ or operat$)).tw. (0)
12 (obesity adj5 (surg$ or operat$)).tw. (113)
13 exp Gastroenterostomy/ or Anastomosis, Roux-en-Y/ or Gastrectomy/ or Biliopancreatic Diversion/ (698)
14 ("gastric bypass" or "gastric surgery" or "restrictive surgery" or "restrictive procedure").tw. (284)
15 ((jejuno?ileal or jejunoileal) adj bypass).tw. (39)
16 (gastrointestinal adj (surg$ or diversion$)).tw. (153)
17 ((biliopancreatic or bilio?pancreatic) adj (diversion or bypass)).tw. (16)
18 ((gastric or silicon) adj band$).tw. (89)
19 gastrectom$.tw. (598)
20 gastroplast$.tw. (83)
21 stomach stapl$.tw. (0)
22 lap band$.tw. (17)
23 "Roux-en-Y".tw. (166)
24 (malabsorptive adj (surg$ or procedure$)).tw. (2)
25 mason$ procedure.tw. (1)
26 duodenal switch$.tw. (6)
27 (lagb or rygb or lrygb).tw. (34)
28 or/8-27 (1571)
29 7 and 28 (481)

Appendix B: Data Extraction and Quality Assessment Forms

B1: Data Extraction Form

Reviewer initials:

Reference (Ref ID, Author, Year, Source, Publication status):

Trial Characteristics

Study design	
Sponsor	
Countries (where was study conducted)	
No. of centres	
Study period	
Inclusion & exclusion criteria	
Study duration	

Patient Characteristics

Outcome Measure	**Group 1**	**Group 2**
# of patients		
Mean age (SD)		
% female		
Other demographics of interest (leave blank space to capture different possible items)		

Outcomes

Outcome Measure	**Group 1**	**Group 2**
# of patients		
# analyzed		
Estimated weight loss (EWL)		
BMI		
Weight		

Appendix B2: Sign 50 checklist

SIGN	**Methodology Checklist 2: Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Guideline topic:	Key Question No:

Before completing this checklist, consider:

1. Is the paper a **randomized controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

Checklist completed by:

Section 1: Internal validity

In a well conducted RCT study…		***In this study this criterion is:***	
1.1	The study addresses an appropriate and clearly focused question.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	The assignment of subjects to treatment groups is randomised	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	An adequate concealment method is used	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	The treatment and control groups are similar at the start of the trial	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.6	The only difference between groups is the treatment under investigation	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?		
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise bias? *Code ++, +, or −*		
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?		

2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	**Notes.** Summarise the author's conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.	

The following section is provided for non-SIGN users of this checklist and is being developed to conform to the standards set by the Guidelines International Network Evidence Tables Working Group.

Members of SIGN guideline groups do not need to complete this section.

SECTION 3: DESCRIPTION OF THE STUDY PLEASE PRINT CLEARLY		
3.1	*Do we know who the study was funded by?*	□ Academic Institution □ Healthcare Industry □ Government □ NGO □ Public funds □ Other
3.2	*How many centres are patients recruited from?*	
3.3	*From which countries are patients selected? (Select all those involved. Note additional countries after "Other")*	□ Scotland □ UK □ USA □ Canada □ Australia □ New Zealand □ France □ Germany □ Italy □ Netherlands □ Scandinavia □ Spain □ Other:

3.4	*What is the social setting (ie type of environment in which they live) of patients in the study?*	□ Urban □ Rural □ Mixed
3.5	*What criteria are used to decide who should be INCLUDED in the study?*	
3.6	*What criteria are used to decide who should be EXCLUDED from the study?*	
3.7	*What intervention or risk factor is investigated in the study? (Include dosage where appropriate)*	
3.8	*What comparisons are made in the study (ie what alternative treatments are used to compare the intervention with). Include dosage where appropriate.*	
3.9	*What methods were used to randomize patients, blind patients or investigators, and to conceal the randomization process from investigators?*	
3.10	*How long did the active phase of the study last?*	
3.11	*How long were patients followed-up for, during and after the study?*	
3.12	*List the key characteristics of the patient population. Note if there are any significant differences between different arms of the trial.*	
3.13	*Record the basic data for each arm of the study. If there are more than four arms, note data for subsequent arms at the bottom of the page.*	

	Arm 1: **Treatment:** **Sample size:** **No. analysed** **With outcome:** **Without outcome:**	**Arm 2:** **Treatment:** **Sample size:** **No. analysed** **With outcome:** **Without outcome>** **Primary outcome?**	**Arm 3:** **Treatment:** **Sample size:** **No. analysed** **With outcome:** **Without outcome>** **Primary outcome?**	**Arm 4:** **Treatment:** **Sample size:** **No. analysed** **With outcome:** **Without outcome** **Primary outcome?**
3.14	*Record the basic data for each IMPORTANT outcome in the study. If there are more than four, not data for additional outcomes at the bottom of the page.*			
	Outcome 1: **Value:** **Measure:** **P value** **Upper CI** **Lower CI** **Primary outcome?**	**Outcome 2:** **Value:** **Measure:** **P value** **Upper CI** **Lower CI** **Primary outcome?**	**Outcome 3:** **Value:** **Measure:** **P value** **Upper CI** **Lower CI** **Primary outcome?**	**Outcome 4:** **Value:** **Measure:** **P value** **Upper CI** **Lower CI** **Primary outcome?**
3.15	**Notes.** Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question. *{Much of this is likely to be contributed by GDG members).*			

Appendix B3: The Cochrane Risk of Bias Tool

Domain	Support for judgement	Review authors' judgement
Selection bias.		
Random sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
Performance bias.		
Blinding of participants and personnel Assessments should be made for each main outcome (or class of outcomes).	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

Detection bias.

Blinding of outcome Assessments should be made for each main outcome (or class of outcomes).	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.

Attrition bias.

Incomplete outcome dataAssessments should be made for each main outcome (or class of outcomes).	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.

Reporting bias.		
Selective reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.
Other bias.		
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Bias due to problems not covered elsewhere in the table.

Appendix C: Excluded studies

1. Aasheim,E.T. et al. Vitamin status after bariatric surgery: a randomized study of gastric bypass and duodenal switch. American Journal of Clinical Nutrition. 90 , 15-22 (2009).

2. Agren G,N.I. A prospective randomized comparison of vertical banded gastroplasty (VBG), loop gastric bypass (GBY) and gastric banding (GB). International Journal of Obesity 13 , 595 (1989).

3. Alami,R.S. et al. Is there a benefit to preoperative weight loss in gastric bypass patients? A prospective randomized trial. Surgery for Obesity & Related Diseases. 3 , 141-145 (2007).

4. Andersen,T., Backer,O.G., Stokholm,K.H., & Quaade,F. Randomized trial of diet and gastroplasty compared with diet alone in morbid obesity. N. Engl. J Med 310 , 352-356 (1984).

5. Andersen,T., Backer,O.G., Astrup,A., & Quaade,F. Horizontal or vertical banded gastroplasty after pretreatment with very-low-calorie formula diet: a randomized trial. International Journal of Obesity. 11 , 295-304 (1987).

6. Andersen,T., Stokholm,K.H., & Nielsen,P.E. Blood pressure and arm circumference during large weight reduction in normotensive and borderline hypertensive obese patients. Journal of Clinical Hypertension. 3 , 547-553 (1987).

7. Andersen,T., Stokholm,K.H., Backer,O.G., & Quaade,F. Long-term (5-year) results after either horizontal gastroplasty or very-low-calorie diet for morbid obesity. International Journal of Obesity. 12 , 277-284 (1988).

8. Andersen,T., Pedersen,B.H., Dissing,I., Astrup,A., & Henriksen,J.H. A randomized comparison of horizontal and vertical banded gastroplasty: what determines weight loss? Scandinavian Journal of Gastroenterology. 24 , 186-192 (1989).

9. Angrisani,L. et al. The use of bovine pericardial strips on linear stapler to reduce extraluminal bleeding during laparoscopic gastric bypass: prospective randomized clinical trial. Obesity Surgery. 14 , 1198-1202 (2004).

10. Angrisani,L. et al. Laparoscopic adjustable gastric banding with truncal vagotomy versus laparoscopic adjustable gastric banding alone: interim results of a prospective randomized trial. Surgery for Obesity & Related Diseases. 5 , 435-438 (2009).

11. Ansay J Vertical banded gastroplasty for morbid obesity. Laparotomy or coelioscopy?A randomized study . Obesity Surgery 6 , 298 (1996).

12. Arceo-Olaiz,R. et al. Maximal weight loss after banded and unbanded laparoscopic Roux-en-Y gastric bypass: a randomized controlled trial. Surgery for Obesity & Related

Diseases. 4 , 507-511 (2008).

13. Azagra,J.S. et al. Laparoscopic gastric reduction surgery. Preliminary results of a randomized, prospective trial of laparoscopic vs open vertical banded gastroplasty. Surg Endosc. 13 , 555-558 (1999).

14. Backer,O., Gudmand-Hoyer,E., & Andersen,B. Randomised trial of jejunoileal bypass versus medical treatment in morbid obesity. Lancet. 2 , 1255-1258 (1979).

15. Bessler,M., Daud,A., Kim,T., & DiGiorgi,M. Prospective randomized trial of banded versus nonbanded gastric bypass for the super obese: early results. Surgery for Obesity & Related Diseases. 3 , 480-484 (2007).

16. Blanco-Engert,R., Weiner,S., Pomhoff,I., Matkowitz,R., & Weiner,R.A. Outcome after laparoscopic adjustable gastric banding, using the Lap-Band and the Heliogast band: a prospective randomized study. Obesity Surgery. 13 , 776-779 (2003).

17. Brolin,R.E., Kenler,H.A., Gorman,J.H., & Cody,R.P. Long-limb gastric bypass in the superobese. A prospective randomized study. Annals of Surgery. 215 , 387-395 (1992).

18. Buckwalter,J.A. A prospective comparison of the jejunoileal and gastric bypass operations for morbid obesity. WORLD-J-SURG. 1 , 757-768 (1977).

19. Buckwalter,J.A. Clinical trial of jejunoileal and gastric bypass for the treatment of morbid obesity: four-year progress report. American Surgeon. 46 , 377-381 (1980).

20. Buddeberg-Fischer,B. et al. Physical and psychosocial outcome in morbidly obese patients with and without bariatric surgery: a 4 1/2-year follow-up. Obes Surg 16 , 321-330 (2006).

21. Champion,J.K. & Williams,M.D. Prospective randomized comparison of linear staplers during laparoscopic Roux-en-Y gastric bypass. Obesity Surgery. 13 , 855-859 (2003).

22. Champion,J.K. & Williams,M. Prospective randomized trial of heated humidified versus cold dry carbon dioxide insufflation during laparoscopic gastric bypass. Surgery for Obesity & Related Diseases. 2 , 445-449 (2006). Ref ID: 310

23. Choban,P.S. & Flancbaum,L. The effect of Roux limb lengths on outcome after Roux-en-Y gastric bypass: a prospective, randomized clinical trial. Obesity Surgery. 12 , 540-545 (2002).

24. Christou,N. & Efthimiou,E. Five-year outcomes of laparoscopic adjustable gastric banding and laparoscopic Roux-en-Y gastric bypass in a comprehensive bariatric surgery program in Canada. Can. J Surg 52 , E249-E258 (2009).

25. Christou,N.V. et al. Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients. Ann Surg 240 , 416-423 (2004).

26. Cottam,D.R., Fisher,B., Sridhar,V., Atkinson,J., & Dallal,R. The effect of stoma size on weight loss after laparoscopic gastric bypass surgery: Results of a blinded randomized controlled trial. Obesity Surgery. #2009. , (2009).

27. Cowan GSM. Long versus short limb Roux-en-Y procedures. Early results in a prospective randomized study of metabolic, nutritional and anthropometric outcomes. Obesity Surgery 6 , 25 (1996).

28. Csendes,A., Maluenda,F., & Burgos,A.M. A prospective randomized study comparing patients with morbid obesity submitted to laparotomic gastric bypass with or without omentectomy. Obesity Surgery. (2004).

29. Dapri,G., re,G.B., & Himpens,J. Reinforcing the staple line during laparoscopic sleeve gastrectomy: prospective randomized clinical study comparing three different techniques. Obesity Surgery. #2010 Apr. , (2004).

30. Dapri,G., Vaz,C., re,G.B., & Himpens,J. A prospective randomized study comparing two different techniques for laparoscopic sleeve gastrectomy. Obesity Surgery. 17 , 1435-1441 (2007).

31. Davila-Cervantes,A. et al. Open versus laparoscopic vertical banded gastroplasty: a randomized controlled double blind trial. Obes Surg 12 , 812-818 (2002).

32. De,P. et al. Prospective randomized controlled trial comparing 2 versions of laparoscopic ileal interposition associated with sleeve gastrectomy for patients with type 2 diabetes with BMI 21-34 kg/m(2). Surgery for Obesity & Related Diseases. 6 , 296-304 (2010).

33. de,W. et al. Open versus laparoscopic adjustable silicone gastric banding: a prospective randomized trial for treatment of morbid obesity. Annals of Surgery. 230 , 800-805 (1999).

34. Eckhout,G.V. & Prinzing,J.F. Surgery for morbid obesity: comparison of gastric bypass with vertically stapled gastroplasty. Colo. Med 78 , 117-122 (1981).

35. Fobi,M.A. Vertical Banded Gastroplasty vs Gastric Bypass: 10 years follow-up. Obes Surg 3 , 161-164 (1993).

36. Fox,S.R., Oh,K.H., & Fox,K.M. Adjustable Silicone Gastric Banding vs Vertical Banded Gastroplasty: a comparison of early results. Obes Surg 3 , 181-184 (1993).

37. Freeman,J.B. & Burchett,H.J. A comparison of gastric bypass and gastroplasty for morbid obesity. Surgery 88 , 433-444 (1980).

38. Govindarajan,R. et al. Efficacy of ketorolac in lieu of narcotics in the operative management of laparoscopic surgery for morbid obesity. Surg Obes Relat Dis. 1 , 530-535

(2005).

39. Gravante,G. et al. Laparoscopic adjustable gastric bandings: a prospective randomized study of 400 operations performed with 2 different devices. Archives of Surgery. 142 , 958-961 (2007).

40. Griffen,W.O.J., Young,V.L., & Stevenson,C.C. A prospective comparison of gastric and jejunoileal bypass procedures for morbid obesity. Annals of Surgery. 186 , 500-509 (1977).

41. Hall,J.C. et al. Gastric surgery for morbid obesity. The Adelaide Study. Annals of Surgery. 211 , 419-427 (1990).

42. Hedenbro,J.L., Frederiksen,S.G., & Lundgren,P.O. Patients accept a shorter hospital time for vertical banded gastroplasty in a short stay unit: A randomized study. Obesity Surgery. 5 , 34-38 (1995).

43. Husemann,B. & Kluy,J.P. VBG and adjustable silicone gastric band - A prospective randomized clinical trial. Obesity Surgery. 7 , 290 (1997).

44. Inabnet,W.B., Quinn,T., Gagner,M., Urban,M., & Pomp,A. Laparoscopic Roux-en-Y gastric bypass in patients with BMI <50: a prospective randomized trial comparing short and long limb lengths. Obesity Surgery. 15 , 51-57 (2005). Ref ID: 360

45. Kasalicky,M., Fried,M., Peskova,M., Bortlik,M., & Votrubova,J. Fixation of a non-adjustable gastric band using an anterior gastric wall cuff (randomized study). [Czech]. Rozhledy v chirurgii : mesicnik Ceskoslovenske chirurgicke spolecnosti. 79 , 227-233 (2000).

46. Kenler,H.A., Brolin,R.E., & Cody,R.P. Changes in eating behavior after horizontal gastroplasty and Roux-en-Y gastric bypass. Am. J Clin Nutr. 52 , 87-92 (1990).

47. Kiviluoto T,S.J.S.T.K.E. Laparoscopic adjustable silicone gastric banding vs. open vertical banded gastroplasty for morbid obesity. A 2-year follow-up. Gastroenterology 116 , S0134. (1999).

48. Laws,H.L. & Piantadosi,S. Superior gastric reduction procedure for morbid obesity: a prospective, randomized trial. Annals of Surgery. #1981 Mar. , (2003).

49. Lawson,M.L. et al. One-year outcomes of Roux-en-Y gastric bypass for morbidly obese adolescents: a multicenter study from the Pediatric Bariatric Study Group. J Pediatr. Surg 41 , 137-143 (2006).

50. Lechner,G.W. & Callender,A.K. Subtotal gastric exclusion and gastric partitioning: a randomized prospective comparison of one hundred patients. Surgery 90 , 637-644 (1981).
51. Lechner,G.W. & Elliott,D.W. Comparison of weight loss after gastric exclusion and partitioning. Archives of Surgery. 118 , 685-692 (1983).

52. Lee,W.J. et al. Laparoscopic Roux-en-Y versus mini-gastric bypass for the treatment of morbid obesity: a prospective randomized controlled clinical trial. Annals of Surgery. 242 , 20-28 (2005).

53. Leyba,J.L. et al. Laparoscopic gastric bypass for morbid obesity-a randomized controlled trial comparing two gastrojejunal anastomosis techniques. Journal of the Society of Laparoendoscopic Surgeons. 12 , 385-388 (2008).

54. Linner,J.H. Comparative effectiveness of gastric bypass and gastroplasty: a clinical study. Arch. Surg 117 , 695-700 (1982).

55. Lujan,J.A. et al. Laparoscopic Versus Open Gastric Bypass in the Treatment of Morbid Obesity: A Randomized Prospective Study. Annals of Surgery. 239 , 433-437 (2004).

56. Miller,K. & Hell,E. The adjustable silicone gastric band (Lap-Band) versus the Swedish Adjustable Gastric Band (SAGB): Preliminary results of a prospective randomized study. Obesity Surgery. 7 , 301 (1997).

57. Miller,K.A. & Pump,A. Use of bioabsorbable staple reinforcement material in gastric bypass: a prospective randomized clinical trial. Surgery for Obesity & Related Diseases. 3 , 417-421 (2007).

58. Miller,K.A. & Pump,A. Mechanical versus suture fixation of the port in adjustable gastric banding procedures: a prospective randomized blinded study. Surgical Endoscopy. 22 , 2478-2484 (2008).

59. Naslund,I., Wickbom,G., Christoffersson,E., & Agren,G. A prospective randomized comparison of gastric bypass and gastroplasty. Complications and early results. Acta Chirurgica Scandinavica. 152 , 681-689 (1986).

60. Naslund,I. The size of the gastric outlet and the outcome of surgery for obesity. Acta Chirurgica Scandinavica. 152 , 5-210 (1986).

61. Naslund,I. Gastric bypass versus gastroplasty. A prospective study of differences in two surgical procedures for morbid obesity. Acta chirurgica Scandinavica. Supplementum. 536 , Date (1987).

62. Naslund,I. Gastric emptying rate after gastric bypass and gastroplasty. Scandinavian Journal of Gastroenterology. 22 , 193-201 (1987).

63. Naslund,I., Jarnmark,I., & Andersson,H. Dietary intake before and after gastric bypass and gastroplasty for morbid obesity in women. International Journal of Obesity. 12 , 503-513 (1988).

64. Nguyen,N.T. et al. Laparoscopic versus open gastric bypass: a randomized study of outcomes, quality of life, and costs. Annals of Surgery. 234 , 279-289 (2001).

65. Nguyen,N.T., Longoria,M., Welbourne,S., Sabio,A., & Wilson,S.E. Glycolide copolymer staple-line reinforcement reduces staple site bleeding during laparoscopic gastric bypass: a prospective randomized trial. Archives of Surgery. 140 , 773-778 (2005).

66. Nguyen,N.T. et al. Effect of staple height on gastrojejunostomy during laparoscopic gastric bypass: a multicenter prospective randomized trial. Surgery for Obesity & Related Diseases. 6 , 477-482 (2010).

67. O'Brien,P.E., Dixon,J.B., Laurie,C., & Anderson,M. A prospective randomized trial of placement of the laparoscopic adjustable gastric band: comparison of the perigastric and pars flaccida pathways. Obesity Surgery. 15 , 820-826 (2005).

68. Olbers,T. et al. Body composition, dietary intake, and energy expenditure after laparoscopic Roux-en-Y gastric bypass and laparoscopic vertical banded gastroplasty: a randomized clinical trial. Annals of Surgery. 244 , 715-722 (2006).

69. Puzziferri,N., Austrheim-Smith,I.T., Wolfe,B.M., Wilson,S.E., & Nguyen,N.T. Three-year follow-up of a prospective randomized trial comparing laparoscopic versus open gastric bypass. Annals of Surgery. 243 , 181-188 (2006).

70. Sanchez,B.R. et al. Comparison of totally robotic laparoscopic Roux-en-Y gastric bypass and traditional laparoscopic Roux-en-Y gastric bypass. Surgery for Obesity & Related Diseases. 1 , 549-554 (2005).

71. Scott DJ,P.D.H.P.C.S.J.DB.S. weight loss similar following Roux-Y gastric bypass and vertical banded gastroplasty for morbid obesity . Gastroenterology 116 , 2528 (1999).

72. Sjostrom,L. et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N. Engl. J Med 351 , 2683-2693 (2004).

73. Sjostrom,L. et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N. Engl. J Med 357 , 741-752 (2007).

74. Sjostrom,L. et al. Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial. Lancet Oncol. 10 , 653-662 (2009).

75. Sorensen,T.I.A., Andersen,B., & Kam-Hansen,L. Total plasma cholesterol in obesity after jejunoileal bypass with 3:1 or 1:3 jejunoileal ratio. A randomized trial. Scandinavian Journal of Gastroenterology. 14 , 865-868 (1979).

76. Sundbom,M. & Gustavsson,S. Randomized clinical trial of hand-assisted laparoscopic versus open Roux-en-Y gastric bypass for the treatment of morbid obesity. British Journal of Surgery. 91 , 418-423 (2004).

77. Suter,M., Giusti,V., Worreth,M., Heraief,E., & Calmes,J.M. Laparoscopic gastric banding: A prospective, randomized study comparing the Lapband and the SAGB: Early

results: Commentary. [French]. Annales de Chirurgie. 130 , 2 (2002).

78. Szewczyk,T. & Modzelewski,B. Perioperative comparison of the MiniMizer extra band with the other laparoscopic gastric bands. Obesity Surgery. 16 , 646-650 (2006).

79. VanWoert J,M.A.A.S.C.J.H.L. A prospective randomized trial (PRT) of gastric bypass (GB) versus vertical banded gastroplasty (VBG) for morbid obesity (MO). Clinical Research 40 , 642 (1992).

80. Viddal,K.O. Intestinal bypass. A randomized, prospective clinical study of end-to-side and end-to-end jejunoileal bypass. Scandinavian Journal of Gastroenterology. 18 , 627-634 (1983).

81. Vila-Cervantes,A. et al. Open versus laparoscopic vertical banded gastroplasty: a randomized controlled double blind trial. Obesity Surgery. 12 , 812-818 (2002).

82. Weiner,R., Bockhorn,H., Rosenthal,R., & Wagner,D. A prospective randomized trial of different laparoscopic gastric banding techniques for morbid obesity. Surgical Endoscopy. 15 , 63-68 (2001).

83. Weiss,H.G. et al. Adjustable gastric and esophagogastric banding: a randomized clinical trial. Obesity Surgery. 12 , 573-578 (2002).

84. Westling,A. & Gustavsson,S. Laparoscopic vs open Roux-en-Y gastric bypass: a prospective, randomized trial. Obesity Surgery. 11 , 284-292 (2001).

85. Yamazaki,K., Kawamura,I., Miyazawa,Y., & Isono,K. [A comparison of gastric bypass and vertical banded gastroplasty for morbid obesity]. Nihon Geka Gakkai Zasshi 91 , 1685-1690 (1990).

Table C1: Excluded studies and the reason for exclusion

Study	Reason for exclusion
Aasheim 2009	Multiple publication
Agren 1989	Abstract only
Andersen 1984	Horizontal gastroplasty - No longer performed
Andersen 1987 i	Horizontal gastroplasty - No longer performed
Andersen 1987 ï	Horizontal gastroplasty - No longer performed
Andersen 1988	Horizontal gastroplasty - No longer performed
Andersen 1989	Horizontal gastroplasty - No longer performed
Angrisani 2004	One procedure - different techniques
Angrisani 2009	One procedure - different techniques
Ansay 1996	One procedure - different techniques
Arceo-Olaiz 2008	One procedure - different techniques
Azagra 1999	One procedure - different techniques
Backer 1997	Jejunoileal bypass – No longer performed
Bessler 2007	One procedure - different techniques
Blanco-Engert 2003	One procedure - different techniques
Brolin 1992	One procedure - different techniques
Buckwalter 1977	Jejunoileal bypass – No longer performed
Buckwalter 1980	Jejunoileal bypass – No longer performed
Buddeberg-Fischer 2006	Study design
Champion 2003	One procedure - different techniques
Choban 2002	One procedure - different techniques
Christou 2004	Study design
Christou 2009	Study design
Cottam 2009	One procedure - different techniques
Cowan 1996	One procedure - different techniques
Csendes 2004	One procedure - different techniques
Dapri 2004	One procedure - different techniques

Dapri 2007	One procedure - different techniques
Davila-Cervantes 2002	One procedure - different techniques
De Paula AL 2010	One procedure - different techniques
De Wit LT 1999	One procedure - different techniques
Eckhout 1981	Study design
Fobi 1993	Study design
Fox 1993	Study design
Freeman 1980	Study design
Gravante 2007	One procedure - different techniques
Griffen 1997	Jejunoileal bypass – No longer performed
Hall 1990	Horizontal gastroplasty - No longer performed
Husemann 1997	Randomization - not appropriate
Inabnet 2005	One procedure - different techniques
Kasalicky 2000	One procedure - different techniques
Kenler 1990	Horizontal gastroplasty - No longer performed
Kiviluoto 1999	Study design
Laws 2003	Horizontal gastroplasty - No longer performed
Lawson 2006	Study design
Lechner 1981	Horizontal gastroplasty - No longer performed
Lechner 1983	Horizontal gastroplasty - No longer performed
Lee 2005	One procedure - different techniques
Leyba 2008	One procedure - different techniques
Linner 1982	Study design
Lujan 2004	One procedure - different techniques
Miller 1997	One procedure - different techniques
Naslund 1986 i	Horizontal gastroplasty - No longer performed
Naslund 1986 ï	Horizontal gastroplasty - No longer performed
Naslund 1987 i	Horizontal gastroplasty - No longer performed
Naslund 1987 ï	Horizontal gastroplasty - No longer performed

Naslund 1988	Horizontal gastroplasty - No longer performed
Nguyen 2001	One procedure - different techniques
Nguyen 2005	One procedure - different techniques
Nguyen 2010	One procedure - different techniques
Olbers 2006	Multiple publication
Puzziferri 2006	One procedure - different techniques
Scott 1990	Study design
Sjostrom 2004	Study design
Sjostrom 2007	Study design
Sjostrom 2009	Study design
Sorensen 1979	Jejunoileal bypass – No longer performed
Sundbom 2004	One procedure - different techniques
Suter 2002	One procedure - different techniques
VanWoert 1992	Abstract only
Viddal 1983	Jejunoileal bypass – No longer performed
vila-Cervantes 2002	One procedure - different techniques
Weiner 2001	One procedure - different techniques
Weiss 2002	One procedure - different techniques
Westling 2001	One procedure - different techniques
Yamazaki 1990	Study design

Appendix D: Detailed assessment of the risk of bias of included trials.

Angrisani 2007

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Unclear	Stated as randomized, but no information was provided about the method of sequence generation
Allocation concealment?	Unclear	Method of concealment was not described in sufficient detail. Quote: Patients were randomly allocated by sealed envelope to 1 of the 2 surgical groups: LAGB or LRYGB.
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Unclear	The reason for lost follow-up was not reported. Quote: Eight patients were excluded from the study after randomization because of their refusal to undergo the procedure to which they had been assigned (5 LRYGB and 3 LAGB) Quote: One LAGB patient was lost to follow-up.
Free of selective reporting?	Unclear	Unclear
Free of other bias?	Unclear	Authors stated that for LRYGB they were in the early phase of the learning curve compared to LAGB.

Dixon 2008

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: Randomization was computer derived, with blocking into 3 groups to allow for orderly recruitment.
Allocation concealment?	Unclear	Not reported.
Blinding of outcome assessors?	No	Quote: The study was not blinded
Incomplete outcome data addressed?	Yes	The reason for lost follow-up was not reported. Quote: One patient randomized to surgery withdrew from the study on the evening prior to scheduled operation and did not agree to be further followed up. The remaining 29 surgically treated patients (97%) completed the 2-year program. Of the conventionally treated patients, 26 (87%) completed the 2-year assessment
Free of selective reporting?	Unclear	Unclear
Free of other bias?	No	The study was industry funded. There is evidence that industry funded trials may overestimate treatment effect [68] Quote: This study was funded by Monash University, which has received an unrestricted grant from Allergan Health. The laparoscopic adjustable gastric bands (Allergan Health) and the laparoscopic ports (Applied Medical) were provided without charge by the manufacturers. Quote: A run-in period of at least 3 months was undertaken in which further alterations to eating, exercise, glucose self-monitoring, and medications were suggested

Himpens 2006

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Unclear	Stated as randomized, but no information was provided about the method of sequence generation. Quote: 80 patient candidates for a laparoscopic restrictive operation were operated consecutively and randomly assigned to a GB (40) or SG (40).
Allocation concealment?	Unclear	Method of concealment not described.
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Unclear	Not reported
Free of selective reporting?	Unclear	The study only reported mean and range, no standard deviations
Free of other bias?	Unclear	Unclear

Howard 1995

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Unclear	Randomized, but no information was provided about the method of sequence generation. Quote: Patients who met these criteria and gave informed consent were randomized to have either VBG or GBP surgery.
Allocation concealment?	Unclear	Not reported
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Unclear	Reasons for dropouts were not provided Quote: Two patients withdrew from the study within 4 weeks of surgery leaving 20 subjects who had a GBP and 22 subjects who had a VBG. Quote: Twelve patients (six GBP and six VBG) were followed for 60 months
Free of selective reporting?	Unclear	Outcomes were not prespecified, but variables measured were listed in the methods section. All but vitamin deficiency were reported in the results section
Free of other bias?	Unclear	Unclear

Karamanakos 2008

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: Computer generated random numbers were used to assign the type of surgery (LRYGBP or LSG)
Allocation concealment?	Unclear	The envelopes were not sequentially numbered Quote: which was written on a card sealed in a completely opaque envelop
Blinding of outcome assessors?	Yes	Quote: Blinding as to the type of the procedure involved the patient and the medical staff, and the independent data collector.
Incomplete outcome data addressed?	Yes	Quote: All patients had a complete evaluation at all time points of the follow-up.
Free of selective reporting?	Unclear	Adverse effect not reported adequately
Free of other bias?	Unclear	Statistically significant difference between the two treatment groups at baseline

Lee 2004

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Unclear	Randomized, but no information reported about the method of sequence generation Quote: Patients were then randomly assigned to LVBG or LGBP by the use of sealed envelopes
Allocation concealment?	Unclear	Method of concealment is not described in sufficient detail. Quote: Patients were then randomly assigned to LVBG or LGBP by the use of sealed envelopes
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	No	Not reported
Free of selective reporting?	Unclear	Not all the outcomes reported in the results section were pre-specified e.g. Laboratory results.
Free of other bias?	Unclear	Unclear

MacLean 1995

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Unclear	Randomized, but no information given about the method of sequence generation Quote: Randomization took place at time of surgery
Allocation concealment?	Unclear	Not reported.
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Unclear	No loss to follow-up in the earlier report, but the updated publication didn't report it.
Free of selective reporting?	Unclear	Didn't report weight loss outcomes as BMI or weight. Measure of variance not reported
Free of other bias?	Unclear	Results were not reported by original treatment assignment

Mingrone 2002

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Unclear	Not reported
Allocation concealment?	Unclear	Not reported
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Unclear	It appears from table 1 that follow-up was 100%, but this was not described in the text
Free of selective reporting?	Unclear	Adverse effects not reported
Free of other bias?	Unclear	Unclear

Morino 2003

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: Randomization was performed 1 day before surgery by means of sealed opaque envelopes containing computer-generated random numbers.
Allocation concealment?	Yes	Quote: Randomization was performed 1 day before surgery by means of sealed opaque envelopes containing computer-generated random numbers.
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Unclear	Reasons for dropouts were not provided Quote: Patients present at follow-up were: 98% at 1 year, 94% at 2 years, 90% at 3 years in the LASGB group and 90%, 88%, and 95%, respectively, in the LVBG group.
Free of selective reporting?	Unclear	Unclear
Free of other bias?	Unclear	Unclear

Nguyen 2009

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Unclear	Randomized, but no information given about the method of sequence generation Quote: After patients gave consent, they were randomly assigned to laparoscopic gastric bypass or laparoscopic gastric banding by use of sealed envelopes with a block of 3 groups to allow for even recruitment
Allocation concealment?	Unclear	Method of concealment was not described in sufficient detail. Quote: After patients gave consent, they were randomly assigned to laparoscopic gastric bypass or laparoscopic gastric banding by use of sealed envelopes with a block of 3 groups to allow for even recruitment
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Unclear	Percentage of patients at each point of follow-up was provided, although the reason of lost follow-up was not reported. Quote: At 2 years, follow-up was available for 84.6% of gastric bypass patients and 91.9% of gastric banding patients. Of the patients with 3 years data, follow-up was available for 84.6% of gastric bypass patients and 93.3% of gastric banding patients. Of the patients with 4 years data, follow-up was available for 83.1% of gastric bypass patients and 93.3% of gastric banding patients. Quote: Fourteen patients in the gastric bypass group and 39 patients in the gastric banding group were excluded because the patients were unwilling to undergo the assigned procedure or inability to obtain insurance coverage for the bariatric operation.
Free of selective reporting?	Yes	Outcomes listed in the methods reported on, measures of variance on outcome were provided.
Free of other bias?	Yes	Study appears free of other sources of bias.

Nilsell 2001

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Unclear	Randomized, but no information given about the method of sequence generation Quote: participants in the study, were randomly allocated by sealed envelope to have one or the other operation on the day before the planned operation
Allocation concealment?	Unclear	Method of concealment was not described in sufficient detail. Quote: participants in the study, were randomly allocated by sealed envelope to have one or the other operation on the day before the planned operation
Blinding of outcome assessors?	No	Quote: After this randomization, the type of operation was not further blinded to patients or staff
Incomplete outcome data addressed?	Unclear	The reason of lost follow-up was not reported Quote: One patient in each group died during the follow-up, from causes unrelated to the bariatric operation. Three patients in the adjustable banding group and 2 in the vertical banded group were lost to follow-up.
Free of selective reporting?	Unclear	Adverse events not reported adequately
Free of other bias?	Unclear	Unclear

O'Brien 2006

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: A computer-derived random allocation sequence, without blocking or stratification, performed the randomization
Allocation concealment?	Yes	Quote: the coordinator contacted the trial office by telephone for allocation.
Blinding of outcome assessors?	No	Quote: The study was not blinded.
Incomplete outcome data addressed?	Unclear	Withdrawals reported, but the reason for the withdrawals not reported. Quote: One patient who was randomly assigned to surgery withdrew from the study on the evening before the scheduled operation and declined to be followed further. The remaining 39 (98%) treated surgical patients and 33 (83%) nonsurgical patients completed the 2-year follow-up program.
Free of selective reporting?	Yes	Outcomes pre-specified in the methods section were reported in the results section
Free of other bias?	Unclear	The study was industry funded. There is evidence that industry funded trials may overestimate treatment effect [68] . Quote : Grant Support**:** By the Department of Surgery, Monash University. INAMED Health, manufacturer of the LAP-BAND System; Novartis, manufacturer of Optifast and U.S. Surgical Corp., manufacturer of disposable laparoscopic instruments, provided the equipment devices or products.

O'Brien 2010

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: Randomization was performed using a computer-derived random allocation sequence to allow orderly admission into both programs.
Allocation concealment?	Unclear	Not reported.
Blinding of outcome assessors?	No	Quote: The study was not blinded
Incomplete outcome data addressed?	Yes	Withdrawal reported as well as the reason for the withdrawal in the flow chart. Quote: Twenty-four of 25 participants in the gastric banding group and 18 of 25 in the lifestyle group completed the study
Free of selective reporting?	Unclear	Protocol not available. All the outcomes in the methods section reported results except for QOL for which a web link was provided for the full results
Free of other bias?	No	Participants participated in a 2-month program prior to surgery Quote: Potential participants undertook a 2-month program that involved best practice recommendations around eating and physical activity. Of 163 potentially eligible participants only 50 were randomized. Reasons for exclusions were provided.Two of the investigators were on the advisory board of the industry

Olbers 2005

Item Authors'	**Judgement**	**Description**
Adequate sequence generation?	Yes	Quote: patients were randomized to either LVBG or LRYGBP (50 in each group) by a computer program that stratified for weight, BMI, age and associated morbidity.
Allocation concealment?	Unclear	Not reported
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Yes	Reasons for missing outcome were provided Quote: The follow-up rate was 97·6 percent. One patient in each group was lost to follow-up 1 year after surgery and two patients who had undergone LVBG could not be contacted at the 2-year follow-up. Two women were pregnant at the 1-year follow-up and another two were pregnant at the 2-year follow-up. Their weights were excluded from the analysis.
Free of selective reporting?	Yes	Outcomes were pre-specified in the methods section
Free of other bias?	Yes	The study appeared to be free of other sources of bias

Peterli 2009

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: Computer-generated random numbers were used to assign the type of surgery (LRYGB or LSG).
Allocation concealment?	Unclear	The envelopes were not sequentially numbered Quote: Computer-generated random numbers were used to assign the type of surgery (LRYGB or LSG), and these were individually written on cards, then sealed in completely opaque envelopes
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Yes	Quote: All patients had a complete evaluation at all time points of the follow-up.
Free of selective reporting?	No	Adverse events not reported.
Free of other bias?	Unclear	Only three months of follow-up. Both procedures were done by the same surgeon. Author was a consultant to the industry which manufactures procedure instruments

Reis 2010

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: A centralized computed-generated randomization was utilized.
Allocation concealment?	Yes	Quote: A centralized computer-generated randomization was utilized
Blinding of outcome assessors?	Unclear	Reported that the person administering the questionnaire was blinded to the surgery. Other outcome assessors not reported whether they were blinded or not
Incomplete outcome data addressed?	Yes	Quote: The follow-up rate was 100%.
Free of selective reporting?	No	Adverse events not reported.
Free of other bias?	No	The study was conducted on males only. Patients were involved in lifestyle modification prior to surgery. Only 20 patients were selected from 117 men. The reasons for exclusions were not provided.

Scozzari 2009

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: Randomization was performed 1 day before surgery by means of sealed opaque envelopes containing computer-generated random numbers
Allocation concealment?	Yes	Quote: Randomization was performed 1 day before surgery by means of sealed opaque envelopes containing computer-generated random numbers.
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Yes	Percentage of patients at each point of follow-up was provided, although the reason for lost follow-up was not given. Quote: In the LASGB group, the follow-up rate was 85.7% (42/49) at 3 years, 81.6% (40/ 49) at 5 years, and 81.6% (40/49) at 7 years. In the LVBG group, the follow-up rate was 82.4%(42/51) at 3 years, 80.4% (41/51) at 5 years, and 80.4% (41/51) at 7 years
Free of selective reporting?	Yes	Outcomes were pre-specified in the methods section
Free of other bias?	Unclear	Unclear

Sovik 2010

Item Authors'	Judgment	Description
Adequate sequence generation?	Yes	Quote: Randomization was performed at Sahlgrenska with LabVIEWTM version 7.1
Allocation concealment?	Unclear	Not reported
Blinding of outcome assessors?	Unclear	Unclear whether outcome assessors were blinded or not. Quote: The result of randomization was known only to the doctors enrolling the patients and the personnel scheduling the operation.
Incomplete outcome data addressed?	Yes	Quote: A total of 61 patients were included in the study; one patient withdrew after randomization, but was not aware of the planned procedure. LRYGB was performed in 31 patients and LDS in 29. All patients completed the 6- month follow-up, although one patient missed the 1-year visit
Free of selective reporting?	Unclear	Not all outcomes were pre-specified in the methods section.
Free of other bias?	No	Not all surgeons performed all types of surgeries. Quote: Before the study, bariatric surgical experience at Aker included 123 LRYGBs (performed by two surgeons) and 15 LDS procedures (performed by one of the two surgeons), and at Sahlgrenska 435 LRYGBs (three surgeons) and 18 LDS procedures (one of the three surgeons)

Sugerman 1987

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	QUOTE: The feasibility of performing either procedure was determined at the time of laparotomy, and a randomized card was pulled that selected the operation to be performed. In order that approximately equal numbers of the two procedures would be performed concurrently, cards designating each operation were combined into groups of five each, "shuffled," and a card "blindly" pulled by the surgical secretary when called by the operating room circulating nurse.
Allocation concealment?	Unclear	Not reported
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Yes	Number of patients analyzed at each point of follow-up along with the reasoning were provided
Free of selective reporting?	Unclear	Not all outcomes were pre-specified in the methods section
Free of other bias?	Unclear	Quote: The randomized study started in June 1982 and was terminated 9 months later, when a statistically significant difference at $p < 0.05$ was noted in favor of the RYGBP.

van Dielen 2005

Item Authors'	**Judgment**	**Description**
Adequate sequence generation?	Yes	Quote: Patients were randomly assigned to LAGB or open VBG using a computer-generated randomization list, made before the start of the study.
Allocation concealment?	Unclear	Not reported
Blinding of outcome assessors?	Unclear	Not reported
Incomplete outcome data addressed?	Yes	Quote: 100% follow-up in both groups was achieved.
Free of selective reporting?	Unclear	Inadequate pre-specifications of the outcomes
Free of other bias?	Unclear	Unclear

APPENDIX E: Forest Plots: Percent of excess weight loss, BMI, and weight loss of various surgical procedures at 2 and 3 years follow up.

Figure E1: Percent of excess weight loss at 2 year: Gastric Bypass

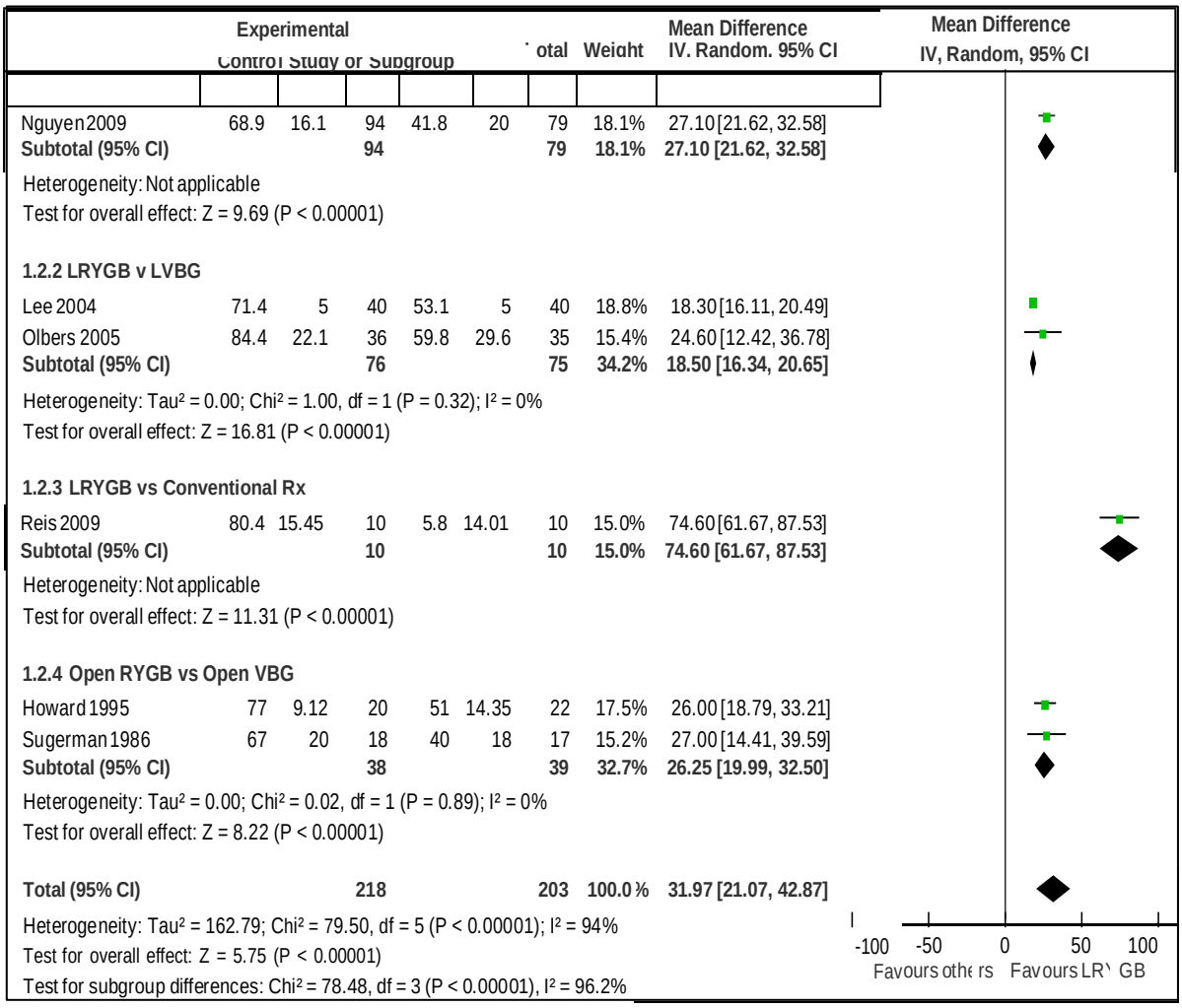

Figure E2: Percent of excess weight loss at 3 year: Gastric Bypass

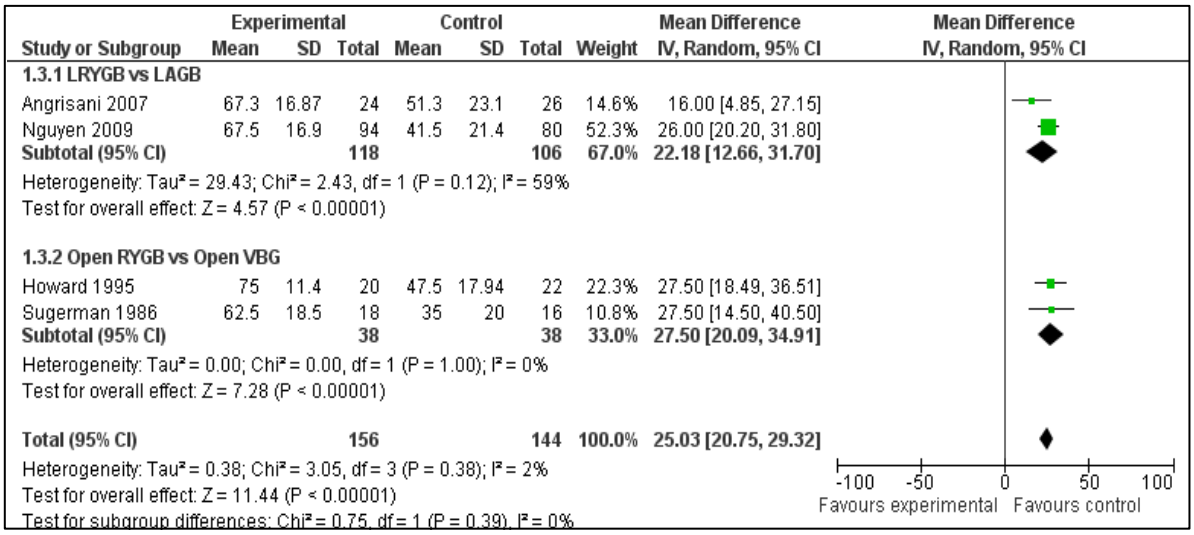

Figure E3: Body mass index loss at 2 year: Gastric Bypass

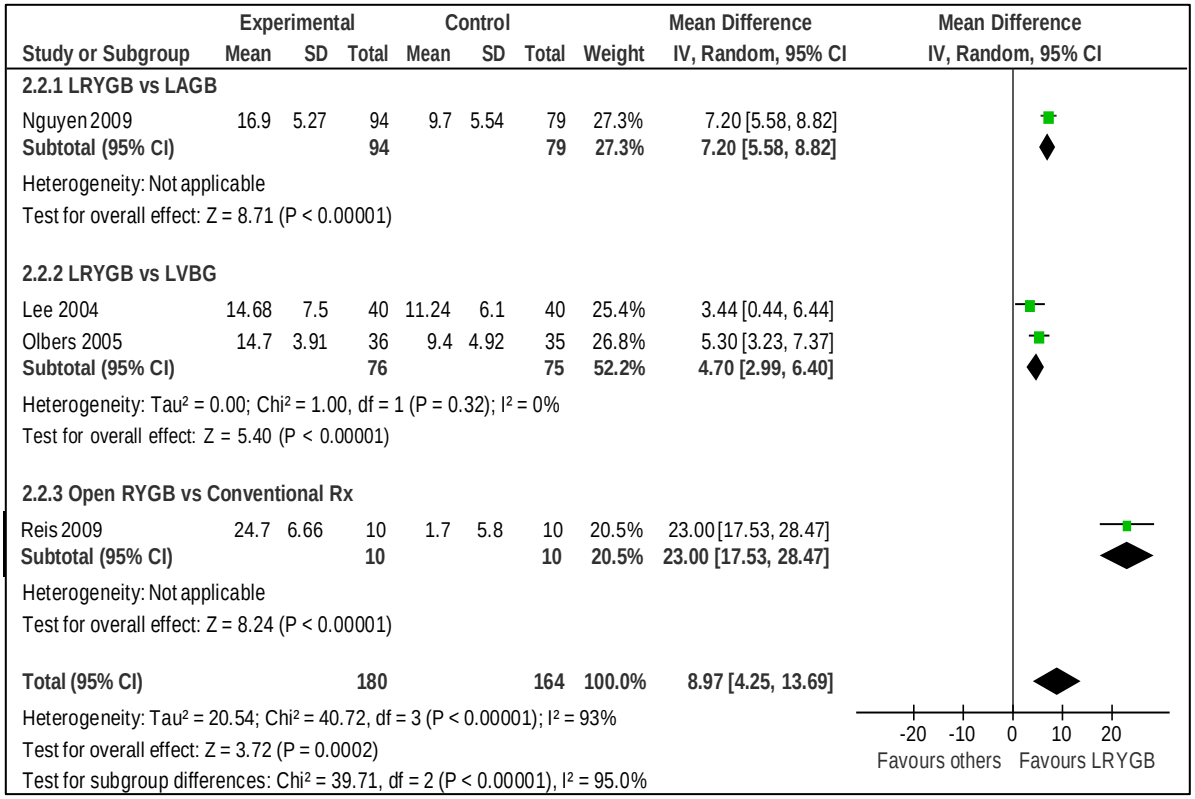

Figure E4: Body mass index loss at 3 year: Gastric Bypass

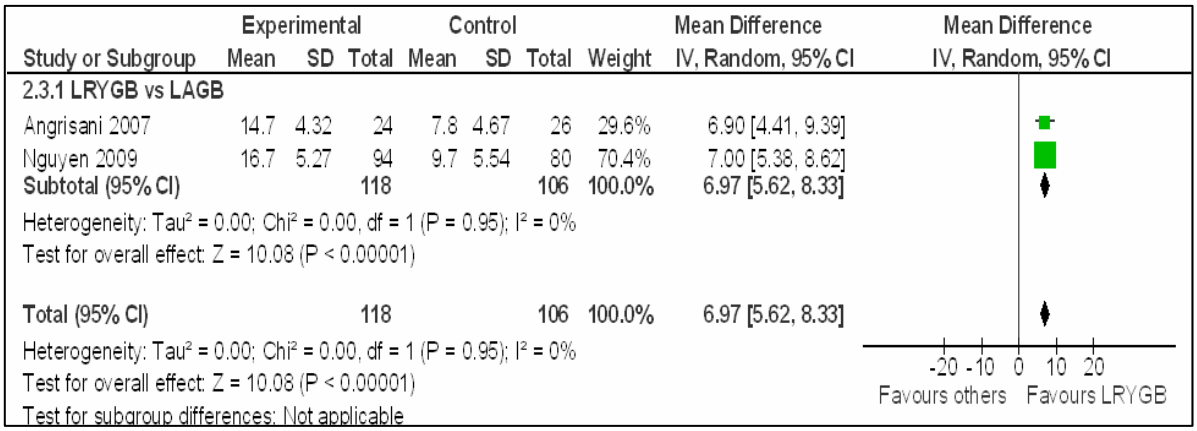

Figure E5: Weigh loss (Kg) at 2 year: Gastric Bypass

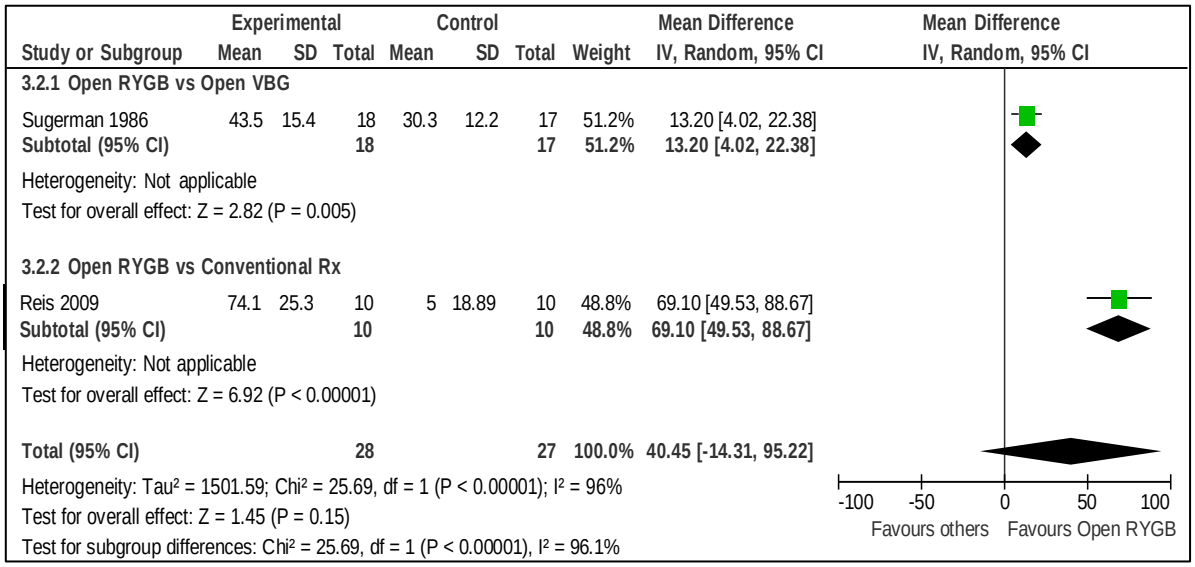

Figure E6: Weigh loss (Kg) at 3 year: Gastric Bypass

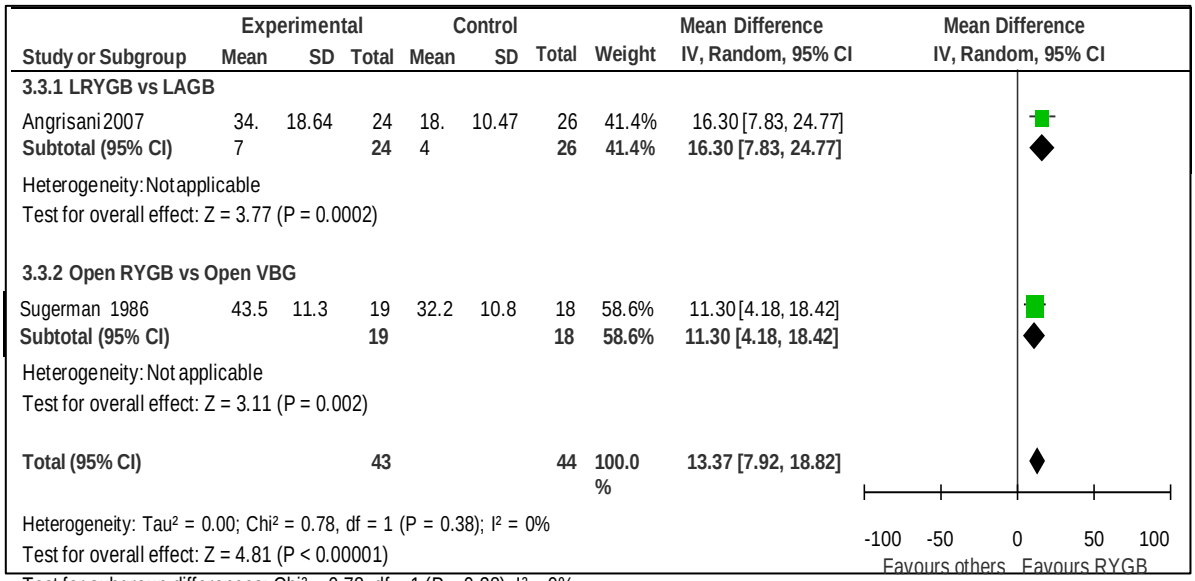

Figure E7: Percent of excess weight loss at 2 year: Adjustable gastric banding

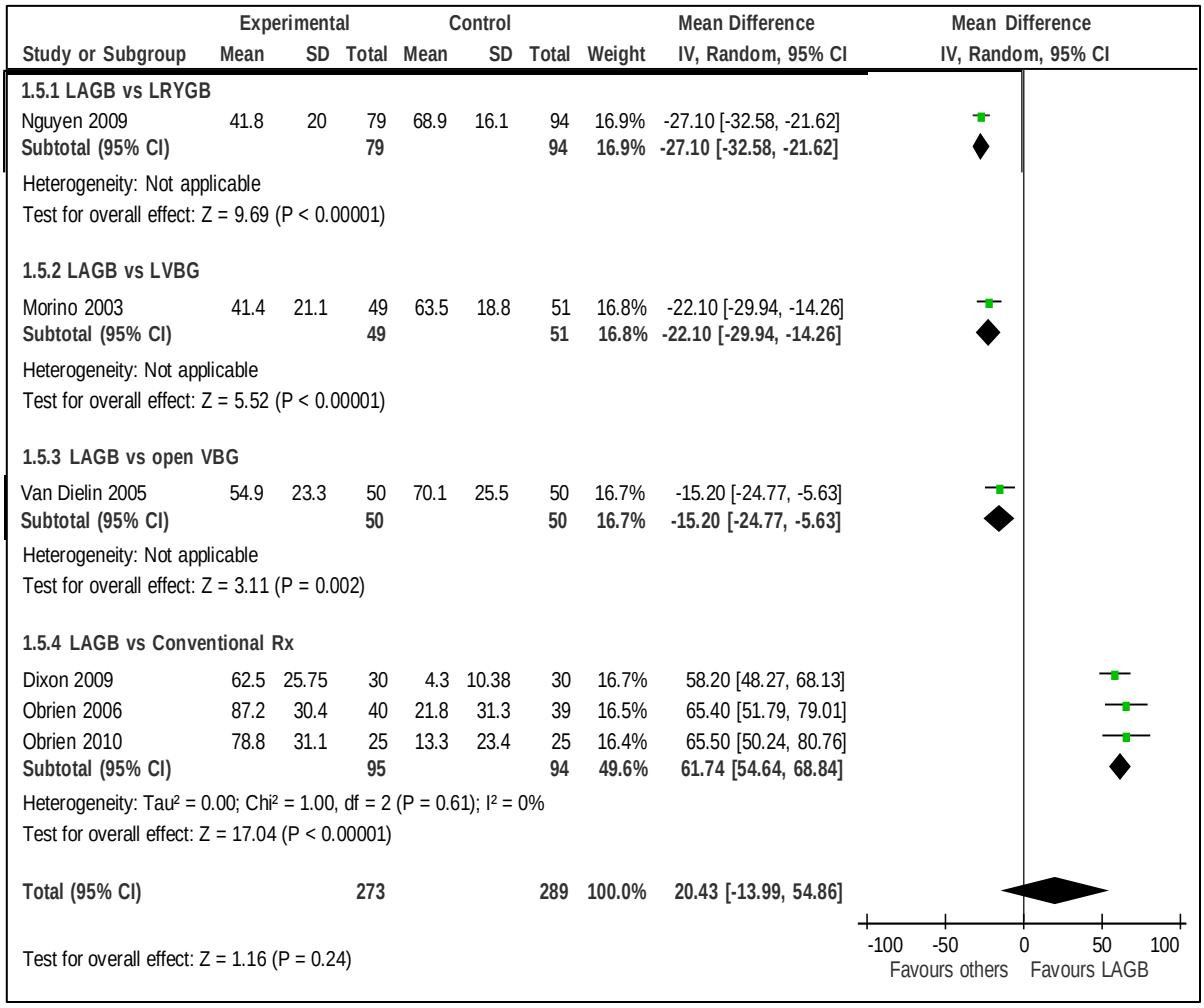

Figure E8: Percent of excess weight loss at 3 year: Adjustable gastric banding

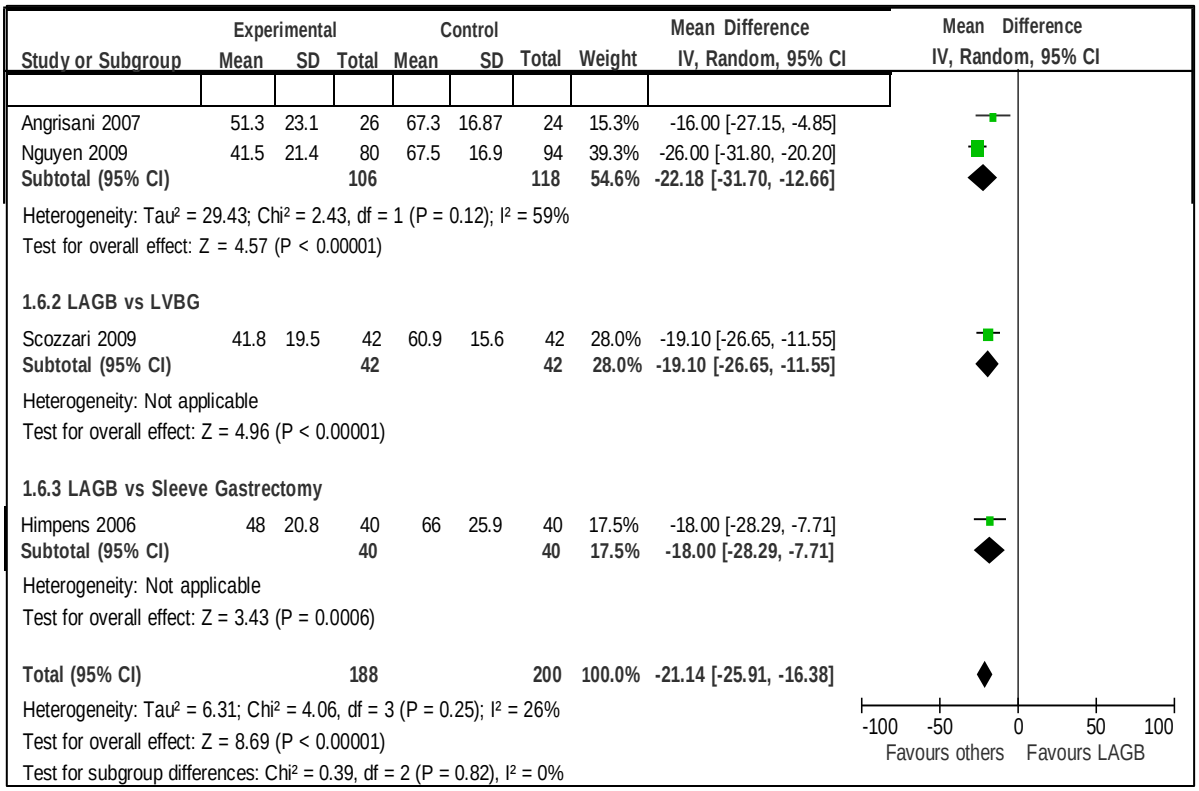

Figure E9: Body mass index loss at 2 year: Adjustable gastric banding

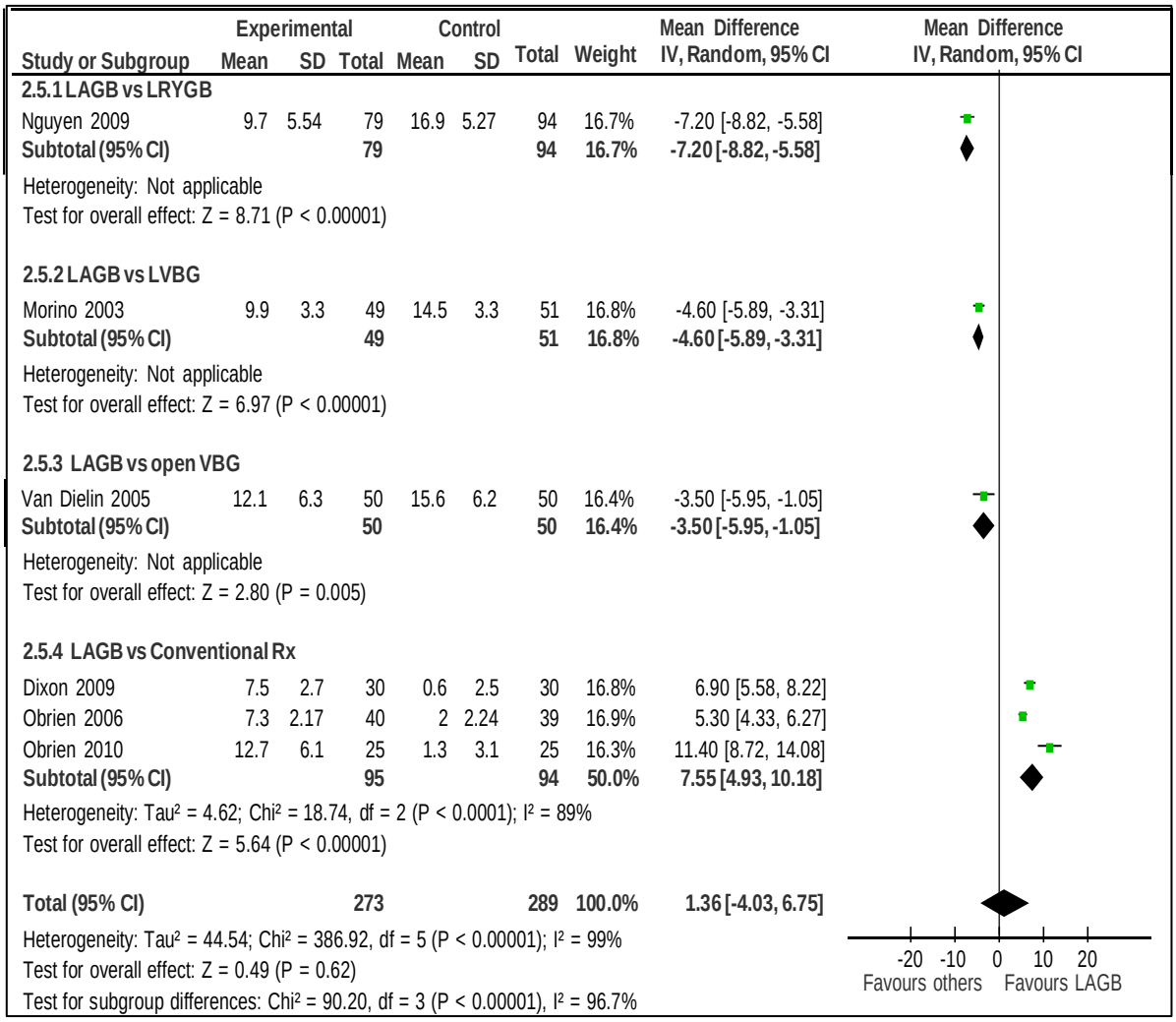

Figure E10: Body mass index loss at 3 year: Adjustable gastric banding

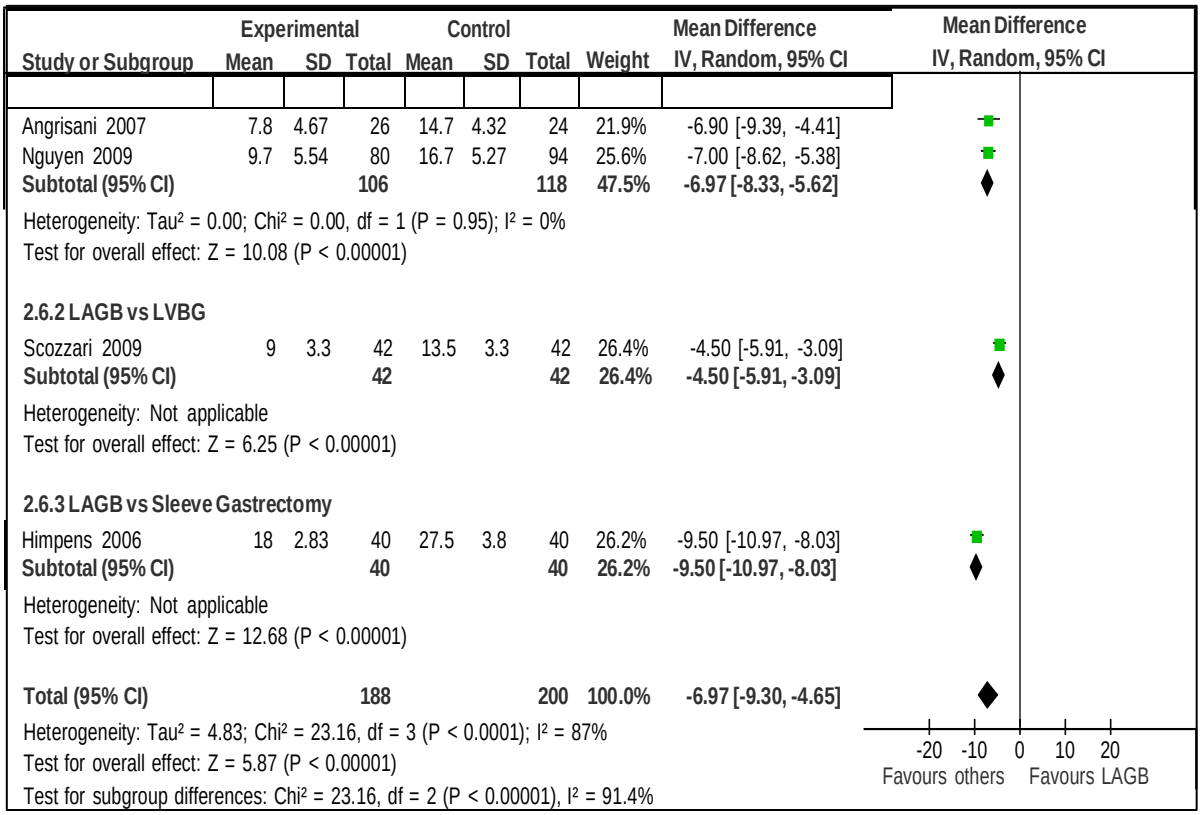

Figure E11: Weight change (Kg) at 2 year: Adjustable Gastric Banding

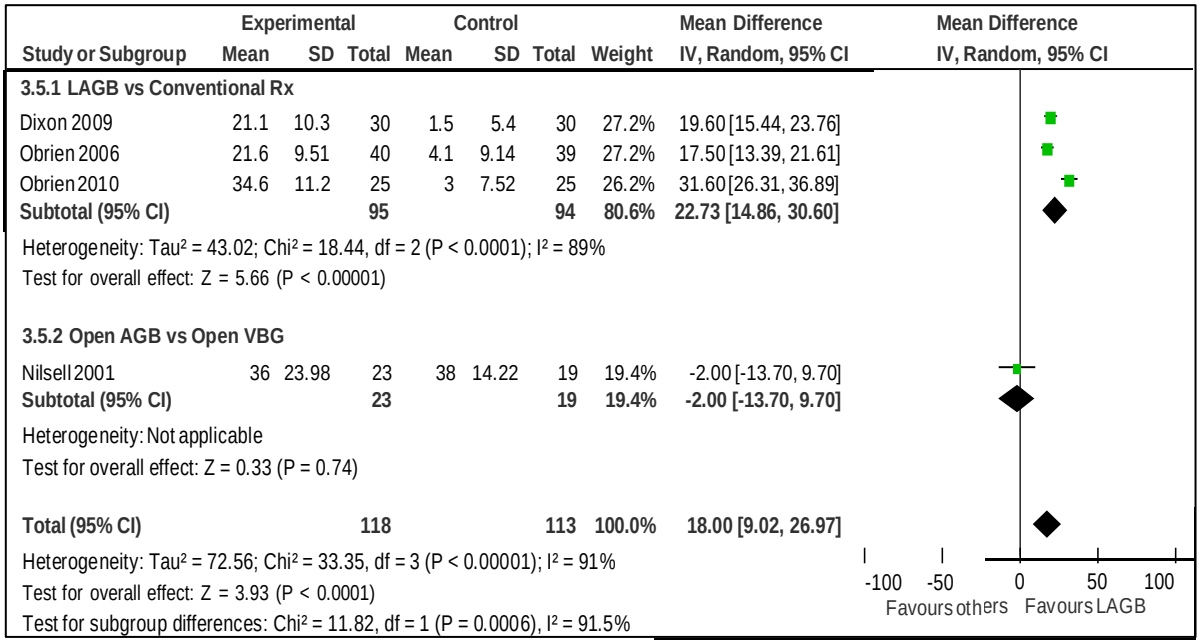

Figure E12: Weight change (Kg) at 3 year: Adjustable Gastric Banding

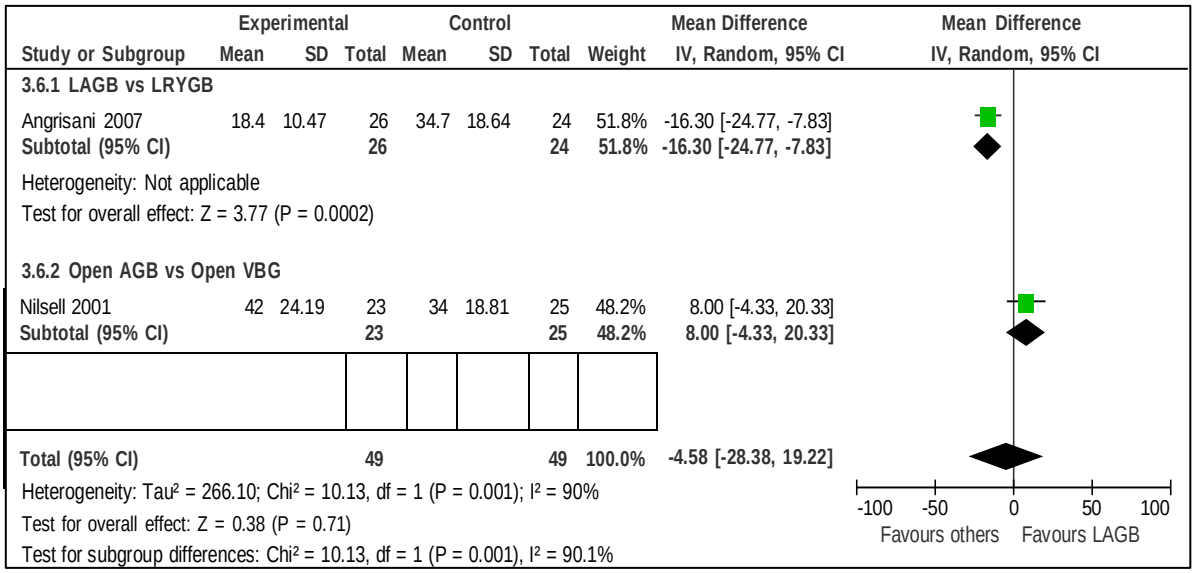

Figure E13: Percent of excess weight loss at 2 year: Vertical Banded Gastroplasty

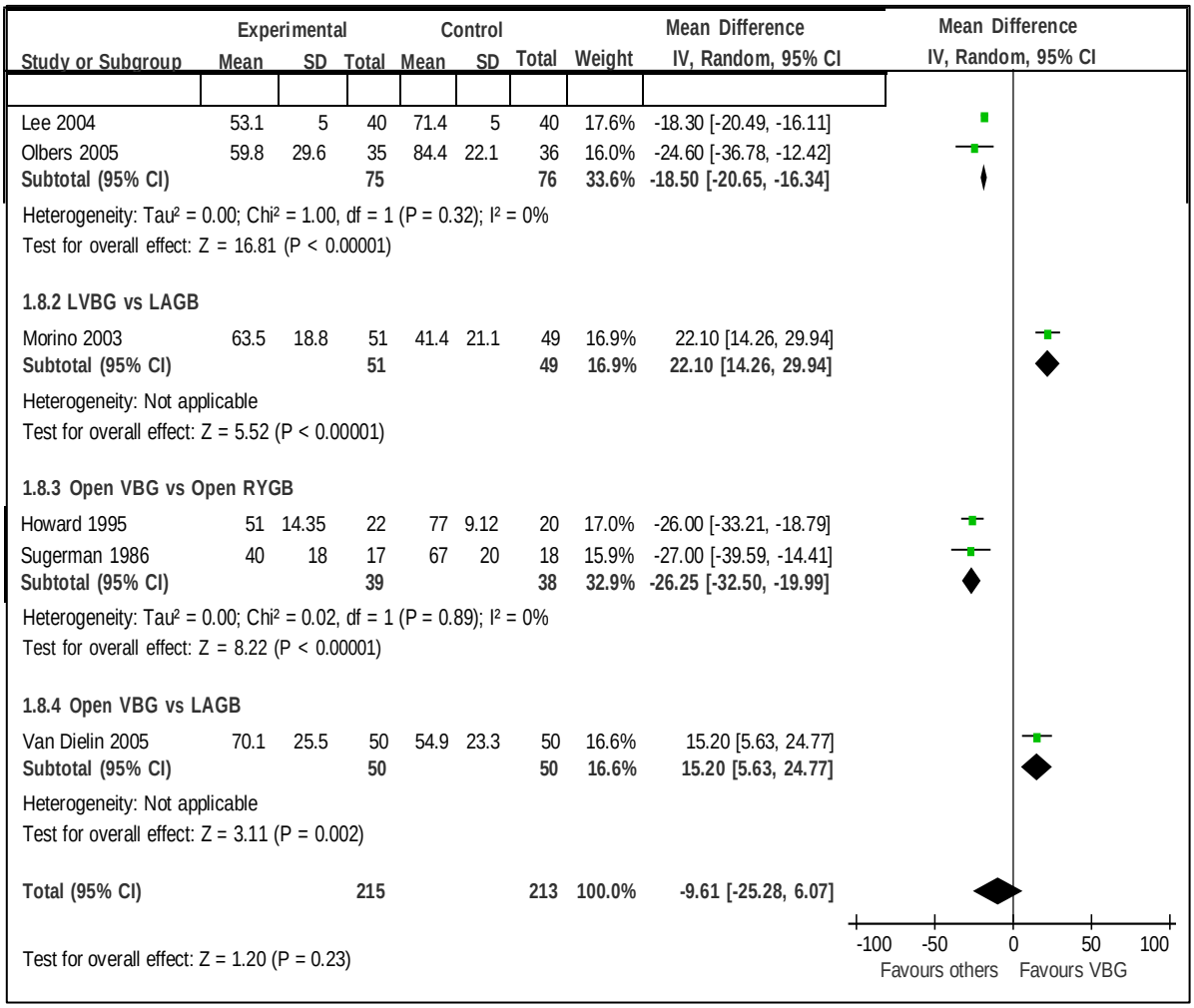

Figure E14: Percent of excess weight loss at 3 year: Vertical Banded Gastroplasty

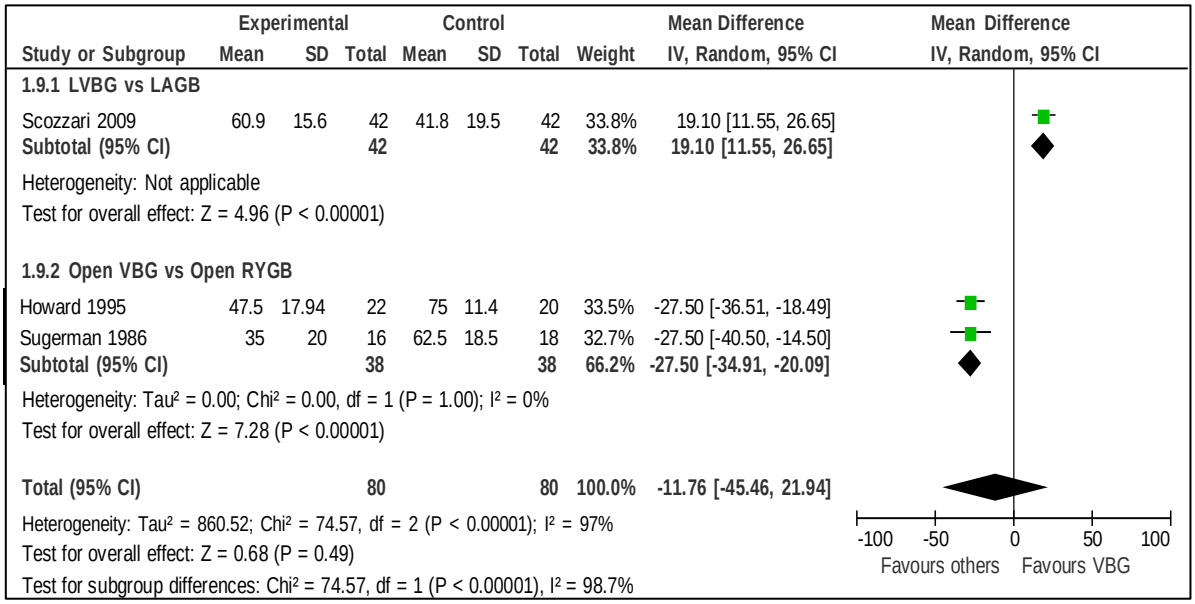

Figure E15: Body mass index loss at 2 year: Vertical Banded Gastroplasty

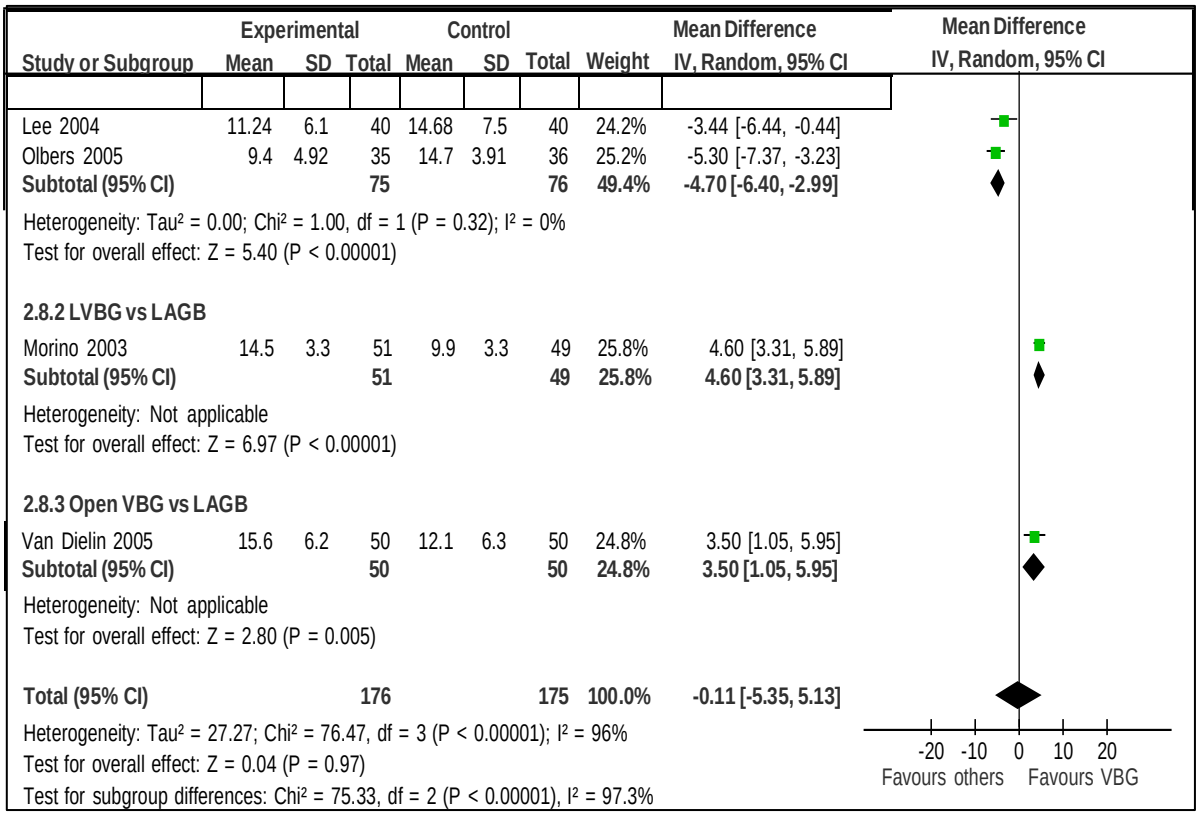

Figure E16: Body mass index loss at 3 year: Vertical Banded Gastroplasty

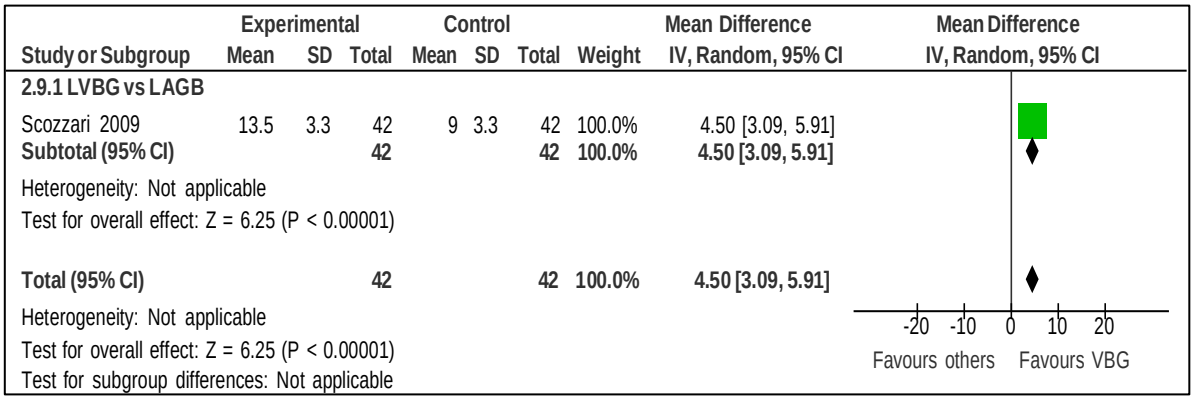

Figure E17: Weight change (Kg) at 2 year: Vertical Banded Gastroplasty

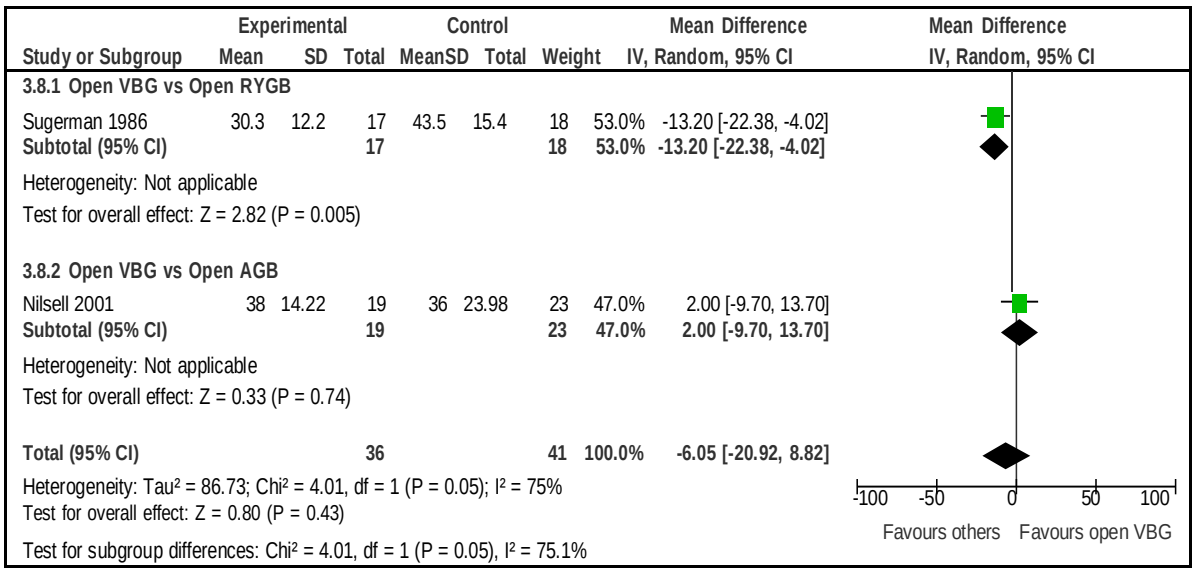

Figure E18: Weight change (Kg) at 3 year: Vertical Banded Gastroplasty

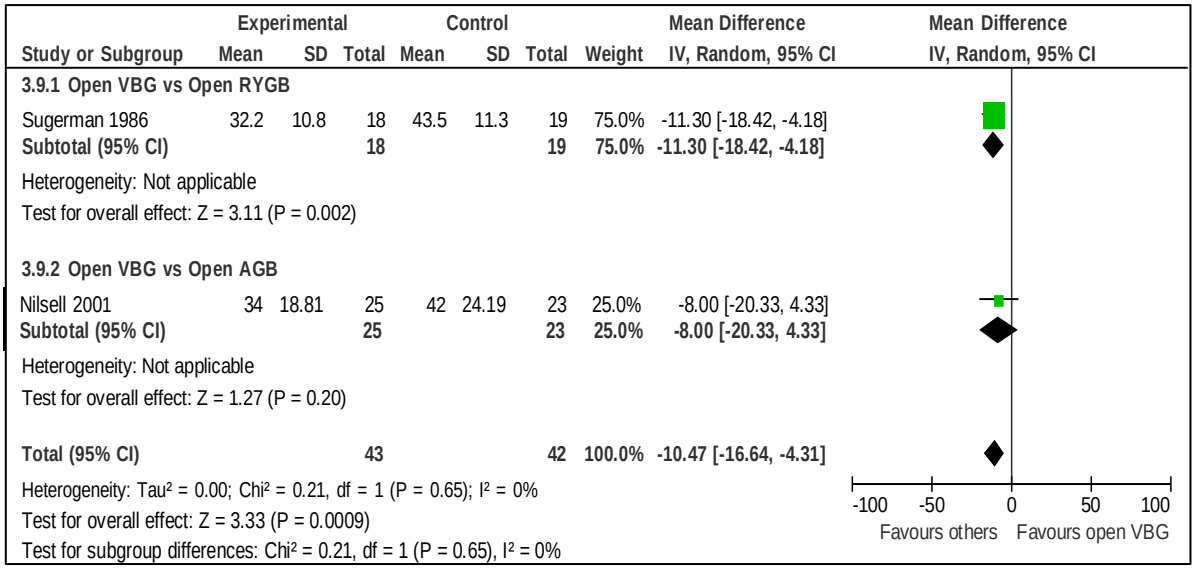

Figure E19: Percent of excess weight loss at 3 year: Sleeve Gastrectomy

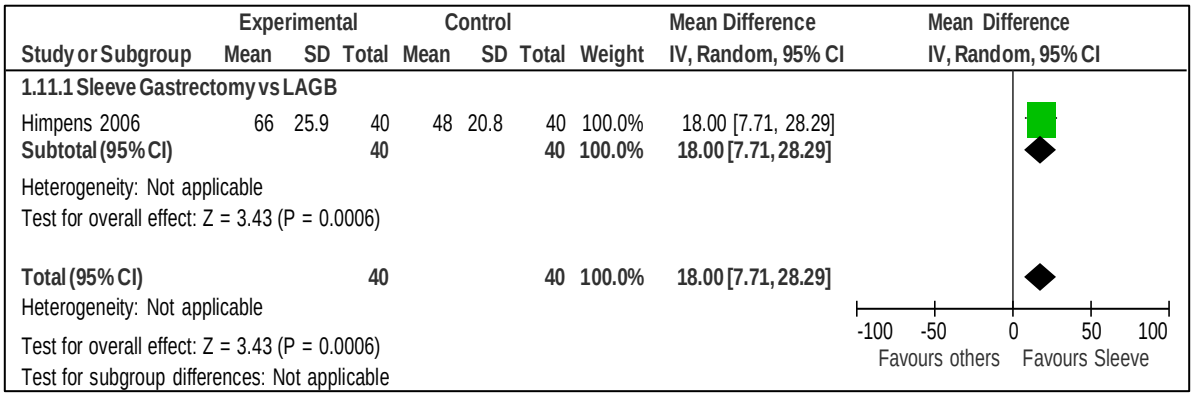

Figure E20: Body mass index loss at 3 year: Sleeve Gastrectomy

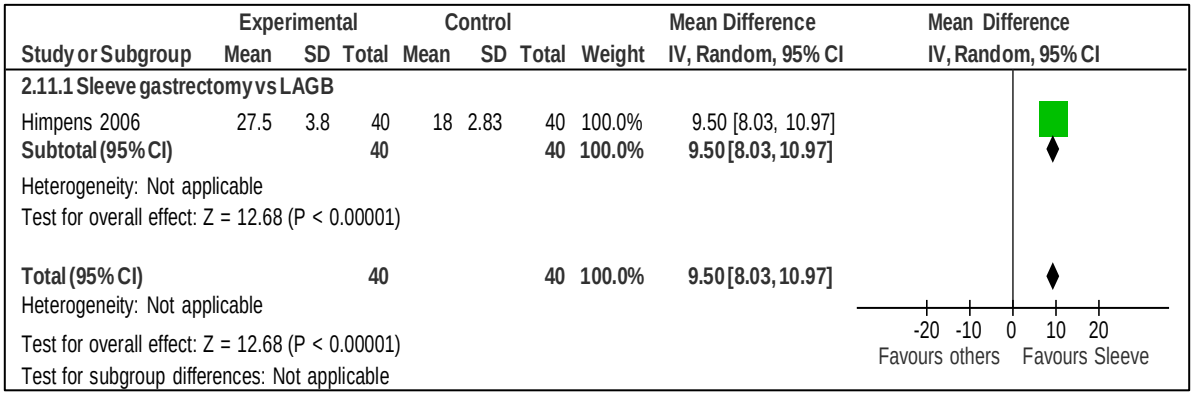

Figure E21: Percent of excess weight loss at 2 year: Conventional Therapy

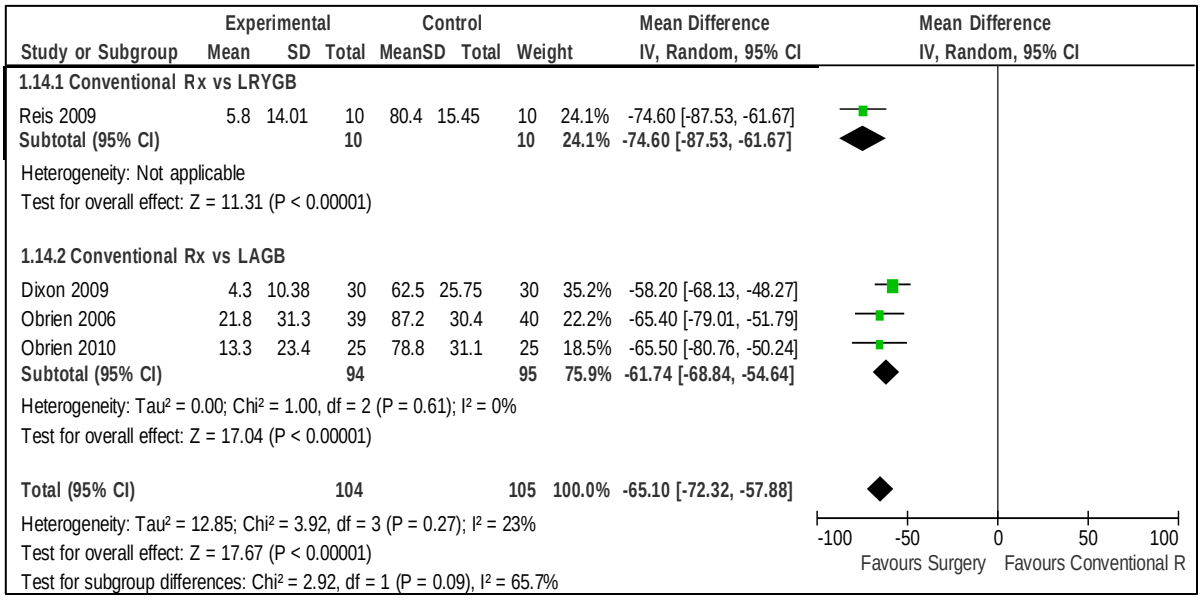

Figure E22:Body mass index loss at 3 year: Conventional Therapy

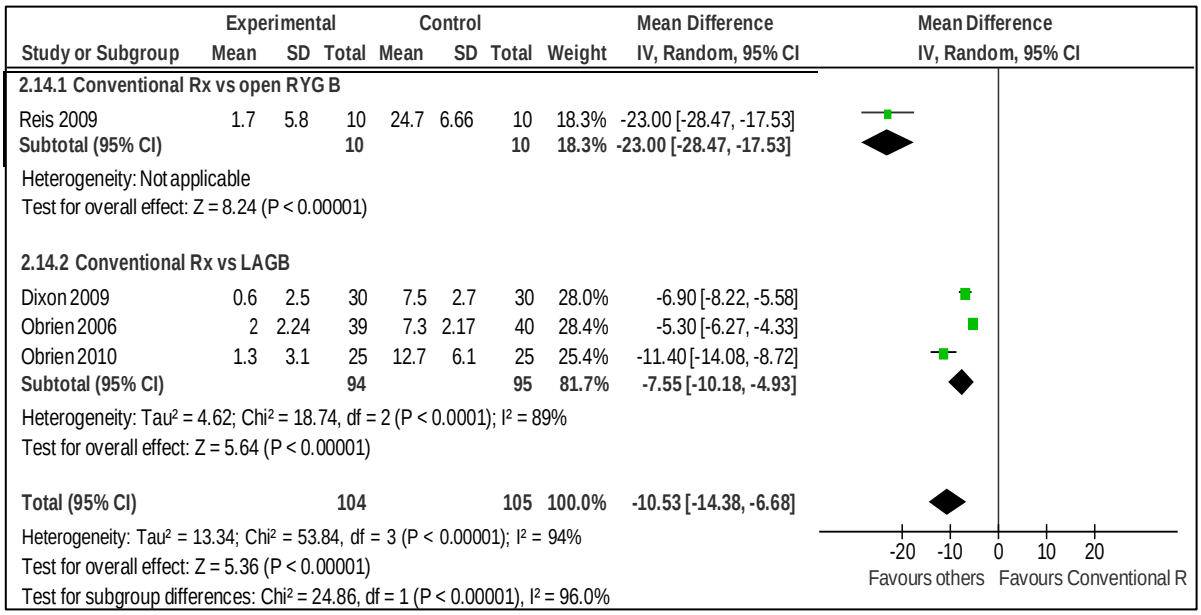

Figure E23: Weight change (Kg) at 2 year: Conventional Therapy