Gloy et al. Meta-analysis bariatric surgery: Appendix

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Appendix Table 1 Search Strategy in MEDLINE via pubmed

1. "obesity"[MeSH Terms]
2. OR "obesity"[All Fields]
3. OR "obese"[All Fields]
4. OR "overweight"[MeSH Terms]
5. OR "overweight"[All Fields]
6. OR ("over"[All Fields] AND "weight"[All Fields])
7. OR "weight loss"[MeSH Terms]
8. OR ("weight"[All Fields] AND "loss"[All Fields])
9. OR "weight loss"[All Fields]
10. **Or/1-9**
11. bariatric surgeries[All Fields]
12. OR bariatric surgery[All Fields]
13. OR bariatric surg*[All Fields]
14. OR bariatric surgery[MeSH Terms]
15. OR "gastric bypass"[MeSH Terms]
16. OR ("gastric"[All Fields] AND "bypass"[All Fields])
17. OR "gastric bypass"[All Fields]
18. OR "digestive system surgical procedures"[MeSH Terms]
19. OR ("digestive"[All Fields] AND "system"[All Fields] AND "surgical"[All Fields] AND "procedures"[All Fields])
20. OR "digestive system surgical procedures"[All Fields]
21. OR ("gastrointestinal"[All Fields] AND "surgery"[All Fields])
22. OR "gastrointestinal surgery"[All Fields]
23. OR "biliopancreatic diversion"[MeSH Terms]
24. OR ("biliopancreatic"[All Fields] AND "diversion"[All Fields])
25. OR "biliopancreatic diversion"[All Fields]
26. OR ("gastric"[All Fields] AND banding[All Fields])
27. OR gastric band*[All Fields]

28. OR LAGB[All Fields]
29. OR (lap[All Fields] AND band [All Fields])
30. OR "gastrectomy"[MeSH Terms]
31. OR "gastrectomy"[All Fields]
32. OR (malabsorptive[All Fields] AND "surgery"[Subheading])
33. OR (malabsorptive[All Fields] AND "surgery"[All Fields])
34. OR (malabsorptive[All Fields] AND "surgical procedures, operative"[MeSH Terms])
35. OR (malabsorptive[All Fields] AND "surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields])
36. OR (malabsorptive[All Fields] AND "operative surgical procedures"[All Fields])
37. OR Roux en Y[All Fields]
38. OR (duodenal[All Fields] AND switch[All Fields])
39. **OR/ 11-38**
40. randomized controlled trial [Publication Type]
41. OR randomized controlled trial [All Fields]
42. OR randomized [All Fields]
43. OR randomised [All Fields]
44. OR randomly [All Fields]
45. **OR/ 40-44**
46. **10 AND 39 AND 45 AND "humans"[MeSH Terms]: 931**

Appendix Table 2 Search Strategy Embase (4 Dec 2012)

No.	Query	Results without updated results
#1		858
#1.36	**#1.28** AND **#1.33** AND **#1.35** AND [humans]/lim AND [embase]/lim	858
#1.35	**#1.1** OR **#1.2** OR **#1.3** OR **#1.4** OR **#1.5** OR **#1.6** OR **#1.7** OR **#1.8** OR **#1.9** OR **#1.10** OR **#1.11** OR **#1.12** OR **#1.13** OR **#1.14** OR **#1.15** OR **#1.16** OR **#1.17** OR **#1.18** OR **#1.19** OR **#1.20** OR **#1.21** OR **#1.34**	158272
#1.34	**gastric** AND **band***	7067
#1.33	**#1.29** OR **#1.30** OR **#1.31** OR **#1.32**	712654
#1.32	**Randomly**	229732
#1.31	**Randomised**	73319
#1.30	**Randomized**	527454
#1.29	**randomized** AND **controlled** AND **trial**	396285
#1.28	**#1.22** OR **#1.23** OR **#1.24** OR **#1.25** OR **#1.26** OR **#1.27**	320394
#1.27	**'weight loss'**/exp	79637
#1.26	**'weight'**/exp AND **loss**	5443
#1.25	**over** AND **'weight'**/exp	5927
#1.24	**'overweight'**/exp	245747
#1.23	**Obese**	89505
#1.22	**'obesity'**/exp	245747
#1.21	**duodenal** AND **switch**	673
#1.20	**'roux en y'**	7093
#1.19	**roux** AND **en** AND **y**	8352
#1.18	**malabsorptive** AND **surgical** AND **'procedures'**/exp	389

No.	Query	Results without updated results
#1.17	**malabsorptive** AND **'surgery'**/exp	**479**
#1.16	**'gastrectomy'**/exp	**34975**
#1.15	**lap** AND **band**	**539**
#1.14	**'gastric banding'**/exp	**3672**
#1.13	**Lagb**	**1009**
#1.12	**gastric** AND **banding**	**4453**
#1.11	**biliopancreatic** AND **diversion**	**986**
#1.10	**'biliopancreatic diversion'**/exp	**1525**
#1.9	**'gastrointestinal surgery'**:ab,ti	**1676**
#1.8	**gastrointestinal** AND **'surgery'**:ab,ti	**93621**
#1.7	**digestive** AND **surgical** AND **'procedures'**:ab,ti	**35859**
#1.6	**'digestive system surgical procedures'**:ab,ti	**0**
#1.5	**gastric** AND **bypass**:ab,ti	**8144**
#1.4	**'gastric bypass'**/exp	**7859**
#1.3	**bariatric** AND **surg***:ab,ti	**11919**
#1.2	**'bariatric surgery'**/exp	**12988**
#1.1	**'bariatric surgeries'**	**156**

Appendix Table 3: Summary of ongoing trials

Trial ID	Title	intervention 1	intervention 2	intervention 3	Status June 2012	completion date	publication indexed
http://ClinicalTrials.gov/show/							
NCT00939679	ERGEM: Effect of Roux-en-Y Gastric Bypass Surgery on Energy Metabolism.	Roux-en-Y gastric bypass surgery	low calorie diet (1,000 kcal/day)	-	ongoing, but not recruiting	April 2013*	no
NCT01047735	A Randomized Trial to Compare Surgical and Medical Treatments for Type 2 Diabetes	Roux-en-Y Gastric Bypass Surgery	Laparoscopic Adjustable Gastric Banding	Lifestyle Weight Loss Intervention	ongoing, but not recruiting	July 2011*	no
NCT01197963	A Surgical Approach to the Management of Type II Diabetes Mellitus in Patients With a BMI Between 25-35 kg/m2	Sleeve Gastrectomy and Ileal transposition	dietary and medical management	-	recruiting	December 2012*	No
NCT01501201	Comparison of Gastric By-Pass and Optimized Medical Treatment in Obese Diabetic Patients in Terms of Mortality, Glycemic Control, and Cost Effectiveness - Prospective, Multicenter, Randomized Study	laparoscopic Roux-en-Y Gastric Bypass (RYGBP)	optimized medical management	-	recruiting	September 2014*	No
NCT01278823	Effect of Bariatric Surgery on Mechanisms of Type 2 Diabetes	laparoscopic roux en y gastric bypass operation	medical management latest type 2 diabetes medications, lifestyle / behavior modification and dietary regimen	-	recruiting	December 2013	No
NCT01295229	Feasibility, Efficacy, and Mechanisms of Surgical vs Medical Diabetes Treatment	laparoscopic Roux-en-Y gastric bypass (RYGB)	Lifestyle Intervention	-	recruiting	June 2012*	no
NCT00641251	Global Randomized Prospective Study of Intensive Medical Management of Type 2 Diabetes, With and Without Gastric Bypass Surgery	intensive medical ma-gement	RYGB & intensive medical management	-	ongoing, but not recruiting	December 2013*	Yes
NCT00428571	Laparoscopic Bariatric Surgery for Treatment of Type 2 Diabetes in Obese Patients With End Organ Damage: A Prospective Randomized Controlled Pilot Study	laparoscopic gastric bypass surgery	laparoscopic adjustable gastric banding	Intensive Medical Management	recruiting	April 2013*	no
NCT01041768	Multicentric Prospective Randomized Controlled Trial on the Effect of Gastric Bypass and Bilopancreatic Diversion on Type 2 Diabetes Mellitus in Patients With BMI Between 30 and 35	Biliopancreatic diversion	gastric bypass	standard antidiabetic care	recruiting	December 2010*	no

Trial ID	Title	intervention 1	intervention 2	intervention 3	Status June 2012	completion date	publication indexed
http://ClinicalTrials.gov/show/							
NCT00626964	Prevention of Coro-ry Heart Disease in Morbidly Obese Patients. Lifestyle Intervention, Low Energy Diet or Bariatric Surgery	Gastric Sleeve	Gastric bypass	Intensive Lifestyle Intervention Program	unknown	January 2011*	no
NCT00888836	Prospective Randomized Controlled Trial on the Effect of Gastric Bypass and Biliopancreatic Diversion on Type 2 Diabetes Mellitus in Patients With BMI > 35 vs. Medical Therapy	Gastric bypass	Bilio-pancreatic diversion	anti-diabetic drugs and behavioral suggestions	completed	October 2011*	Mingrone 2012
NCT01231308	Roux-en-Y-Gastric Bypass (RYGB) Versus Lifestyle Modification Plus Medical Therapy in the Treatment of Type 2 Diabetes in Overweight-to-Moderately Obese Patients: A Randomized Clinical Trial	Roux-en-Y-Gastric Bypass	Intensive lifestyle modification and Optimal medical Therapy	-	recruiting	October 2013*	no
NCT01352403	Severe Obesity: Bariatric Surgery vs. Life-Style-Intervention Wurzburg Adipositas Study - WAS	gastric bypass	intensive life style intervention	-	recruiting	June 2016	no
NCT00965302	Sleeve Gastrectomy vs Medical Management for Remission of Diabetes in Mild to Moderately Obese Patients	Laparoscopic sleeve gastrectomy	Intensive medical management	-	enrolling	April 2011*	no
NCT00432809	STAMPEDE: Surgical Therapy And Medications Potentially Eradicate Diabetes Efficiently	Advanced medical therapy for diabetes	P laparoscopic Roux-en-Y Gastric Bypass (RYGB)	laparoscopic sleeve gastrectomy	ongoing, but not recruiting	January 2012*	Schauer 2012
NCT01073020	Surgery or Lifestyle With Intensive Medical Management in the Treatment of Type 2 Diabetes (SLIMM-T2D)	Laparoscopic Adjustable Gastric Band	Procedure: Roux-en-Y Gastric Bypass (Surgery)	Intensive Medical Diabetes & Weight Management	recruiting	January 2013*	
NCT01053130	The Effect of Weight Loss Surgery on Preservation of Kidney Function and Cardiovascular Disease Risk Factors in Obese Patients With Stages 3-4 Chronic Kidney Disease: a Randomised Controlled Trial	laparoscopic sleeve gastrectomy	weight management program	-	recruiting	January 2012*	no publication
NCT01353066	Multicenter Randomized Prospective Trial on the Effects of Intensive Medical Treatment of Type 2 Diabetes With and Without Roux-in-Y Gastric Bypass Surgery on Carotid Intima Media Thickness in Grade I Obesity (BMI 30,0-34,9 kg/m2)	Intensive Medical Treatment	IMM+Roux-en-Y Gastric Bypass (RYGBP)	-	Not yet open	Not reported	no publication

Trial ID	Title	intervention 1	intervention 2	intervention 3	Status June 2012	completion date	publication indexed
http://ClinicalTrials.gov/show/							
-Research Register: http://public.ukcrn.org.uk/search/ , Controlled Trials http://www.controlled-trials.com/, EU Clinical Trials Register (EUCTR) (https://www.clinicaltrialsregister.eu/): No eligible ongoing trial found * Final data collection date for primary outcome measure - = not applicable, because no third intervention included							

Appendix Table 4: Definition of Type 2 diabetes and metabolic syndrome remission

Diabetes remission	
Study	**Definitions**
Dixon 2008	= fasting plasma glucose ≤ 7mmol/L (126 mg/dL) and HbA1c ≤ 6.2% without medication ,
Mingrone 2012	= fasting plasma glucose ≤ 5.6mmol/L and HbA1c ≤ 6.5% for one year without medication,
Schauer 2012	= HBA1c ≤ 6% without diabetes medication.
Liang 2013	Not reported
Metabolic syndrome	
Study	**Definitions**
Dixon 2008, Dixon 2012 and O'Brien 2006	defined by the US National Cholesterol Education Program Adult Treatment Panel III criteria. At least 3 of the following criteria had to be met: waist circumference ≥ 102 cm for men and ≥ 88 cm for women; triglycerides level: ≥ 150 mg/dL (1.7 mmol/L); high-density lipoprotein cholesterol: ≤ 40 mg/dL (1.04 mmol/L) in men and ≤ 50 mg/dL (1.29 mmol/ L) in women; plasma pressure: systolic, ≥ 130 mmHg and diastolic, ≥85 mmHg; fasting plasma glucose: ≥ 110 mg/dL (6.1 mmol/L).
O'Brien 2010	defined metabolic syndrome by the age-specific adolescent criteria of Joliffe and Janssen (Jolliffe and Janssen 2007) linked to the Adult Treatment Panel III21 criteria.
Schauer 2012	did not report a definition.

Appendix Table 5: List of included studies and corresponding publications

Study identification	**Reference**
Mingrone 2012	Mingrone, G., S. Panunzi, et al. (2012). "Bariatric surgery versus conventional medical therapy for type 2 diabetes." N Engl J Med 366(17): 1577-1585. Pokala, S. (2012). "Gastric bypass or biliopancreatic diversion increases remission from type 2 diabetes in obese adults." Annals of Internal Medicine 157(2): 2-12.
Schauer 2012	Schauer, P. R., S. R. Kashyap, et al. (2012). "Bariatric surgery versus intensive medical therapy in obese patients with diabetes." N Engl J Med 366(17): 1567-1576.
Reis 2010	Reis, L. O., W. J. Favaro, et al. (2010). "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(5): 736-744.
O'Brien 2006	O'Brien, P. E., J. B. Dixon, et al. (2006). "Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program: A randomized trial." Annals of Internal Medicine 144(9): 625-633. Dixon, J. B., B. J. Strauss, et al. (2007). "Changes in body composition with weight loss: obese subjects randomized to surgical and medical programs." Obesity (Silver Spring) 15(5): 1187-1198.
Ikramuddin 2013	Ikramuddin, S., J. Korner, et al. (2013). "Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: the Diabetes Surgery Study randomized clinical trial." JAMA **309**(21): 2240-2249.
Liang 2013	Liang, Z., Q. Wu, et al. (2013). "Effect of laparoscopic Roux-en-Y gastric bypass surgery on type 2 diabetes mellitus with hypertension: A randomized controlled trial." Diabetes Research and Clinical Practice.
O'Brien 2010	O'Brien, P. E., S. M. Sawyer, et al. (2010). "Laparoscopic adjustable gastric banding in severely obese adolescents: A randomized trial." JAMA - Journal of

	the American Medical Association 303(6): 519-526.
Dixon 2008	Dixon, J. B., P. E. O'Brien, et al. (2008). "Adjustable gastric banding and conventional therapy for type 2 diabetes: A randomized controlled trial." Obstetrical and Gynecological Survey 63(6): 372-373.
Dixon 2012	Dixon, J., L. Schachter, et al. (2012). "Surgical versus conventional therapy for weight loss treatment of obstructive sleep apnea: A randomized controlled trial." Obesity Research and Clinical Practice 6: 29. Dixon, J. B., L. M. Schachter, et al. (2012). "Surgical vs conventional therapy for weight loss treatment of obstructive sleep apnea: A randomized controlled trial." JAMA - Journal of the American Medical Association 308(11): 1142-1149.
Mingrone 2002	Mingrone, G., A. V. Greco, et al. (2002). "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(2): 455-462.
Heindorff 1997	Heindorff H, Hougaard K, Larsen PN. Laparoscopic adjustable gastric band increases weight loss compared to dietary treatment: A randomized study. *Obesity surgery* 1997;7(4):300-01.

Appendix Table 6: Patient recruitment

Study	Recruitment	Site	Period	Patients assessed for eligibility (n)	Inclusion criteria
Mingrone 2012	Patients visiting the Catholic University anti-diabetic center in Rome, Italy	Day Hospital of Metabolic Diseases and Diabetology of the Catholic University of Rome, Italy	April 2009 to October 2011	72	Age 30 to 60 years, BMI 35 or more, a history of type 2 diabetes of at least 5 years, a glycated hemoglobin level of 7.0% or more
Schauer 2012	Use of electronic medical records and advertisements in local media	Cleveland Clinic, Cleveland, USA	March 2007 to January 2011	218	Age 20 to 60 years, BMI of 27 to 43, a diagnosis of type 2 diabetes (glycated hemoglobin level, >7.0%, uncontrolled)
Reis 2010	Selection from 117 men undergoing evaluation and follow-up for gastric bypass	University of Campinas, Sao Paulo, Brazil	First semester of 2007	117	NR (only exclusion criteria given: Exclusion criteria were co-morbidities requiring regular drug usage (statin, antihypertensive, oral anti-diabetic), endocrine disease (except mild hypogonadism) or recent hormonal manipulation (thyroid／other hormonal reposition／block in the last 3 months), testicular impairment, previous history of alcohol or tobacco abuse and phosphodiesterase type-5 inhibitor usage.
Ikramuddin 2013	Recruitment of patients participating in a lifestyle and medically managed weight control program through mass media advertisements, contact with professional groups, presentations at public events and a practice based database	University of Minnesota, Columbia University Medical Center, National Taiwan University Hospital, Min Sheng General Hospital, Mayo Clinic in Rochester, USA and Taiwan	April 2008 to December2011	2648	Age 30 to 60 years, BMI > 28 in accordance with the WHO Asia-Pacific classification for obesity T2DM diagnosed according to WHO criteria, T2DM with hypertension of 5–10 years with hypertension defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic (DBP) ≥90 mmHg as per 1999 WHO/ISH criteria; insulin therapy in combination with oral administration of drugs for 12 months; glycated hemoglobin (HbA1c) ≥ 7%; seronegative for antibodies against insulin, islet cells and glutamic acid decarboxylase (GAD), C-peptide level ≥ 0.3 mg/L.
Liang 2013	NR	Southwest Hospital of third military medical University in Chongqing , China	June 2008 to July 2011	NR	Age 30 to 67 years, BMI 30.0 to 39.9, under a physician's care for type 2 diabetes for at least 6 months before recruitment, had hemoglobin A1c (HbA1c) levels of 8.0% or higher at the time of entry, and had a serum C-peptide level higher than 1.0 ng/mL (to convert C-peptide to nanomoles per liter, multiply by 0.331) 90 minutes after a liquid mixed meal (250 calories, 6 g fat, 40 g carbohydrate, and 9 g protein), absence of conditions that would contraindicate surgery, such as serious cardiovascular disease, previous gastrointestinal surgery, psychological concerns, or history of malignancy
O'Brien 2006	Newspaper advertisement	Community Clinic Melbourne dedicated to obesity management or in the clinics of a university department of surgery.	May 2000 to November 2001	340	Age 20 to 50 years; BMI of >30; identifiable problems, including an obesity-related comorbid condition; had attempted to reduce weight over at least the previous 5 years.

O'Brien 2010	Newspaper advertisement	Community Clinic of Melbourne or at a special clinic at the Centre for Adolescent Health, Royal Children's Hospital, Surgery at a private clinic, Melbourne Australia	May 2005 to September 2008	163	Age 14 to 18 years; BMI >35; identifiable medical complications or psychosocial difficulties and evidence of attempts to lose weight by lifestyle means for more than 3 years.
Dixon 2008	Newspaper advertisement	University Obesity Research Center, Melbourne Australia	December 2002 to November 2004	158	Age 20 to60 years, BMI of 30 - 40, type 2 diabetes diagnoses within previous 2 years, no renal impairment or diabetic retinopathy
Dixon 2012	Potential participants were screened initially at sleep clinics and referred to trial physicians	7 sleep clinics Melbourne, Australia	September 2006 to March 2009	130	Age 18 to 60 years, BMI 35 to 55, apnea-hypopnea index (AHI) of 20 events/hour or more diagnosed within the previous 6 months with recommendation to commence CPAP therapy and at least 3 prior significant weight loss attempts
Mingrone 2002	NR	Istituto di Medicina Internae Geriatria, Universita` Cattolica del Sacro Cuore, Rome, Italy	June 1998 to December 2000	NR	NR (only exclusion criteria given: pregnancy, history or diagnosis of diabetes, heart disease, hypertension, or other chronic diseases, hormone replacement therapy chronic steroid therapy, a history of alcohol abuse or drug abuse, and glucose intolerance, defined as a 2 h glucose levels of >140mg/dL after a 75g oral glucose load and of stable weight within plus minus 2 kg, 6 months before testing.
Heindorff 1997	NR	Department of Gastrointestinal Surgery, University Copenhagen	October 1995 - 1996	NR	NR

Appendix Table 7: Description of study groups

Study	study groups (n)	Bariatric surgery group 1	Bariatric surgery group 2	Non-surgical treatment group (control)			Follow-up visits	Follow-up time
				In general	Diet	physical activity		
Mingrone 2012	3	Laparoscopic RYGB; Daily multivitamin and mineral supplementation	Open BPD; Daily multivitamin and mineral supplementation	Treatment by a diabetologist, dietician, and nurse; programs for diet and lifestyle modification	Reduced energy and fat intake (<30% total fat)	Increased (>30 minutes of brisk walking every day, possibly moderate intensity aerobic activity twice a week.	At months 1,3,6,9,12, and 24	2 years
Schauer 2012	3	Laparoscopic RYGB; Daily multivitamin and mineral supplementation**;** **+same therapy as non-surgical group**	Laparoscopic SG; Daily multivitamin and mineral supplementation; **+same therapy as non-surgical group**	Recommendations of the American Diabetes Association 2011 (weight management, lifestyle counseling, frequent home glucose monitoring, treatment by diabetes specialist, diabetes education, behavioral modification	Recommendations by the American Diabetes Association (American Diabetes 2011): either low-carbohydrate, low-fat calorie-restricted, or Mediterranean diets; encouraged to participate in the Weight Watchers program	> 150 min/week of moderate intensity aerobic physical activity (50–70% of maximum heart rate); in the absence of contraindications, encouraged to perform resistance training three times per week	Every 3 months	1 year
Reis 2010	2	weight loss plan with nutritional education for low energy diet and intensive behaviour modification for daily physical activity guided by multidisciplinary team of nutritionist, physical educator, psychologist before and after surgery: distal gastrectomy involving three-quarters of the stomach with a 250–300 mL residual stump and Roux-en-Y reconstruction.	-	general multidisciplinary team direction no intensive program	general information about healthy food choices	General guidance on increasing physical activity	At months 4 and 24	2 years
Ikramuddin 2013	2	Laparoscopic RYGB, low-caloric diet with meal replacement 2 weeks before operation, Daily multi and mineral supplementation**;** **+same therapy as non-surgical group**	-	The lifestyle-medical management protocol consisted of 2 components—lifestyle modification designed to produce maximum achievable weight loss and medications to control glycemia and cardiovascular disease risk factors while facilitating weight loss. Only US Food and Drug Administration–approved medications were used. Both groups met regularly with a trained interventionist to discuss strategies for facilitating weight management and increasing physical activity, including self-monitoring, stimulus control, problem solving, social support, cognitive behavior modification, recipe modification, eating away from home, and relapse prevention	All lifestyle/medical management participants were given calorie intake targets of 1200, 1500, or 1800 kilocalories per day, depending on body weight, with the goal of producing a weight loss of 1 to 2 pounds per week. Portion-controlled diets using meal replacements, structured menus, and calorie counting were encouraged to help participants stay within calorie limits	Both groups were advised to progressively increase their level of moderate-intensity physical activity (such as walking) to a total of 325 minutes per week	24 weekly meetings over the first 6 months, biweekly meetings between months 7 and 9, and monthly meetings between months 10 and 12	1 year

Liang 2013	3	Laparoscopic RYGB,	-	Usual care, treated by a multi-disciplinary team, individualized medical treatment with aim HbA1c<7%, blood pressure < 40/90mmHg, fat intake below 30%, second control group received Exenatide (Exendin-4, GLP-1 analogue) treatment	Nutritional goal based on an individual energy intake and reducing fat intake to <30%, saturated fat to <10% and increasing high fiber intake	>30 min of brisk walking every day associated with moderate-intensity aerobic activity twice a week	At baseline, 3, 6, 9 and 12 months	1 year
O'Brien 2006	2	LAGB; (Inamed, Santa Barbara, CA); lifestyle changes, good eating practices, increased physical activity	-	Behavioral modification, education and professional support on appropriate individualized eating and exercise behavior	First 6-months: very-low-calorie diet (500 to 550 kcal/d) using Optifast (Novartis, Fremont, Michigan) daily for 12 weeks, followed by a transition phase over 4 weeks combining some very-low-calorie meals with 120 mg of orlistat, and then orlistat before all meals, followed by further courses of very-low-calorie diets or orlistat as tolerated	Exercise advice, no further details	Every 2 weeks during the very-low-calorie diet program, then every 4 to 6 weeks	2 years
O'Brien 2010	2	LAGB (Allergan, Irvine, California); eating rules centered on having 3 or fewer small protein-containing meals per day, eaten slowly (1 min/ bite), at least 30 minutes of formal exercise per day and to maintain a high level of activity through the day.	-	Behavioral modification, parents were invited to participate in a specific educational program that included sports motivational talks, nutritional education, and discussions of the psychological aspects of adolescence	Individualized diet plans ranging between 800 and 2000 kcal/d, depending on age and weight status	Increased, target of 10 000 steps per day on pedometer) with a structured exercise schedule of at least 30 minutes a day; decrease of sedentary activities with a limit of 2-hour computer or television screen time, increase of formal exercise including bicycle riding, walking, and swimming plus informal individual and group activities. A personal trainer was provided to each participant for a 6-week period.	Every 6 weeks	2 years
Dixon 2008	2	LAGB (Inamed Health, Santa Barbara, CA)**;** **+same therapy as non-surgical group**	-	Open access to a general physician, dietician, nurse, diabetes educator, lifestyle modification program	Individualized diet plans to reduce intake of energy intake, fat (<30%) and saturated fats, recommendation of food intake with low glycemic index and high fiber foods, very low calorie diets and medications continued to be available and applied if appropriate	Increased, 10 000 steps per day and 200 minutes per week of structured activity including moderate intensity aerobic activity and resistance exercise	Every 6 weeks	2 years

Dixon 2012	2	LAGB (Allergan Health)**;** **+same therapy as non-surgical group**	-	Open access to a bariatric physician, sleep physician, and dietician, management of obstructive sleep apnea, dietary, physical activity, and behavioral programs were individualized.	Dietary Guidelines for Australian Adults and the Australian Guide to Healthy Eating; planned daily deficit of 500 kcal from estimated energy requirements; Initial very low –energy diet (Optifast, Nestle, Australia) program, with meal very low calorie diets continued to be available and used more or less intensively	Walking and 200 minutes/week of structured activity, including moderate-intensity aerobic activity and resistance exercise	Every 4 to 6 weeks	2 years
Mingrone 2002	2 (4)	BPD	-		20kcal/7kg fat free mass (FFM), 55% carbohydrates, 30% fat and 15% protein. The caloric content of the diet was modified every 6 months according to the DEXA measurement of FFM.	Not reported	Unclear, at least every 6 months	2 years
Heindorff 1997	2	LAGB	-	Dietary treatment, no further details	Not reported	Not reported	Every 4 weeks	40 weeks

Legend: FFM = fat-free mass; LAGB = Laparoscopic Adjustable Gastric Banding; RYGB = Roux-en-Y Gastric Bypass; SG = Sleeve Gastrectomy

Appendix Table 8: Summary on risk of bias assessment

Study		Mingrone 2012	Schauer 2012	Reis 2010	O'Brien 2006	Ikramuddin 2013	Liang 2013	O'Brien 2010	Dixon 2008	Dixon 2012	Mingrone 2002	Heindorff 1997
A) Risk of selection bias	Was the sequence generation adequate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
	Was group allocation concealed?	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Unclear
	Judgment	*Low*	*Low*	*Low*	*Low*	*Low*	*Unclear*	*Unclear*	*Unclear*	*Unclear*	*High*	*Unclear*
B) Risk of performance bias	Blinding of patients	No	No	No	No	No	No	No	No	No	No	No
	Blinding of health care providers	No	No	No	No	No	Unclear	No	No	No	No	No
	Judgment	*High*	*High*	*High*	*High*	*High*	*High*	*High*	*High*	*High*	*High*	*High*
C) Risk of Detection bias (body weight loss)	Blinding of data collectors	Yes	No	No	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	*Unclear*
	Blinding of outcome adjudicators	Yes	No	No	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Unclear
	Blinding of data analysts	Yes	No	No	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Unclear
	Judgment	*Low*	*High*	*High*	*Unclear*	*Low*	Unclear	*Unclear*	*Unclear*	*Unclear*	*Low*	Unclear
D) Risk of attrition bias	Were all randomized patients analyzed?	No	Yes	Yes	No	Yes*	No	No	Yes	Yes	Yes	Yes
	Were patients analyzed in the groups to which they were randomized?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	low	Yes

	Incomplete outcome data addressed? **(continuous data)**	Yes (incomplete outcome data was balanced across groups, non-surgical group: 1% of patients randomized were not analyzed and in the bariatric surgery group: 0.5%.	Yes (Missing data was addressed by last observation carried forward incomplete outcome data was: non-surgical group: 18% bariatric surgery group: 1% of patients randomized; reasons for missing outcome data were likely to be related to true outcome)	Yes (No missing data)	No (Missing data was not addressed in the analysis, in-complete outcome data was not balanced. Non-surgical treatment group: 18%, bariatric surgery group: 3% of patients randomized; reasons for missing outcome data were likely to be related to true outcome)	Yes* (missing data were imputed by multiple imputation for the data presented in the publication, but not for the data sent by email. Missing data was balanced across groups for body weight loss but not for other outcomes: non-surgical group: 5-13%, bariatric surgery group: 5%; of patients randomized)	No (Missing data was not addressed in the analysis. Missing data was not balanced across groups: Non-surgical group: 3% Bariatric surgery group: 14%, reasons unclear	No (Missing data was not addressed in the analysis, incomplete outcome data was not balanced across groups: non-surgical group: 28% of patients randomized were not analyzed and bariatric surgery group: 4%; reasons for missing outcome data were likely to be related to true outcome)	No (Baseline data carried forward analysis for missing data was used. This was not regarded as appropriate, Missing data: non-surgical group: 13%, bariatric surgery group: 3% of patients randomized . Thus this did not represent a conservative case scenario and is likely to overestimate the surgical effect)	Yes (missing data were imputed by multiple imputation, Missing data: non-surgical group: 13%, bariatric surgery group: 7%; of patients randomized)	yes (no missing data)	Yes (No missing outcome data)
	Judgment	*Low*	*Low*	*Low*	*High*	*Low*	*Unclear*	*High*	*High*	*Low*	*Low*	*Low*

	Incomplete outcome data addressed? **(diabetes remission)**	Yes, to account for missing data, a conservative case scenario was assumed: all 2 missing patients in the non-surgical group achieved diabetes remission. However a risk ratio was not reported	Yes Missing data was addressed by last observation carried forward incomplete outcome data was: non-surgical group: 18% bariatric surgery group: 1% of patients randomized; reasons for missing outcome data were likely to be related to true outcome	n.a.	n.a.	n.a.	No	n.a.	Yes To account for missing data, a conservative case scenario was assumed: all 4 missing patients in the non-surgical group achieved diabetes remission. However a risk ratio was not reported			n.a.
	Judgment	*Low*	*Low*	n.a.	n.a.	n.a.	High	n.a.	*Low*	*Unclear*	*n.a.*	*n.a.*

	Incomplete outcome data addressed? **(Metabolic syndrome remission)**	n.a.	Yes Missing data was addressed by last observation carried forward incomplete outcome data was: non-surgical group: 18% bariatric surgery group: 1% of patients randomized; reasons for missing outcome data were likely to be related to true outcome	n.a.	No Missing data was not addressed in the analysis, incomplete outcome data was not balanced across groups	n.a.	n.a.	No Missing data was not addressed in the analysis, incomplete outcome data was not balanced across groups	No Missing data was not addressed in the analysis, incomplete outcome data was not balanced across groups	Yes missing data were imputed by multiple imputation	n.a.	n.a.
	Judgment	n.a.	*Low*	n.a.	*High*	*n.a.*	*n.a.*	*High*	*High*	*Low*	n.a.	n.a.
E) Risk of reporting bias	Were expected outcomes reported or outcomes addressed pre-specified?	Yes	Yes	Unclear, adverse events were poorly reported	Yes	Yes	Unclear, adverse events were poorly reported;	yes	Yes	Yes	No adverse events were not reported in the publication but upon request	No
	Are exact data available? **(body weight loss)**	Yes	Yes	Yes	Yes	Yes	No, body weight at the end of follow up is not reported	yes	Yes	Yes	Yes	Yes

	Are exact data available? **(other outcomes)**	One year data was not reported for most data, except for glycated HBA1c, which is however only presented in figure.	Yes	Yes	Quality of life data only presented in figure, meaning no point estimates are available for this outcome; numbers for relative change in body weight in table differs from numbers in text.	Yes	Yes	Quality of life data only presented in figure, no exact data available	No (loss of excess body weight: measure of variance only presented in figure; BMI baseline values in table different from text on p. 319 "weight loss"; no measure of variance given for BMI at 24 months)	yes	yes	n.a.
	Judgment	*Low*	*Low*	*Low*	*Low*	*Low*	*Low*	*Low*	*Low*	*Low*	*Low*	*Low*
F) Other forms of bias	Funding	Mixed industry/ public	Mixed industry/ public	Not reported	Mixed industry/ public	Mixed industry/ public	Public	Mixed industry/public	Mixed industry/public	Mixed industry/ public	public	NR
	Other	No other	yes, block randomization was used in an unblinded trial which can mean it is possible to predict future assignments	Unclear selection criteria of patients, unclear inclusion criteria	Yes , less than half of the patients assessed for eligibility were finally included	No	Unclear, how many patients were assessed for eligibility	No other	Yes, block randomization was used in an unblinded trial which can mean it is possible to predict future assignments	No other	Yes, recruitment of patients was poorly described	Due to lack of full text publication, information was unclear for most items

*for data in the publication yes, but not for data additionally obtained.

Appendix Table 9: Adverse events

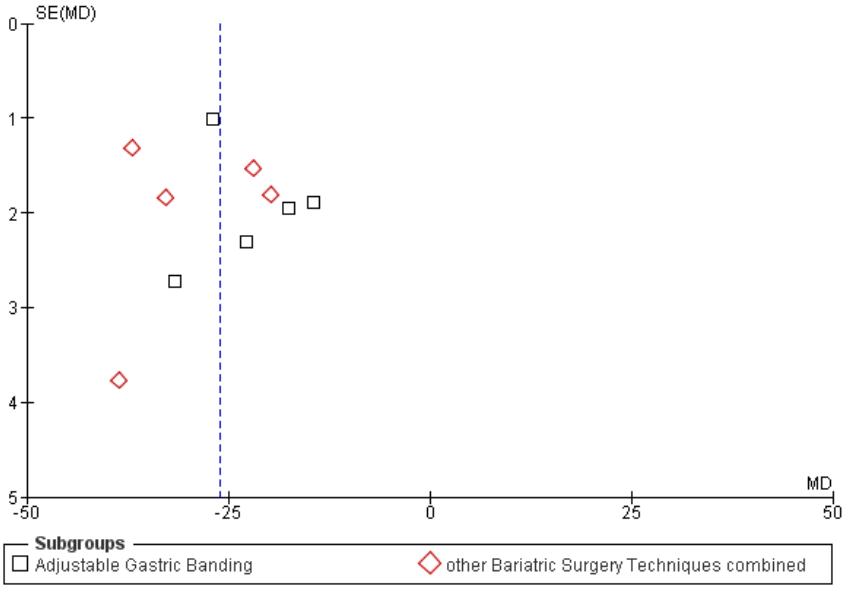
Study	Mingrone 2012			Schauer 2012			Ikramuddin 2013		Liang 2013			O'Brian 2006		O'Brian 2010		Dixon 2008		Dixon 2012		Mingrone 2002		Heindorff 1997	
Study group	control	BPD	RYGB	control	RYGB	SG	control	RYGB	control 1	control 2	RYGB	control	AGB	control	AGB	AGB	control	control	AGB	control	BPD	control	LAGB
Patients (n)	20	19	19	43	50	49	60	60	36	34	31	31	39	25	25	30	30	30	30	33	46	8	8
Acute abdomen																		1					
Anastomotic ulcer					4																		
Anoxic brain injury							0	1															
Angina																	1	1					
Arrhythmia or palpitations				2		1																	
Band removed																1							
Bleeding								1, anasto motic ulcer; 1, uterine															
Blood transfusion needed					1	1																	
Bronchitis							1	0															
Buttock abscess																							
Cardiac and renal failure																		1					
Cataract							0	1															
Cellulitis				1																			
Cholecystectomy					1							4	1	1	1				1				
Depression														1	1			1					

Diarrhea							0	1				1					1	2					
Duodenal ulcer																		1					
Duodenitis							1	0															
Excessive weight gain				3																			
Epilepsy																		1					
Febrile episodes																1							
Gastric pouch enlargement														6	2			1					
Gastritis								1															
Gastrointestinal leak						1		2, Anastomotic leak															
Headache							0	1										1, severe					
Hemoglobin decrease > 5g/dL					1																		
Hernia		1			1													1					
Hyper-triglyceridemia							5	1															
Hypo-albuminemia		2					0	4															
Hypoglycemic episode				35	28	39	4	5								1	1						
Hypokalemia				1	2	2																	
Intestinal occlusion			1																				
Intolerance to metformin																1	3						
intolerance to orlistat												8											
Intravenous treatment for dehydration/ dehydration					4	2	0	1										1					

Iron deficiency anemia		2	2	3	6	6	0	13															
Ketoacidosis					1																		
Kidney stone				1														1					
Nephrolithiasis							2	1															
Neuropathy							2	2															
Obstruction								1 (small bowel)															
Osteopenia (BMD T score, -2)		1																			3		
Osteoporosis (BMD T score, -2.7)		1																					
Pain							1 chest	1, abdo-minal; 1, back,										3, joint	4, joint				
Pancreatitis							1	0															
Pancreatic cancer							2	0															
Perforation																							1
Pleural effusion						1																	
Pneumonia					2														1				2
Pyelonephritis							1	0															
Reoperation		1	1		3	1							4		7	3			1				
Rupture of suture or staple line																							
Suicide attempt							1	0															
Stricture								1															
Transient renal insufficiency					1																		
Toe amputation							0	1															
Urinary tract infection							0	1															
Ureteral stone							1	1															

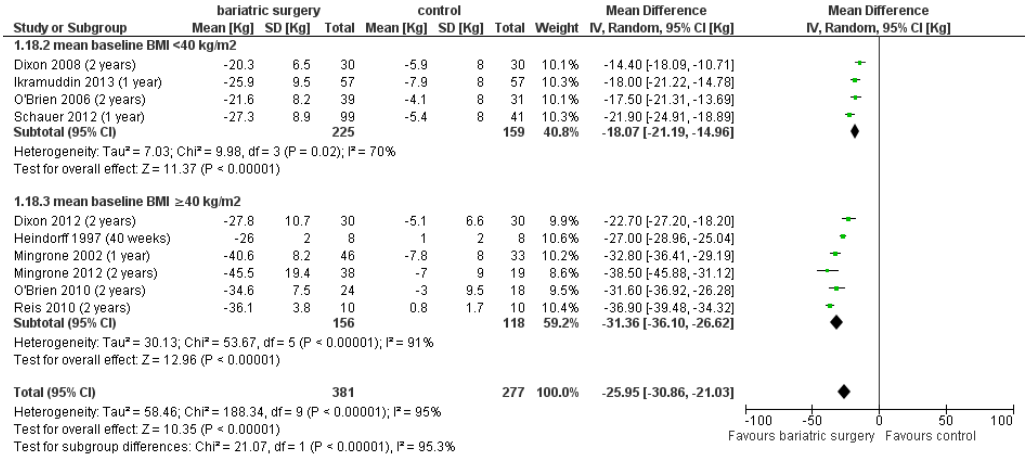
Vasculitic rash																	1						
Vitamin-deficiencies (B and D)							7	15															
Vomiting/nausea									3	13	5												
Wound /5 mm port site infection					1			1			6		1			1							
Wound hematoma								1															

Risk of bias across studies



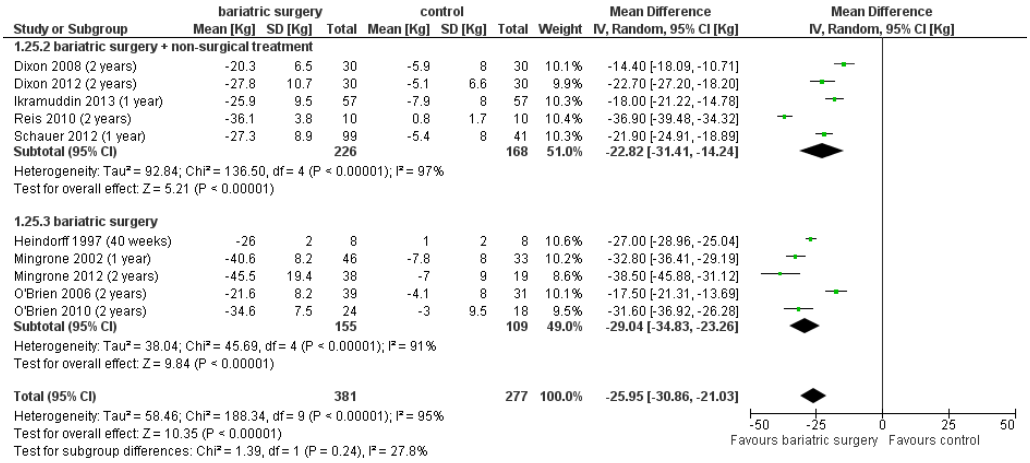
Appendix Figure 1: **Funnel plot**

Body weight, body composition



Appendix Figure 2: Body weight change after bariatric surgery versus non-surgical treatment (control) for patients (subgroups according to mean baseline BMI).

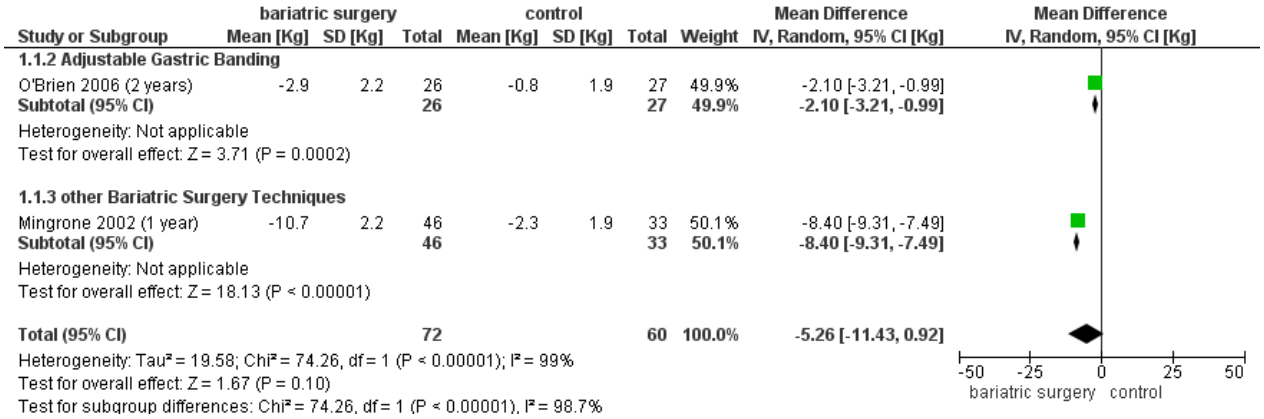
A subgroup analysis was done for the studies which included patients with a mean body mass index (BMI) < 40 at baseline compared to studies which included patients with a mean BMI ≥40 at baseline. Standard deviations (SD) were derived from 95% CI for O'Brien 2010 and Dixon 2012, and were imputed by taking the median SD of the respective groups of the other studies for O'Brien 2006 and Mingrone 2002. Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, I^2= measure of inconsistency (scale: 0 to 100%), IV = Inverse Variance Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).



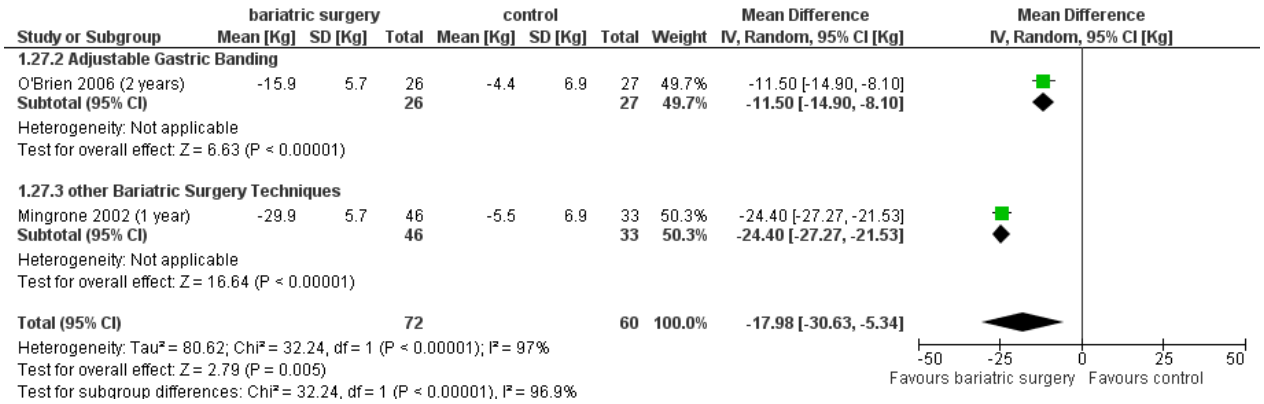
Appendix Figure 3: Body weight change after bariatric surgery versus non-surgical treatment (control) for patients (subgroups according to bariatric surgery plus non-surgical treatment versus bariatric surgery).

A subgroup analysis was done for the studies which offered the treatment of the non-surgical treatment group to the bariatric surgery group as well versus studies which offered none or some other accompanying treatment in the bariatric surgery group. Standard deviations (SD) were derived from the 95% CI for O'Brien 2010 and Dixon 2012, and were imputed by taking the median SD of the respective groups of the other studies for O'Brien 2006 and Mingrone 2002. Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, I^2= measure of inconsistency (scale: 0 to 100%), IV = Inverse Variance Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).

A)



B)

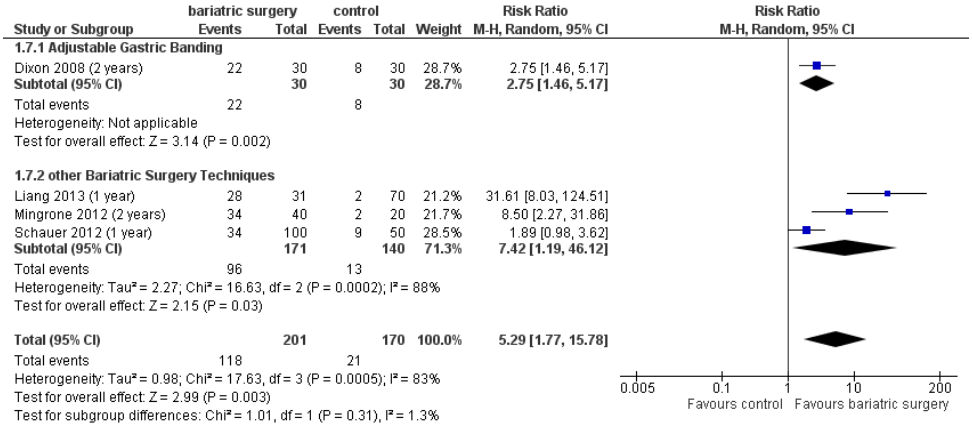


Appendix Figure 4: Change in FFM (A) and FM (B) after bariatric surgery versus non-surgical treatment (control) for obesity.

A subgroup analysis was done for the studies which used AGB versus other bariatric surgery techniques (BPD). FFM and FM were estimated with Dual-X-Ray Absorptiometry (DEXA). Data for O'Brien 2006 was taken from another publication of the same study, but with more missing data (Dixon 2007) for Mingrone 2002 the same SD was assumed. The total DEXA weight loss was -18.8 ± 6.1 and -5.1 ± 7.7 in O'Brien 2006 and - 40.6 and - 7.8 Kg in Mingrone 2002 for the bariatric surgery versus non-surgical treatment group, respectively.

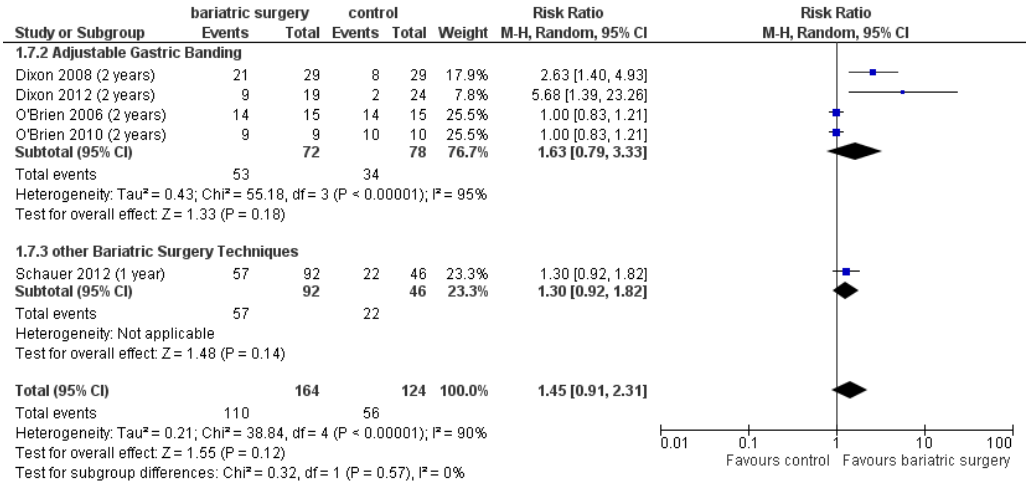
Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, FFM = fat-free mass, FM = Fat mass, I^2= measure of inconsistency (scale: 0 to 100%), IV = Inverse Variance Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).

Diabetes and metabolic syndrome remission



Appendix Figure 5: Type 2 Diabetes Remission after bariatric surgery versus non-surgical treatment (control) for obesity (conservative case scenario).

A subgroup analysis was done for the studies which used AGB versus other bariatric surgery techniques (RYGB, SG or BPD). For the pooled analysis a conservative case scenario was assumed. All missing patients in the non-surgical treatment groups were treated as if they had achieved diabetes remission (n = 20), whereas missing patients in the bariatric surgery groups did not.
Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, I^2= measure of inconsistency (scale: 0 to 100%), M-H = Mantel-Haenzel Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).

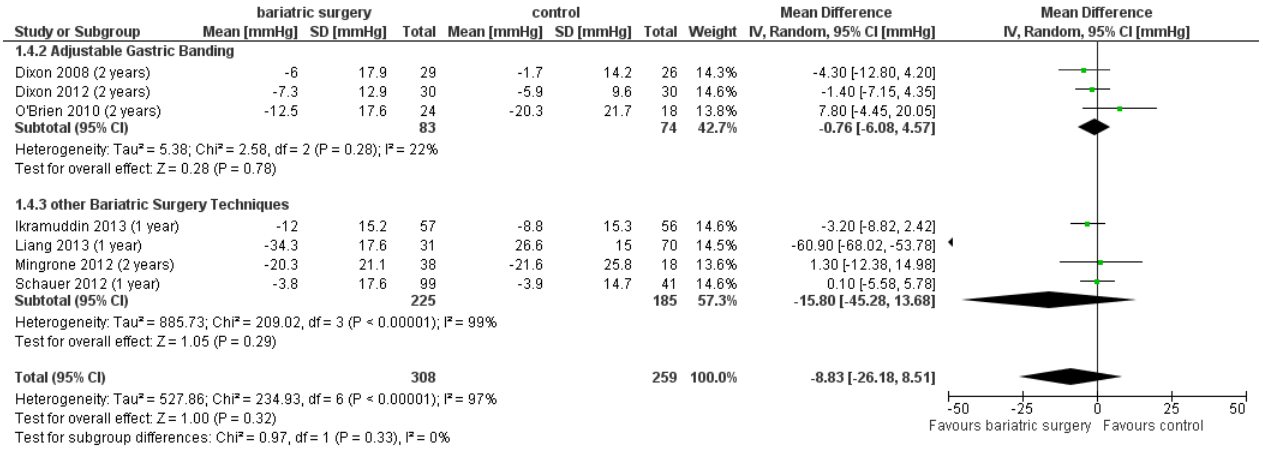


Appendix Figure 6: Metabolic Syndrome Remission after bariatric surgery versus non-surgical treatment (control) for obesity (conservative case scenario).

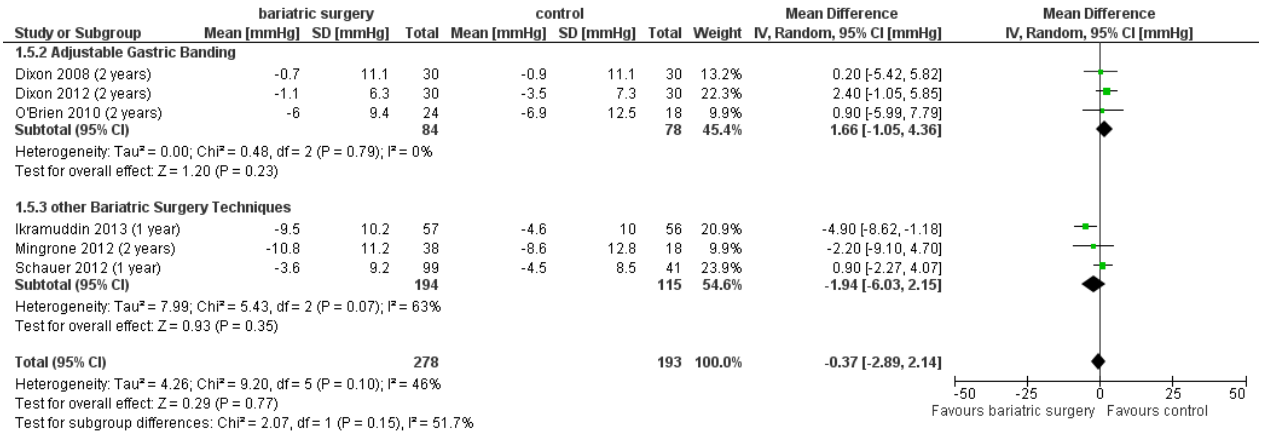
For the pooled analysis a conservative case scenario was assumed. A subgroup analysis was done for the studies which used AGB versus other bariatric surgery techniques (RYGB, SG or BPD). All missing patients in the non-surgical treatment groups were treated as if they had achieved metabolic syndrome remission (n = 24), whereas missing patients in the bariatric surgery groups did not.
Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, I^2= measure of inconsistency (scale: 0 to 100%), M-H = Mantel-Haenzel Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).

Blood parameters and blood pressure

A)

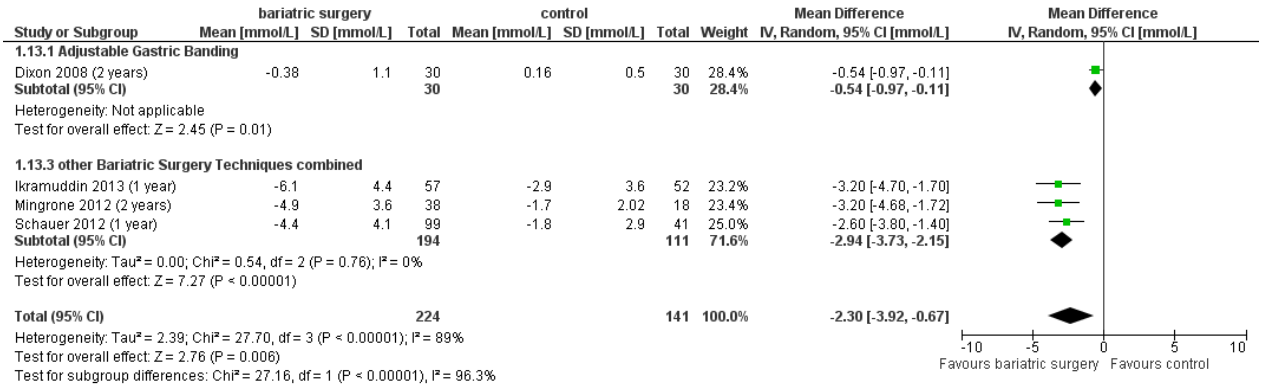


B)



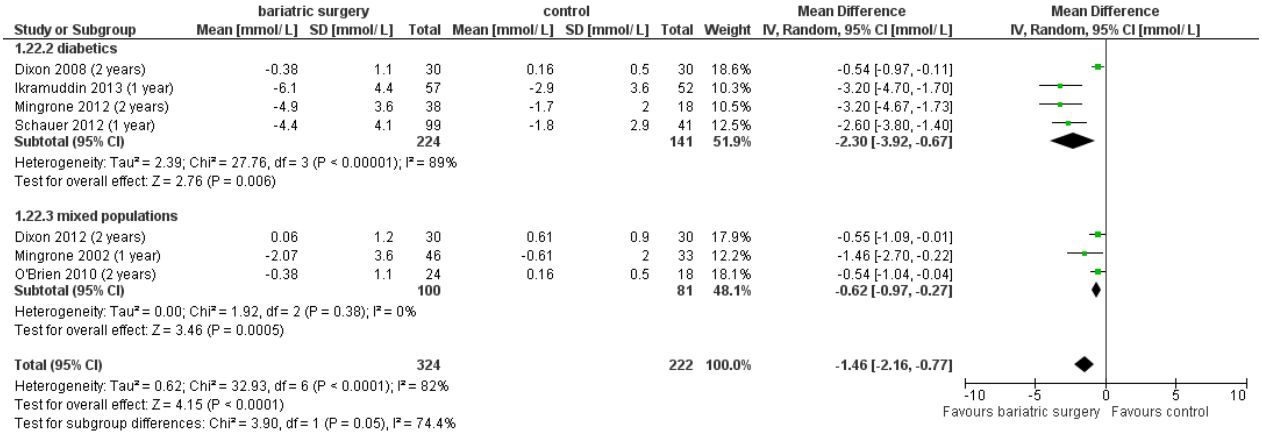
Appendix Figure 7: Change in systolic (A) and diastolic (B) blood pressure after bariatric surgery versus non-surgical treatment (control) for obesity.

A subgroup analysis was done for the studies which used AGB other bariatric surgery techniques (RYGB, SG, or BPD). Standard deviations (SD) were derived from 95% CI for Dixon 2012 and were imputed by taking the median SD of the respective groups of the other studies for Liang 2013.
Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, I^2= measure of inconsistency (scale: 0 to 100%), IV = Inverse Variance Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).



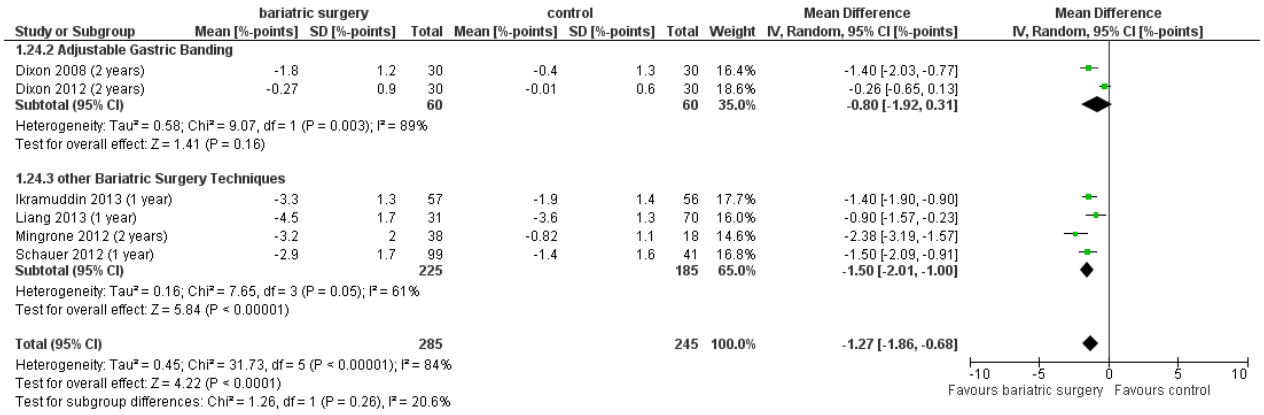
Appendix Figure 8: Change of fasting glucose level after bariatric surgery versus non-surgical treatment (control) for obesity (diabetics only, subgroups according to AGB versus other bariatric surgery techniques).

All patients included in the pooled analysis were diabetics at baseline. A subgroup analysis was done for the studies which used AGB versus other bariatric surgery techniques (RYGB, SG or BPD). The conversion factor used from mg/dL to mmol/L was 0.055.
Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, I^2= measure of inconsistency (scale: 0 to 100%), IV = Inverse Variance Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).



Appendix Figure 9: Change of fasting glucose levels after bariatric surgery versus non-surgical treatment (control) for obesity (subgroups according to diabetics versus mixed populations).

Subgroup analysis compared studies which included diabetics only versus mixed populations at baseline. The conversion factor used from mg/dL to mmol/L was 0.055. Standard deviations (SD) were imputed for Mingrone 2002 by taking the median SD of the respective groups of the other studies, and from 95% CI for Dixon 2012.
Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, I^2= measure of inconsistency (scale: 0 to 100%), IV = Inverse Variance Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).



Appendix Figure 10: Change of glycated HbA1c after bariatric surgery versus non-surgical treatment (control) for obesity (subgroups according to AGB versus other bariatric surgery techniques).

A subgroup analysis was done for the studies which used AGB other bariatric surgery techniques (RYGB, SG, or BPD). Standard deviations (SD) were derived from p-value for Liang 2013 and from 95% CI for Dixon 2012. Abbreviations: BPD = biliopancreatic diversion, CI = confidence intervall, df = degrees of freedom, I^2= measure of inconsistency (scale: 0 to 100%), IV = Inverse Variance Statistical Method, Random = random effects model, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy).